Evidence-based medicine and the patient—the example of cardiovascular disease prevention

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Evidence-based medicine and the patient—the example of cardiovascular disease prevention

Thesis presented
for the degree of
Doctor of Philosophy
in the subject of
Public Health

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Evidence-based medicine and the patient—the example of cardiovascular disease prevention

ABSTRACT

Background
Patient ideas about cardiovascular diseases (CVDs) differ widely from those of clinicians. The failure to understand these explanatory models has been suggested to be a key barrier to effective CVD prevention. Nonetheless, currently available decision-support interventions for CVD prevention have had limited patient involvement in their development.

Aims
Through four studies, this thesis seeks to use qualitative and quantitative methods to identify barriers and recommend best practices for supporting decisions in CVD prevention: both for education, and communicating the risk of benefit and harm from treatment.

Methods
Study i analyses data from the South London Stroke Register, examining factors associated with the diagnosis and treatment of risk factors prior-to-stroke. Study ii systematically reviews qualitative studies of patient perspectives on hypertension and medication taking. Study iii systematically reviews randomized controlled trials (RCTs) and qualitative studies examining the effectiveness of different strategies for communicating CVD risk. Study iv is a qualitative study of patient perspectives on CVD risk in two south London general practices.

Results
Study i found low but increasing prescribing rates of all preventative medication classes; prescribing did not differ by ethnicity or socio-economic status. Study ii included 52 qualitative studies. Participants experienced hypertension as symptomatic and strongly associated with stress. Many actively avoided medication, or self-adjusted medication use at times of lower stress or symptoms; concerns about serious adverse effects were widespread. Study iii included 23 RCTs, and found communicating CVD risk did not affect clinical outcomes, and only modestly improved decision quality; different formats produced similar results. Four qualitative studies found the risks were widely perceived as too small or distant to merit taking action. Study iv found many did not trust CVD risk estimates, perceiving they were not applicable to them as individuals, and omitted pertinent personal characteristics.
Conclusions

This thesis proposes strategies to improve the effectiveness of decision support interventions, including acknowledgement of widespread concerns about symptoms and medication adverse effects, and using a population ranking to communicate risk.
## Contents

1 **Introduction** ................................................. 16
   1.1 Motivation for the thesis .................................. 16
   1.2 Sharing decisions in cardiovascular diseases .......... 17
   1.3 Aims, objectives, and organisation of the thesis .... 19

2 **Literature review** ........................................... 21
   2.1 Literature review methods ................................ 22
   2.2 Preventing cardiovascular disease ....................... 22
      2.2.1 Effects of lifestyle change on cardiovascular disease rates 26
      2.2.2 Drug treatment to prevent cardiovascular disease .... 30
      2.2.3 The prevention paradox in cardiovascular disease .... 34
      2.2.4 Risk prediction algorithms ............................. 37
      2.2.5 The problem of adherence ............................. 39
      2.2.6 The rule of halves, and subsequent improvements in care quality 42
   2.3 Informing patients about cardiovascular disease prevention .... 44
      2.3.1 Education .............................................. 44
      2.3.2 Motivation for communicating risk .................. 51
      2.3.3 Strategies for communicating risk .................... 52
      2.3.4 Risk communication in cardiovascular disease prevention .... 55
      2.3.5 Applying population-based evidence to individuals .... 56
      2.3.6 External validity in cardiovascular disease prevention trials .... 57
      2.3.7 Uncertainty ............................................. 64
      2.3.8 Sharing decisions with patients—consultation style and decision aids ............................ 65
      2.3.9 Decision aids in cardiovascular disease prevention .... 67
      2.3.10 Assessing information needs for decision making .... 72
      2.3.11 Development process of decision aids for cardiovascular disease prevention .... 73
      2.3.12 Competing motivations ............................... 75
   2.4 Conclusions ............................................... 81

3 **Theoretical framework: the patient in evidence-based medicine** 82
   3.1 Introduction .................................................. 82
   3.2 History of, and motivation for, evidence-based medicine .... 83
      3.2.1 The Evidence Based Medicine framework ............... 85
      3.2.2 Evidence Based Medicine as a social movement ....... 87
   3.3 The lack of the patient in Evidence Based Medicine ....... 88
   3.4 Why involve patients? — the Shared Decision Making movement .... 90
   3.5 How should decisions be shared in practice ............... 92
      3.5.1 Patient explanatory models of illness ................ 93
6.4.1 Comparison with qualitative studies in other medical conditions 158
6.4.2 Comparison with the biomedical literature 158

7 Effects of different strategies for communicating cardiovascular risk—a systematic review of randomized controlled trials and qualitative studies 163
7.1 Introduction 163
7.2 Methods 165
7.2.1 Identifying papers 165
7.2.2 Inclusion criteria—RCTs 166
7.2.3 Inclusion criteria—qualitative studies 166
7.2.4 Data extraction 167
7.2.5 Synthesising results 167
7.2.6 Quality appraisal—quantitative papers 168
7.2.7 Quality appraisal—qualitative papers 169
7.3 Results 169
7.3.1 Characteristics of included studies 169
7.3.2 Methods evaluated in the studies 169
7.3.3 Quality of studies 171
7.3.4 RCTs comparing risk communication v usual care 171
7.3.5 Heterogeneity in analyses—possible causes 177
7.3.6 Adherence to treatment 178
7.3.7 RCTs comparing different risk communication strategies v each other 178
7.3.8 Summary of GRADE data for main outcomes 193
7.3.9 Qualitative studies 195
7.3.10 Report of qualitative thematic synthesis 199
7.3.11 Desire for shared decision making 202
7.4 Discussion 202

8 Patient perspectives on future CVD risk 207
8.1 Introduction 207
8.2 Methods 209
8.2.1 Ethics 209
8.2.2 Eligibility criteria 209
8.2.3 Data capture and coding 214
8.3 Results 215
8.3.1 Characteristics of participants 215
8.3.2 Consequences of high blood pressure 218
8.3.3 Explanations for hypertension 219
8.3.4 Reluctance to consider future risk of illness 221
8.3.5 Response to example risk charts 223
8.3.6 Interpreting population risks—“I think I might be that one” 226
8.3.7 Using peers as a reference group 229
8.3.8 Risk factors important to individuals 230
8.3.9 The doctor knowing a patient as an individual 232
8.3.10 Testing treatments for side-effects 234
8.3.11 Mistrust of statistics 236
8.3.12 A lay model of future risk 237
8.4 Discussion 237
8.4.1 Parallels between lay perspectives, and academic research on risk 240
8.4.2 Comparison with peers—an acceptable risk language 240
8.4.3 Strengths and weaknesses of the sampling strategy 241
8.4.4 Risk factors important to individuals 242
8.4.5 Comparison with other studies 243
8.4.6 Conclusions 243

9 Discussion 245
9.1 Introduction 245
9.2 Triangulation of results 246
9.3 Overview of thesis results 246
9.4 Difference between patient perspectives and current interventions 251
  9.4.1 Stress and symptoms 252
  9.4.2 Need for ‘culturally sensitive’ interventions 255
  9.4.3 Risk factors perceived as important - ‘people like you’ 256
  9.4.4 ‘I think I would be that one’ 258
  9.4.5 ‘Build up’ of medication in the body 259
9.5 How to address patient concerns in communication 260
9.6 Implications for risk communication 261
9.7 Implications for future research 266
9.8 Strengths and weaknesses of the research 267
9.9 Conclusions 269

References 270

Appendix A Publications and presentations 310
Appendix B Ethical approvals 335
Appendix C Patient literature for the qualitative study 342
Appendix D Topic guide for semi-structured interviews 346
Appendix E Search strategies for the systematic reviews 349
  E.1 Systematic review from Chapter 6 349
  E.2 Systematic review from Chapter 7 349
Appendix F Characteristics of excluded studies 351
## Listing of figures

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Expected effects of population-based prevention strategies versus targeting high-risk groups</td>
<td>35</td>
</tr>
<tr>
<td>2.2</td>
<td>Performance of QRISK2 for predicting future CVD</td>
<td>36</td>
</tr>
<tr>
<td>2.3</td>
<td>Predicted versus observed CVD risk with the Framingham Score</td>
<td>40</td>
</tr>
<tr>
<td>2.4</td>
<td>Improvements from the rule of halves: Hypertension awareness, treatment, and control rates in the general population, England, from 1994–2011; data from the Health Survey for England</td>
<td>43</td>
</tr>
<tr>
<td>2.5</td>
<td>Frequently used strategies for communicating CVD risk</td>
<td>54</td>
</tr>
<tr>
<td>2.6</td>
<td>The problem with averages: treatment effects on individuals</td>
<td>58</td>
</tr>
<tr>
<td>2.7</td>
<td>Estimates of the effectiveness of statins on all-cause mortality using four definitions of a primary prevention population</td>
<td>59</td>
</tr>
<tr>
<td>2.8</td>
<td>Equation for personalising meta-analysis data</td>
<td>61</td>
</tr>
<tr>
<td>3.1</td>
<td>The Evidence Based Medicine hierarchy of evidence quality</td>
<td>86</td>
</tr>
<tr>
<td>3.2</td>
<td>Schematic showing the updated model for evidence-based decision making by Haynes et al.</td>
<td>89</td>
</tr>
<tr>
<td>3.3</td>
<td>A model for Shared Decision Making in practice</td>
<td>93</td>
</tr>
<tr>
<td>4.1</td>
<td>Schematic outlining the methodological steps used in a typical systematic review</td>
<td>103</td>
</tr>
<tr>
<td>4.2</td>
<td>PRISMA diagram demonstrating the necessity of adding a title screening step for qualitative research</td>
<td>107</td>
</tr>
<tr>
<td>4.3</td>
<td>Example of line-by-line coding in qualitative synthesis</td>
<td>117</td>
</tr>
<tr>
<td>4.4</td>
<td>Example of the thematic groupings from the systematic review in Chapter 6</td>
<td>118</td>
</tr>
<tr>
<td>5.1</td>
<td>Recruitment area for the South London Stroke Register</td>
<td>123</td>
</tr>
<tr>
<td>5.2</td>
<td>Trends in risk factors prior to stroke from the South London Stroke Register</td>
<td>128</td>
</tr>
<tr>
<td>5.3</td>
<td>Trends in prescribed medication before stroke in those with known risk factors from the South London Stroke Register</td>
<td>131</td>
</tr>
<tr>
<td>6.1</td>
<td>PRISMA flowchart: flow of studies through the systematic review of qualitative studies</td>
<td>141</td>
</tr>
<tr>
<td>6.2</td>
<td>PRISMA flowchart: flow of studies through the systematic review of RCTs and qualitative studies</td>
<td>170</td>
</tr>
<tr>
<td>7.1</td>
<td>Risk of bias assessment of the included RCTs</td>
<td>172</td>
</tr>
<tr>
<td>7.2</td>
<td>Forest plot: systolic blood pressure, risk communication v control</td>
<td>179</td>
</tr>
<tr>
<td>7.3</td>
<td>Forest plot: diastolic blood pressure, risk communication v control</td>
<td>180</td>
</tr>
<tr>
<td>7.4</td>
<td>Forest plot: serum total cholesterol, risk communication v control</td>
<td>181</td>
</tr>
<tr>
<td>Section</td>
<td>Title</td>
<td>Page</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>7.6</td>
<td>Forest plot: serum LDL cholesterol, risk communication v control</td>
<td>182</td>
</tr>
<tr>
<td>7.7</td>
<td>Forest plot: change in body mass index, risk communication v control</td>
<td>183</td>
</tr>
<tr>
<td>7.8</td>
<td>Forest plot: Framingham CVD risk estimates; risk communication v control</td>
<td>184</td>
</tr>
<tr>
<td>7.9</td>
<td>Forest plot: Decisional conflict score, risk communication v control</td>
<td>185</td>
</tr>
<tr>
<td>7.10</td>
<td>Forest plot: anxiety, risk communication v control</td>
<td>186</td>
</tr>
<tr>
<td>7.11</td>
<td>Forest plot: worry about developing cardiovascular disease, risk communication v control</td>
<td>187</td>
</tr>
<tr>
<td>7.12</td>
<td>Sensitivity analysis: excluding heart age intervention; systolic blood pressure, risk communication v control</td>
<td>188</td>
</tr>
<tr>
<td>7.13</td>
<td>GRADE assessment of studies: effects of risk communication v no risk communication</td>
<td>194</td>
</tr>
<tr>
<td>7.14</td>
<td>Risk of bias assessment of the included qualitative studies</td>
<td>198</td>
</tr>
<tr>
<td>8.1</td>
<td>Example decision aid shown in interviews</td>
<td>211</td>
</tr>
<tr>
<td>8.2</td>
<td>A model of lay understanding of CVD risk</td>
<td>238</td>
</tr>
<tr>
<td>9.1</td>
<td>The reference class problem—a hypothetical risk model with identical performance to QRISK2, but with contradictory results</td>
<td>258</td>
</tr>
<tr>
<td>9.2</td>
<td>Example decision aid illustrating thesis conclusions (Part 1 of 2)</td>
<td>264</td>
</tr>
<tr>
<td>9.3</td>
<td>Example decision aid illustrating thesis conclusions (Part 2 of 2)</td>
<td>265</td>
</tr>
</tbody>
</table>
## List of Tables

2.1 Estimates of the population attributable risk for major modifiable risk factors from the INTERHEART and INTERSTROKE studies .......................... 25

2.2 Effects of drug classes for the primary prevention of CVD .......................... 31

2.3 Summary of RCTs assessing hypertension educational interventions ........................................... 46

2.4 Decision aids for CVD prevention; summary of RCTs .................................................. 69

2.5 Development of decision aids for CVD prevention .................................................. 77

3.1 Changes in practice due to Evidence Based Medicine: examples of where expert opinion has been found incorrect by high quality research evidence 84

5.1 Trends in demographics and vascular risk factors diagnosed prior-to-stroke 127

5.2 Association of demographics and stroke subtype With risk factors .......................... 132

5.3 Association of demographics and stroke subtype with prescribed preventative medication .................................................. 133

6.1 Description of included studies (Lay perspectives on hypertension and medication taking) .................................................................. 144

6.2 Lay concepts of hypertension causation by country .................................................. 150

6.3 Symptoms most widely associated with hypertension .................................................. 153

6.4 Alternative treatments used by country .................................................. 156

6.5 Sensitivity analysis for key results .................................................. 157

7.1 RCTs comparing risk communication versus usual care; characteristics of studies .................................................. 173

7.2 RCTs comparing different risk communication strategies versus one another; characteristics of studies .................................................. 189

7.3 Qualitative studies about risk communication; characteristics of studies 196

8.1 Characteristics of participants .................................................. 216

9.1 Summary of key findings from the individual studies .................................................. 249
List of Boxouts

2.1 Example of patient information from the updated Evidence Based Medicine framework .................................................. 64
2.2 Quality criteria in the IPDASi guidelines for patient involvement in the development of decision aids ............................. 73
2.3 A decision aid which promotes a particular decision .......................................................... 76
3.1 Five steps for practising evidence-based medicine .......................................................... 85
4.1 Seven steps of meta-ethnography .................................................................................. 109
4.2 Prompts for appraising qualitative research .................................................................. 113
7.1 Description of the Decisional Conflict Scale ................................................................. 165
List of Abbreviations

95% CI 95% confidence interval.
ACE angiotensin-converting enzyme.
AF atrial fibrillation.
ARB angiotensin II receptor blocker.
BMI body mass index.
BP blood pressure.
CCB calcium channel blocker.
CPRD Clinical Practice Research Datalink.
CVD cardiovascular disease.
DA decision aid.
EBM Evidence Based Medicine.
HDL high-density lipoprotein.
HES Hospital Episode Statistics.
HR hazard ratio.
ICH intracerebral haemorrhage.
INR International Normalised Ratio.
IPDAS International Patient Decision Aids Standards.
LDL low-density lipoprotein.
MI myocardial infarction.
MINAP Myocardial Ischaemia National Audit Project.
MMAS-8 Morisky medication adherence scale.
MRC Medical Research Council (UK).
NHS National Health Service (UK).
NICE the National Institute for Health and Care Excellence (UK).

NOAC Novel Oral Anticoagulant.

NRT nicotine replacement therapy.

ONS Office for National Statistics (UK).

OR odds ratio.

PAR population attributable risk.

RAS renin-angiotensin system.

RCT randomized controlled trial.

RR risk ratio.

SDM shared decision making.

TIA transient ischaemic attack.

UK United Kingdom.

US United States.

WHO World Health Organisation.
Dedicated to Rachel, Marcel, and Lief
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Finally, I am enormously grateful for the invaluable practical and moral support of my wife Rachel, without whom the thesis would not have been completed.
1.1 Motivation for the thesis

Before taking up my first permanent post as a general practitioner (GP), I wrote an editorial about the importance of communicating health statistics to patients.¹ But since, I have been struck by how difficult it is to do in practice. A typical clinical encounter might be with a person who feels entirely healthy, but has attended due to concern (sometimes their own concern, but often concern of another) about a risk factor for cardiovascular disease (CVD). Often, patients attended after a family member or friend became ill, or following a blood pressure or cholesterol check at work.

In this scenario, most current guidelines recommend conducting a global risk assessment (i.e. the effects of all CVD risk factors are considered together, rather than treating, say, blood pressure alone).²³ First, the clinician would collect data on key CVD risk factors, measuring blood pressure and lipid profile. These data are combined with that
on age, sex, and smoking status, among others, and used to produce a risk estimate via an algorithm embedded in the patient record. This risk estimate is expressed as the percentage probability of developing CVD in the following 10 years. Guidelines then recommend that the clinician communicates this risk estimate to the patient, using techniques found to be helpful in communicating health risks more generally: natural frequencies such as ‘5 in 100’ alongside smiley face charts. Next, estimates of the likely benefits and downsides of available options are communicated (typically taking medication, making changes to lifestyle, or doing nothing). Patients are then encouraged to make a decision aligned with their own preferences and values.

Despite persisting for a number of years with this approach, I never got the sense that it was particularly successful. In reality, there is often a substantial amount of health education to cover in these consultations. Hypertension in particular is an abstract concept to cover, and often misunderstood. Patients often have myriad questions, from understanding the cause of elevated risk factors, to wanting very specific advice on dietary changes. Very frequently patients questioned whether our blood pressure readings were reliable, and attributed elevated readings as due to some stress, or having rushed to their appointment. Nearly always, patients resisted my suggestions of starting or increasing the dose of medication.

Consultations often overran, and I often sensed that patients left more confused than when they started. It seemed to me that understanding statistics from CVD research was a low priority for most. This led me to wonder how to improve these consultations. In particular, what are the educational needs of patients in this situation? And why were patients not responding to risk information as expected?

1.2 Sharing decisions in cardiovascular diseases

Highly effective, and inexpensive strategies already exist which would prevent the majority of CVDs: namely, healthier lifestyles and drug treatment of hypertension, dyslipidaemia, and atrial fibrillation (AF). However, the benefit from these strategies predicted by clinical trials has not been achieved in practice, and rates of risk factor detection, treatment, and control remain suboptimal. Low adherence to prescribed treat-
ments is likely to be a substantial contributor to this, with more than 50% of people stopping hypertension treatment within 12 months of initiation.\textsuperscript{9,10}

The risk threshold at which guidelines recommend initiating preventative medication has been reduced, motivated by low cost of medication and the desire to obtain the largest population-level reductions.\textsuperscript{11,12} However, individuals in the lower risk populations now treated stand to gain a more modest benefit. The consequence is that decisions to use medication are now based on more finely balanced benefits and harms than they used to be.\textsuperscript{13–15}

As a consequence, national and international CVD prevention guidelines now focus on estimating a patient’s individual risk, and communicating this information to them alongside estimates of the effects of treatment.\textsuperscript{3,11,12} Patients are encouraged to use this information to inform their own decisions about use of primary prevention.

Across a wide range of health conditions, decision aids have been demonstrated to improve decision making quality,\textsuperscript{16} and there have been suggestions (as yet unproven) that they may improve adherence to treatment.\textsuperscript{17} Decision aids (which are typically booklets, or computer-based tools) combine health-related education with individualised estimates of the probability of benefit and harm from available treatment options.\textsuperscript{18}

The optimal content and format of such a tool for CVD prevention specifically is not clear. The majority of current decision aids provide no justification for their educational content.\textsuperscript{1} In practice, most use simplified versions of the type of information about risk factors and disease causation which might be found in a medical textbook. However, in 1975, Sackett demonstrated that educating patients about hypertension and the importance of treatment did not affect adherence to treatment;\textsuperscript{19} numerous subsequent RCTs have reported similar results.\textsuperscript{20} None of the educational interventions in the RCTs were informed by any assessment of what patients needed to or wanted to know.

Several qualitative studies have concluded that culturally-specific education might be important.\textsuperscript{21–24} However, the overwhelming majority of decision aids have not taken into account the results of these and many other qualitative studies examining patient understanding about cardiovascular risks.

\textsuperscript{1}these will be reviewed in Chapter 2
For the risk communication component, most current decision aids use absolute risks presented as natural frequencies, often accompanied by graphical risk charts; a practice based on the results of extensive psychological research.\textsuperscript{25} Decision making in \textit{CVD} prevention, however, has some unique characteristics which have attracted less research attention.

Given \textit{CVD} may take decades to manifest after the detection of risk, decision-making is fluid: patients may revise their preferences and decisions over time, and are contemplating outcomes in the distant future.\textsuperscript{26} Much decision making research concerns surgery or screening tests, where the patient’s decision is about a one-time procedure carried out by a clinician. By contrast, the responsibility for implementing \textit{CVD} prevention decisions (whether taking medication or lifestyle change) rests with the patient, and decisions are often not adhered to in practice.\textsuperscript{26} The best risk prediction algorithms for \textit{CVDs} are still highly inaccurate for individual use,\textsuperscript{27} yet there is little research or consensus on how to account for uncertainty when communicating risk.\textsuperscript{28} Lastly, strategies unique for \textit{CVD} prevention such as \textit{heart age} have been used in some decision aids.\textsuperscript{29} A systematic review (search date 2008) evaluating risk communication strategies in \textit{CVD} prevention specifically found insufficient evidence to recommend any particular format.\textsuperscript{30}

\subsection*{1.3 Aims, objectives, and organisation of the thesis}

This thesis aims to examine strategies for sharing research evidence to inform patient decisions about \textit{CVD} prevention, and particularly how research on patient experiences and understandings about health can be used to improve information provision. The thesis seeks to understand why existing decision-support and educational interventions have failed to produce important improvements in either the quality of decision making or clinical outcomes.

The thesis seeks to achieve these aims by using the results of qualitative research (both synthesis of existing research and a new study conducted for the thesis) together with quantitative research on risk communication strategies. Specifically, the thesis sets out to address the following objectives:
• To critically review the literature around decision making in CVD prevention (Chapter 2)

• To set out the theoretical basis for involving patients in decisions around CVD prevention, and the importance of patient explanatory models about illness for CVD prevention (Chapter 3).

• To describe methodological difficulties around the use of systematic reviews which incorporate qualitative research, and how these may be overcome (Chapter 4).

• To investigate trends over time in risk factors for CVD and the use of preventative treatment in a cohort of patients with stroke, and investigate whether age, sex, ethnicity, or socioeconomic status affect the use of preventive medication (Chapter 5).

• To systematically review qualitative studies conducted in people with hypertension, and investigate the link between patient health understanding, and health behaviours and medication taking (Chapter 6).

• To systematically review RCTs of CVD risk communication strategies to determine the effects on decision making quality and clinical outcomes (Chapter 7).

• To investigate patient perspectives on future CVD risk through a qualitative study conducted in two general practices in south London (Chapter 8).

• To systematically review qualitative studies examining patient perspectives on CVD risk communication strategies, in order to uncover possible reasons for the success or failure or these strategies (Chapter 7).

• To bring together the findings from Chapters 2–7 (known as triangulation) and discuss the implications for educational and decision-support interventions around CVD prevention (Chapter 7.4).
This thesis investigates strategies for sharing research evidence to inform patient decisions about cardiovascular disease (CVD) prevention. This chapter reviews the rationale, development, and contents of current strategies, together with evidence of their effectiveness, and is structured as follows:

First, the concept of CVD prevention will be introduced. Research on CVD risk factors will be reviewed, together with strategies for risk factor reduction. Studies examining the empirical effects of risk factor modification (which provide the raw data to be communicated to patients) will be reviewed. The use of risk algorithms to target preventative treatment at those at highest risk will be examined, and methods for individualising estimates of treatment efficacy described.

Secondly, the relevance of the patient to CVD prevention will be discussed. The current international state of risk factor control will be described, and low adherence to
treatments, a key barrier to effective CVD prevention, will be introduced. Lastly, the empirical research supporting sharing decision making will be discussed. Strategies for communicating risk, decision aids, and health education will be reviewed, and their efficacy as applied to CVD prevention evaluated.

2.1 Literature review methods

This chapter provides a critical survey of research relevant to the thesis, and covers a number of topics, necessarily drawing upon multiple research disciplines and methods. Formal systematic review methods (which lend themselves to answering a highly-focused question from a narrow range of study designs) would therefore not be appropriate.

The following strategy was used. Multiple iterative searches of PubMed and Google Scholar covering the topic areas were conducted between February 2011 and April 2012, and updated from March–December 2015. A recent systematic review was identified where possible for each topic as a starting point. The data from these reviews were augmented by retrieval of the primary publications of the included studies, searches for relevant subsequent studies, and scrutiny of citation lists. The retrieved studies are not discussed exhaustively; instead the most relevant were selected, favouring high-quality recent studies with the most rigorous methods for the topic (for example, RCTs for evaluations of interventions, and cohort studies for investigation of risk factors). Key older studies are additionally reported where appropriate to provide important context.

For clarity, citation of a primary study indicates that data was taken from the primary publication itself; where data was taken from a secondary source such as a systematic review, the review has been cited.

2.2 Preventing cardiovascular disease

CVDs comprise coronary artery disease, peripheral vascular and aortic disease, and stroke. CVDs are the number one cause of death and disability in both developed
and developing countries, causing 30% of all deaths worldwide, but are eminently preventable.\textsuperscript{8}

\textbf{CVDS} share a common aetiology of atherosclerosis, and common risk factors,\textsuperscript{31} comprising those which are non-modifiable (age, ethnicity, sex, and genetics), and modifiable (poor diet, being overweight, smoking, inactivity, dyslipidaemia, and hypertension).\textsuperscript{31} Diabetes independently increases the risk of all \textbf{CVDS},\textsuperscript{32} and \textit{AF} is an important risk factor for stroke.\textsuperscript{33} Social factors (including socio-economic deprivation and low educational attainment) have been additionally recognised as risk factors for CVD;\textsuperscript{34} this relationship is partly explained by increased levels of conventional risk factors among deprived populations,\textsuperscript{35} and also through inadequate access to health care.\textsuperscript{36}

The \textit{Framingham Study} is an ongoing cohort study of a predominantly white and middle-aged community in the town of Framingham, Massachusetts, United States (US), which in 1948 enrolled 5,209 men and women aged from 30–62 years.\textsuperscript{37} The results from this study were seminal in understanding of the aetiology and risk factors for \textbf{CVDS}, and identifying targets for prevention. By the time data from the 2- and 6-year follow ups were analysed, it was clear that those with hypertension, elevated cholesterol, and left cardiac ventricular hypertrophy had an associated increase in the risk of subsequent coronary heart disease.\textsuperscript{38,39} More recently, \textit{INTERHEART} and \textit{INTERSTROKE} (in 2004 and 2010 respectively) examined the population attributable risk (\textit{PAR})\textsuperscript{1} for key risk factors.\textsuperscript{40,41} These were large case-control studies conducted in multiple countries internationally, and including data from high-, middle-, and low-income countries. The key results from these studies are summarised in Table 2.1 on Page 25. These studies demonstrated that 10 key modifiable risk factors account for around 90% of the incidence of stroke and myocardial infarction (\textit{MI}).

Hypertension is the greatest overall risk factor, accounting for 20–25% of total CVD incidence worldwide, and 37%–54% of CVD deaths (in south east Asia, and high-income European countries respectively).\textsuperscript{42–45}

A 2011 World Health Organisation (\textit{WHO}) report concluded that the majority of \textbf{CVDS} could be prevented by optimising risk factor management,\textsuperscript{8} and even modest

\footnote{Population Attributable Risk may be defined as the absolute reduction in disease incidence expected if the risk factor were absent in the population.}
population-level improvements would be associated with a 25% relative reduction in incidence.\textsuperscript{46}
Table 2.1: Estimates of the PAR for major modifiable risk factors from the INTERHEART\textsuperscript{40} and INTERSTROKE\textsuperscript{41} case-control studies with 95% CIs. Note that the PARs may exceed 100% in total, since CVD risk factors interact in their effect.\textsuperscript{47} A: defined as hip-to-waist ratio, top v bottom tertile; B: self-reported composite score including fruit and vegetables, fish, and meat for INTERSTROKE; self-reported daily fruit and vegetables for INTERHEART; C: INTERHEART used a cut-off of > 3 drinks per week, finding (moderate) alcohol was protective; INTERSTROKE used a cut-off of > 30 drinks per month, finding (heavier) alcohol intake increased stroke risk; D: cardiac causes include: AF and atrial flutter, previous MI, and valvular heart disease; E: dyslipidemia was defined as an elevated ApoB/ApoA I ratio, which are the key protein components of LDL and HDL cholesterol respectively. F: total PAR is an estimate of proportion of disease which would be avoided if all risk factors removed, calculated with a multi-variable model.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Stroke</th>
<th>Myocardial infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>hypertension</td>
<td>35% (30–39%)</td>
<td>23% (22–25%)</td>
</tr>
<tr>
<td>smoking</td>
<td>19% (15–23%)</td>
<td>36% (34–39%)</td>
</tr>
<tr>
<td>overweight\textsuperscript{A}</td>
<td>27% (19–36%)</td>
<td>34% (30–37%)</td>
</tr>
<tr>
<td>poor diet\textsuperscript{B}</td>
<td>18% (11–30%)</td>
<td>13% (10–17%)</td>
</tr>
<tr>
<td>diabetes</td>
<td>5% (3–10%)</td>
<td>12% (11–14%)</td>
</tr>
<tr>
<td>inactivity</td>
<td>29% (15–49%)</td>
<td>26% (20–32%)</td>
</tr>
<tr>
<td>teetotaller\textsuperscript{C}</td>
<td>not assessed</td>
<td>14% (9–20%)</td>
</tr>
<tr>
<td>excessive alcohol\textsuperscript{C}</td>
<td>4% (1–15%)</td>
<td>not assessed</td>
</tr>
<tr>
<td>psychosocial stress</td>
<td>5% (2–10%)</td>
<td>29% (23–34%)</td>
</tr>
<tr>
<td>depression</td>
<td>3% (3–10%)</td>
<td>not assessed</td>
</tr>
<tr>
<td>cardiac causes\textsuperscript{D}</td>
<td>7% (5–9%)</td>
<td>not assessed</td>
</tr>
<tr>
<td>dyslipidaemia\textsuperscript{E}</td>
<td>25% (16–37%)</td>
<td>54% (50–59%)</td>
</tr>
<tr>
<td>total\textsuperscript{F}</td>
<td>90% (85–94%)</td>
<td>90% (88–92%)</td>
</tr>
</tbody>
</table>
2.2.1 Effects of lifestyle change on cardiovascular disease rates

This section summarises the evidence of the associations between lifestyle or behavioural risk factors and CVD incidence, and discusses the effects of interventions for increasing healthy lifestyles.

Smoking cessation

In those who smoke, smoking provides the greatest contribution to CVD risk. Numerous large, high-quality cohort studies have found that CVD risk reduces quickly after smoking cessation, with ex-smokers having a similar CVD risk to never-smokers around 15 years after quitting.\(^{48-52}\)

Cahill et al. conducted a network meta-analysis evaluating a total of 26 drug treatments, using data from 267 RCTs identified from 12 source Cochrane systematic reviews.\(^{53}\) Nicotine replacement therapy (NRT), bupropion, varenicline and cytisine were all found to significantly increase the odds of abstinence compared to placebo (odds ratios (ORS) with 95% Credible Intervals\(^1\); NRT 1.84 [1.71 to 1.99], bupropion 1.82 [1.60 to 2.06], varenicline 2.88, [2.40 to 3.47], and cytisine 3.98, 95% CI 2.01 to 7.87). The trials did not evaluate the effects of smoking cessation interventions on later CVD.

Weight loss

Obesity, which affects around 10% of the world’s population,\(^8\) is a major risk factor for CVD, with observational studies finding a linear increase in risk of CVD and mortality with increasing body mass index (BMI).\(^{55,56}\) There is consistent evidence from observational studies that intentional weight loss leads to improvement in cardiovascular risk factors, including reduced blood pressure, reduced left ventricular mass, and reduced resting heart rate.\(^{55}\) Direct evidence of weight loss on clinical CVD outcomes is lacking.

Although reducing body weight may be achieved in theory by reducing food intake and increasing physical exercise, in practice most find achieving this goal challenging, and effective interventions to help are lacking.\(^{57}\) The effects of weight loss interventions

\(^1\)95\% Credible Intervals are a standard method for describing uncertainty in Bayesian analyses; there is a 95\% probability that the true population mean lies between the lower and upper bounds.\(^{54}\)
were examined by a systematic review (search date 2014) which compared interventions (typically one-to-one support and counselling with a clinician over 6 months to 2 years) delivered in primary care, and included fifteen RCTs with a total of 4,539 participants.\textsuperscript{58} It found modest difference in weight loss, with those receiving the intervention achieving an additional 1.4 kg weight loss at 12 months, and 1.2 kg weight loss at 24 months.

**Dietary change**

Aside from the aim of weight reduction, various components of dietary intake have been associated with changes in CVD risk factors, including salt, alcohol, fresh fruit and vegetables, and types of fat intake.\textsuperscript{59} The volume and type of dietary fat intake has been associated with changes in levels of blood lipids, and in turn, increased levels of total cholesterol, \textit{LDL} cholesterol, and triglycerides have found to be associated with increased risk of CVD.\textsuperscript{60} A key study was the \textit{Seven Countries Study}, a analysis of 15 cohort studies including a total of 11,579 men, which discovered low rates of CVD and mortality in Mediterranean populations where the main dietary fat was olive oil.\textsuperscript{61} Later, the US Nurses Health Study followed up 80,082 woman who completed dietary questionnaires, finding no association between total fat intake and CVD, but that saturated fats and trans-fats were associated with substantial increases in CVD rates.\textsuperscript{62} Further observational studies linked have linked saturated fat intake with increased blood cholesterol, and particularly myristic and palmitic acids found in meat and dairy products.\textsuperscript{60} Polyunsaturated fat intake has been associated with reduced total blood cholesterol.\textsuperscript{60}

A systematic review and meta-analysis (search date 2010) of clinical trials and observational studies found strong evidence that adhering to a \textit{Mediterranean diet}\textsuperscript{1} improved several risk factors for CVD (including reducing blood cholesterol, waist circumference, and blood pressure).\textsuperscript{63} However, a subsequent Cochrane systematic review which included RCTs but excluded observational studies (search date 2012) found only 1 RCT which examined CVD rates directly as an outcome.\textsuperscript{64} This large RCT (48,835 women) assessed an intensive programme to educate and monitor dietary intake, with the aim

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\textsuperscript{1}defined as a diet which contains high levels of mono-unsaturated fats typically from olive oil; high in fruit, vegetables, grains, and low-fat dairy products; with weekly fish, poultry, and nuts; with low consumption of red meats, and moderate alcohol intake
of increasing fruit, vegetables, and grains. The intervention was successful in chang-
ing diet: there were high levels of adherence, significant reductions in fat consumption (a mean reduction in quantity of >8%), and increases in the intake of grains (0.5 mean additional portions per day), and fruit and vegetables (1.1 additional portions per day). Nonetheless the trial found no significant difference in CVD (hazard ratio (HR) for CVD events: 0.98, 95% CI 0.92 to 1.05, mean follow up time 8.1 years).65

Observational studies and animal experiments have consistently found an association between high dietary salt intake and increased blood pressure.66 A systematic review and meta-analysis of 34 high quality RCTs found that ‘modest’ reduction in dietary salt significantly reduces blood pressure; the effects of salt reduction on CVD outcomes have not been directly measured.67 Participants mean baseline salt consumption was 8.9 g/day, and the mean reduction with intervention was 4.4 g/day; this led to a reduc-
tion in systolic blood pressure of 4 mmHg, and diastolic of 2 mmHg. Though these re-
ductions in blood pressure are modest for individuals, the authors argue that if applied to a population are likely to result in substantial reduction in the CVD burden. A 2011 systematic review found only 7 RCTs of salt reduction which directly measured CVD rates, but reported insufficient power to draw precise conclusions.68 Thus, although re-
ducing salt intake seems likely to reduce CVD rates (based on strong observational data), the absence of strong RCT evidence makes the size of benefit expected by reducing salt intake difficult to quantify.

**Increasing physical activity**

Sedentary lifestyle is strongly associated with a substantial increase in CVD: a meta-
alysis of 27 large cohort studies published in 1990 estimated that inactivity is associ-
ated with a near doubling in the risk in heart disease (risk ratio (RR) 1.9, 95% CI 1.6 to 2.2),69 and its effect is independent of other known risk factors.69

**Intensive lifestyle change**

One systematic review (search date 2011, 55 RCTs with a total of 163,471 participants) found no significant benefit of intensive lifestyle interventions targeting multiple risk
factors in the general population.\textsuperscript{70} The review did find a significant reduction in mortality (OR 0.78, 95\% CI 0.68 to 0.89) and CVD (OR 0.71, 95\% CI 0.61 to 0.83) in the subgroup with both hypertension and diabetes. However, the included trials were reported to be of very low quality, with poor reporting of randomisation methods, very high dropout rates, and in most cases insufficient description of what the intervention comprised. Despite the lack of evidence to support lifestyle intervention targeting individuals, large scale public health programmes targeting CVD risk factors for a whole population have been associated with substantial reductions in CVD and other illnesses with related risk factors.\textsuperscript{71}

**Evidence quality for lifestyle change**

High quality observational studies have consistently found associations between being overweight, poor diet, and sedentary lifestyle and increased rates of CVD. However, for most of these factors there is no RCT evidence available to quantify the effects of lifestyle change, and a paucity of effective interventions to improve lifestyles.

Observational studies are at risk of bias from confounding factors.\textsuperscript{72} Such studies are able to demonstrate associations between a putative risk factor and CVD, but do not provide evidence that these factors themselves cause CVD.\textsuperscript{73} For example, some of the apparent benefits of high dietary fruit and vegetables might instead be caused by high income or other healthy behaviours found in those with ‘healthy’ diets; improving the diet alone in low-income populations with additional risk factors may not achieve the expected benefit. These studies would therefore tend to overestimate the size of benefit expected from reducing risk factors. These biases occur particularly frequently in nutritional research.\textsuperscript{74,75}

There are additionally limitations in the RCT evidence which does exist. Systematic reviews of behavioural change interventions have found that the included randomized trials have substantial risk of bias.\textsuperscript{70,76} Trials examining behavioural change have particular challenges in achieving adequate blinding, and ensuring participants adhere to their allocated intervention.\textsuperscript{77} Finally, the research base is overwhelmingly skewed towards pharmaceuticals both in terms of trial numbers and size.\textsuperscript{78} The statistical estimates of
the effects of lifestyle change are therefore less certain than the equivalent for medica-

tion.

From the perspective of risk communication, the effects of lifestyle change are more
difficult to quantify precisely for individuals, both due to limitations in the evidence
base and the lack of effective interventions available to offer. As will be shown later in
this chapter, existing decision aids tend to provide detailed textual and statistical inform-
ination on the expected effects of drug treatment, but brief verbal descriptions of the
effects of lifestyle change.

2.2.2 Drug treatment to prevent cardiovascular disease

This section describes the empirical evidence from RCTs of the effects of pharmaceuti-
cal treatments for CVD. This data forms the evidence base which underpins patient risk
information about the benefits and harms of treatment.

A variety of pharmaceutical treatments have been shown to be effective in the pri-
mary prevention of CVD, and their effects are summarised in table 2.2. Meta-analyses
of large high quality RCTs have found that antihypertensive drugs significantly reduce
all-cause mortality, heart disease, and stroke in people without a prior history of CVD when compared with placebo.\textsuperscript{79}

The main classes of drug used to treat hypertension are those which block the renin-
angiotensin system (RAS) (angiotensin-converting enzyme (ACE) inhibitors, and an-
giotensin II receptor blockers (ARBs)), calcium channel blockers (CCBs), and thiazide-
like diuretics.\textsuperscript{80} United Kingdom (UK) and international guidelines recommend the use of the ACD algorithm to initiate and increase drug treatment for hypertension (where ACE inhibitors/ARBs, CCBs, and thiazide-like diuretics are added sequentially), aiming for a target clinic blood pressure reading of 140/90mmHg.\textsuperscript{80} The different classes of antihypertensive appear to vary in their effectiveness,\textsuperscript{81} and particular classes are preferred in certain populations. For example, drugs acting on the RAS are favoured in people with diabetes, since they have been found to reduce the risk of diabetic renal complications.\textsuperscript{82} Calcium channel blockers are favoured in black ethnic groups follow-

\textsuperscript{ia}also known as the primary prevention population
ing a subgroup analysis of 6,423 black ethnic participants from the ALLHAT trial, which found that lisinopril was associated with increased incidence of stroke and serious adverse effects (gastrointestinal bleeding and angioedema) when compared with amlodipine. Antihypertensive drugs have additionally been found effective in RCTs in older people (aged >80 years).

The most frequent adverse effects with hypertension drugs are: cough with ACE inhibitors (15%), ankle oedema with CCBs (15% to 30%), and hypokalaemia with thiazide diuretics. However, all three classes of drugs are associated with a very large number of different adverse effects affecting all systems which occur less frequently, and which range in severity from serious (sudden death with thiazide diuretics), to minor (rash with CCBs).

<table>
<thead>
<tr>
<th>Intervention</th>
<th>CHD</th>
<th>Stroke</th>
<th>Mortality</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide diuretics</td>
<td>28% (16 to 39%)</td>
<td>37% (29 to 43%)</td>
<td>11% (3 to 18%)</td>
<td>[79]</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>19% (6 to 30%)</td>
<td>35% (18 to 48%)</td>
<td>17% (5 to 28%)</td>
<td>[79]</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>23% (-9 to +45%)</td>
<td>42% (16 to 59%)</td>
<td>14% (-9 to +32%)</td>
<td>[79]</td>
</tr>
<tr>
<td>Statins</td>
<td>27% (20 to 33%)</td>
<td>22% (11 to 32%)</td>
<td>14% (6 to 21%)</td>
<td>[88]</td>
</tr>
<tr>
<td>Warfarin (for AF)</td>
<td>13% (-238 to 68%)</td>
<td>59% (39 to 63%)</td>
<td>29% (5 to 48%)</td>
<td>[89]</td>
</tr>
</tbody>
</table>

Table 2.2: Relative risk reductions (RRRs) (with 95% CI) for different drug classes in the primary prevention of CVD; CHD = coronary heart disease.

A 2013 Cochrane review found eighteen RCTs (56,934 participants) examining the effects of statin treatment versus placebo, limiting their inclusion to trials conducted principally in a primary prevention population. A 2005 meta-analysis of individual patient data of 90,056 participants from 14 large RCTs was able to analyse key subgroups, finding that statins significantly reduced cardiovascular events, and that the relative improvement in outcomes was similar in both high- and low-risk strata of the population. A secondary analysis of 183 RCTs of statin therapy evaluated the effects of being industry-sponsored. A network meta-analysis design was used, which allowed the authors to adjust for the differences in effect which would be expected by the use of different statins, and at different doses. They found no important difference in the primary outcome of LDL cholesterol between industry, and non-industry sponsored trials, pro-

\[\text{defined as } \leq 10\% \text{ of the trial population having existing CVD}\]
viding some reassurance for this class of drugs at least.

Statins have been associated with frequent adverse effects. Observational studies have found that myopathy occurs in 1.5–10%, but was reported to occur in 0.05% in the Cholesterol Treatment Trialists’ Collaboration analysis of RCT data. Even after adjusting for the fact that muscle problems occur frequently in the general population not taking statins, this still represents a 100-fold difference between observational and RCT estimates. The Cholesterol Treatment Trialists’ Collaboration did not have access to the full data on statin adverse effects from the pharmaceutical companies for their analysis of RCTs data.

A 2009 Cochrane review identified 5 RCTs with 2313 participants evaluating warfarin versus placebo for preventing stroke and transient ischaemic attack (TIA) in people with AF. The review found that warfarin significantly reduced stroke and all-cause mortality compared with placebo (see Table 2.2).

This review found no significant difference between warfarin and placebo in the adverse effects of intra-cranial or extra-cranial haemorrhage but the confidence intervals were wide (RRS with 95% CI S 2.38, [0.54 to 10.50] for intracerebral haemorrhage (ICH), and 1.07, [0.53 to 2.12] for extra-cranial haemorrhage). An earlier analysis of the same RCTs estimated the annual risk of major haemorrhage to be 1.3% with warfarin compared with 1% with no treatment. Risk of haemorrhagic adverse effects with warfarin has been found to increase in certain groups, for example in older people, in those who drink excessive alcohol, and those with uncontrolled hypertension; knowledge of these factors can be used to estimate individual bleeding risk.

Warfarin dosing is variable, necessitating frequent checks of clotting via the International Normalised Ratio (INR) blood test. In addition to the patient inconvenience of frequent blood testing, INRs outside of a narrowly defined target range are associated with increased risk of haemorrhage.

These limitations motivated the development of a group of drugs known as the Novel Oral Anticoagulants (NOACs), which include dabigatran, rivaroxaban, apixaban, and edoxaban. A 2014 systematic review and network meta-analysis compared RCTs of warfarin with these NOACs.

\[ \text{Correspondence to the Editor of BMJ, obtained from http://www.documentcloud.org/documents/1341683-rorycollinsreply.html} \]
farin, novel anticoagulants, aspirin, and placebo for stroke prevention in AF, identifying 16 RCTs with a total of 82,396 participants.\textsuperscript{99} Dabigatran and apixaban were associated with reduced risk of stroke compared with warfarin (ORs with 95\% CIs: 0.66 [0.53 to 0.82] and 0.78 [0.65 to 0.94] respectively). There was no significant difference in stroke between either edoxaban or rivaroxaban and warfarin (ORs with 95\% CIs: 0.87 [0.74 to 1.02] and 0.88 [0.74 to 1.04] respectively). Edoxaban, apixaban, edoxaban, and dabigatran were all associated with significantly lower rates of major bleeding, but the differences were small in absolute terms.

**Limitations in evidence of harms**

In order that patients and clinicians can make informed decisions about treatment, it is important that good quality information is available on potential harms as well as benefits. However, such information is much more difficult to obtain. First, RCTs typically have a beneficial effect as the primary outcome, which determines its sample size; such trials do usually not have sufficient statistical power to detect drug adverse effects.\textsuperscript{100} Relatively small sample sizes and short follow up periods make rare and long-term side effects difficult to detect using this design.\textsuperscript{101}

Second, adverse effects information is often poorly reported. Saini et al. conducted an analysis of adverse effects reporting in systematic reviews, evaluating 92 newly published Cochrane reviews assessing the efficacy of interventions, and 230 recent reviews published elsewhere focusing on adverse effects.\textsuperscript{102} Their primary outcome was whether the systematic review presented an analysis of the primary harm from all included studies (either tabular data or meta-analysis). Lack of this data may result from inadequate or selective reporting by the authors of the included clinical trial (which is the case in most clinical trials\textsuperscript{101}), or from incomplete analysis by the authors of the systematic review. The analysis found 86\% (79/92) of Cochrane reviews, and 76\% (173/230) of systematic reviews of harms did not adequately report drug adverse effects by this criteria. For example, a Cochrane review examining first-line drugs for hypertension did not report information on specific harms.\textsuperscript{79} Instead, this review only reported the composite outcome withdrawals due to adverse effects, which provides no information on the type of
adverse effect or its severity.

Third, in practice, RCTs often select participants with a single illness (excluding those with serious co-morbidities), and frequently exclude elderly people, pregnant women, and children—groups who have a higher risk of adverse effects. Although CVD prevention medications are frequently co-prescribed, most RCTs examine monotherapy. Interactions between agents can produce adverse effects which are therefore unexpected. For example, CCBs (used frequently for hypertension) have been found to produce harmful interactions with both simvastatin and clopidogrel; both were noted a considerable time after the medications were in widespread use.

Information for some frequent adverse effects may be available from RCTs, but most will come from observational studies and pharmacovigilance data from drug manufacturers and regulators, which are often based on individual case-reports. Such data tends to provide only a rough estimate of adverse effect likelihood, and without the ability to individualise to patients at particularly high or low risk. The quality of information available on adverse effects is, in general, substantially lower than that of beneficial effects.

2.2.3 The prevention paradox in cardiovascular disease

In 1981, Rose described the Prevention Paradox, which states that most CVD would be expected to occur in people at low risk, since only a very small proportion of people will have risk factor levels located at the top end of the distribution. Targeting people at high risk leads to large absolute benefits for this group, but ignores the bulk of the population in whom most CVD occurs. Thus, paradoxically, whole-population measures lead to small average benefits for any individual, but the largest reduction in disease across a whole population. This has important implications for communicating risk to individuals. Interventions which are broadly targeted will produce the largest absolute population benefits, will appear the least effective to individuals.

Figure 2.1 on Page 35 illustrates the expected effects of two strategies for reducing blood pressure. The left half of the diagram illustrates an approach which targets a whole population. This might represent a multi-faceted approach aimed at increasing
exercise, improving diet, and reducing smoking in a population. A key example of this approach is the North Karelia project, a Finnish community health programme which led to significant improvements in CVD and all-cause mortality. This might be expected to produce a small reduction in blood pressure for any individual, but with a large number benefiting. The right half of the diagram illustrates the effect of targeting a high-risk group, such as with the National Health Service (UK) (NHS) Health Check programme. The relatively small group identified as high risk would expect substantial improvements in blood pressure with drug treatment, but the majority of the population (in which most CVD would be expected to occur) have no change. This problem is compounded since screening programmes are more likely to attract healthy participants. Groups with lower participation in screening programmes for cancer include those with low income, fewer years of education, and ethnic minority groups. Analysis of data from the NHS Health Check programme has found participation to be similar among socio-economic groups, but socio-economic deprivation was associated with lower rates of complete risk data being collected; additionally smokers were less likely to attend that non-smokers. Thus, unless risk factor screening programmes are targeted systematically across the whole population including harder-to-reach groups, socio-economic and ethnic disparities in health may be worsened.

In practice, a risk score cut-off is typically used to identify those at high risk who should be treated. Figure 2.2 (Page 36) depicts the performance of one such risk score (Qrisk2) using a 20% 10-year risk cut-off. This illustrates some trade-offs of this ap-
Women

Men

All women/men

Develop cardiovascular disease in following 10 years

QRisk2 high risk group

Figure 2.2: Scaled rectangle chart demonstrating the performance of QRisk2 for identifying men and women who will develop CVD in the following 10 years. Note that most people predicted to be at high risk will not go on to develop CVD (false positives), and that most people who do develop CVD would have been identified as low risk (false negatives). Adapted from the validation study by Collins & Altman with permission.117

proach. Most of those who test positive will not go on to develop CVD (as would be expected with a 20% 10-year risk cut-off; by definition the risk of not developing CVD in this group will be up to 80%). Furthermore, high-risk people make up only a minority of those who will go on to develop CVD; the bulk of CVD occurs in those who would be identified as being at low risk.

Lowering thresholds for treatment is one strategy for achieving a greater population reduction in CVD. A simulation study, showed that targeting aggressive cholesterol and blood pressure lowering treatments with a 20% cut-off prevented substantially more CVD than a 30% cut-off.120 However, the simulation found that neither strategy performed as well as a modest reduction in blood pressure and cholesterol across a whole population. This paradox has motivated the polypill concept, a strategy whereby all people over the age of 55 would be offered a pill containing a low dose of several preventative medications.121 The polypill has the additional economic advantage of avoiding costly risk assessments, enabling resources to be used for treating a greater number of people.122
The prevention paradox is a key factor which led to a change in guidelines in the UK and US, which have recently reduced the recommended high-risk cut-off from 20% to 10%.\textsuperscript{11,12} This change will reduce the number of false negatives, that is, those who are predicted to be at low risk but go on to develop CVD nonetheless. The trade-off will be an increase in false positives (those who are predicted at high risk but do not develop CVD), and a reduced average absolute benefit from treatment for individuals. In practice, the WHO recommends a combination of population-based strategies and targeting high risk populations.\textsuperscript{8}

### 2.2.4 Risk prediction algorithms

National and international guidelines recommend the use of risk estimation tools to provide patients with individual risk estimates,\textsuperscript{123,124} examples of which include the Framingham score, QRISK2, and ASSIGN.\textsuperscript{125,126} These tools are based on statistical models which incorporate information on a range of measurable risk factors (usually including age, sex, blood pressure, smoking status, family history, and blood lipid measurements), and predict a risk of developing CVD typically over the following 5 or 10 years. For settings without easy access to computers, the WHO have published a pocketbook of data tables, allowing risk to be estimated by hand.\textsuperscript{127}

The Framingham Heart Study produced multi-variable models to allow an individual’s CVD risk to be quantified from their risk factors.\textsuperscript{128} Data from the study has been used to generate tools which predict the risk of heart disease,\textsuperscript{129} and later the risk of all CVD,\textsuperscript{130} in people with no prior history of CVD.

The Framingham risk scores are based on multi-variable Cox proportional-hazards models,\textsuperscript{131} which measure the association between known risk factors at baseline (in this case: age, total and HDL cholesterol, systolic blood pressure, treatment for hypertension, smoking, and diabetes) and later incidence of CVD. Separate models were fitted for men and women.

The coefficients generated by these models can then be multiplied by the risk factor values of a patient seen in clinical practice to produce an individualised risk of CVD over the following 10 years. The calculation is typically done by computer using risk
factor values already recorded in a patient’s electronic health record. The methods of the Framingham risk scores became a prototype for many Framingham adaptations, and CVD risk tools based on other datasets, which aim to improve performance for the needs of particular populations worldwide. A key limitation of the Framingham score is the ethnic and geographical homogeneity of the source population. Framingham risk estimates have been found to perform reasonably well in populations unlike the source cohort (see Figure 2.3 on Page 40), but do have a higher rate of misclassification in European populations, and in those over the age of 65. A validation in a US multi-ethnic cohort (comprising White [42%], Chinese [12%], African American [26%], and Hispanic [20%]) of five different risk algorithms (all recommended by various current guidelines) found that all algorithms substantially overestimated CVD risk; the best performing algorithm overestimated by 25%, and the worst by 115%. Studies from the UK indicate that the effects of ethnicity differ from the effects found in the US: CVD risk has been found to be higher in UK south Asian ethnic groups (the largest ethnic minority group in the UK) compared with white Europeans; within the south Asian group, there was substantial heterogeneity in CVD risk between people of Indian, Bangladeshi, and Pakistani origin. Additionally, although black African and Caribbean UK populations have an increased risk of CVD compared with white ethnic populations, this difference appears smaller than that found in the US between white and African American populations.

In the UK, these deficiencies motivated the development of QRISK, and later QRISK2, which additionally incorporated self-reported ethnicity. These risk algorithms were not based on a traditional cohort study, but instead rely on large scale analysis of routinely collected data from electronic primary care records.

This approach has disadvantages. First, since it relies on routine data, several variables have lower levels of completeness than research quality cohort studies. The least completely recorded variables were total cholesterol (36% of men, 37% women) and HDL cholesterol (25% men, 27% women)—the authors used imputed lipid values in the majority of cases.

One weakness of using risk tools based exclusively on primary care records is incom-
pleteness of case ascertainment. A study by Herrett et al. linked data from overlapping UK data sources covering 17,964 people with MI (Clinical Practice Research Datalink (CPRD), Hospital Episode Statistics (HES), the Myocardial Ischaemia National Audit Project (MiNAP) disease registry, and the Office for National Statistics (UK) mortality register), and found that using primary care data alone missed 26% of cases of MI.\textsuperscript{39}

This is one possible explanation for the fact the Framingham score (derived from a research-quality cohort study) was found to overestimate CVD incidence by 5% when validated using routinely collected primary care data.\textsuperscript{119}

However, as a result of these trade-offs, QRISK has some advantages. First, it is derived directly from a UK population, and therefore avoids some of the generalisability problems of Framingham.\textsuperscript{125} Second, it incorporates information on ethnicity and socio-economic deprivation (using area-level measures by postcode); the absence of these variables in the Framingham score being possible contributors to its reduced accuracy in the UK.\textsuperscript{140} Third, it is derived from a vastly larger population than Framingham (2,343,759 patient records used in the latest version of QRISK\textsuperscript{41} versus 8,491 from the Framingham cohort\textsuperscript{39}), which should in theory increase the precision of the resultant risk estimates.

On an independent validation sample of UK primary care records, QRISK2 has been found to perform better than the Framingham score,\textsuperscript{117} and is now recommended as a first choice by the UK by the National Institute for Health and Care Excellence (UK) (NICE).\textsuperscript{12} As described above, however, use of primary care records data alone is likely to underestimate true CVD rates, and the QRISK algorithms have not been validated using linked overlapping datasets.

### 2.2.5 The problem of adherence

A large proportion of people prescribed medication for CVD prevention do not go on to take it regularly—estimates of the rate of poor adherence or non-adherence range from 30–50\textsuperscript{,}	extsuperscript{142} and adherence\textsuperscript{1} is similarly low across all medication classes.\textsuperscript{144} The

\textsuperscript{1}Terminology describing how patients take medication has changed, with the term compliance (describing how well patients comply with the doctors treatment decision) being used less, since it doesn’t allow for patients being involved in decisions.\textsuperscript{10} Concordance has been increasingly used as an alternative, since it incorporates the concept that patients and doctors will come to agreement. This thesis will use
WHO has stated that poor adherence to medication is the most important impediment to risk factor control, and has recommended research into interventions to promote adherence.\textsuperscript{145} Haynes describes the scale of the problem of adherence thus:

Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments\textsuperscript{1}

The causes of poor adherence have been widely studied, and can be considered as unintentional (practical barriers to treatment, including cost, access to health care, poor social support, complex drug regimens, and forgetting) or intentional (related to patient motivation to take treatment).\textsuperscript{10}

**Measuring adherence**

Measuring adherence is challenging, and there is a range of measures each with strengths and weaknesses. The simplest method is to ask the patient to report their own adherence.\textsuperscript{147} This method has been criticised as being particularly susceptible to bias in cases where trial participants are not blinded, which is the case in most adherence research.\textsuperscript{148}

\begin{itemize}
  \item the term *adherence*, defined as the proportion of people who keep adequately to an agreed treatment plan, no matter how it was decided.\textsuperscript{143}
  \item \textsuperscript{1}This quotation is very widely attributed to the Cochrane review by Haynes et al.\textsuperscript{146} but the quote does not appear in any versions currently available.\textsuperscript{146}
\end{itemize}
However, the method has been found valid: patients have been found to overestimate their own adherence (by around 17%), but self-report is still reasonably accurate at identifying non-adherers.\textsuperscript{147}

A systematic review by Christensen \textit{et al.} (search date 2009) examined studies using electronic pill boxes to monitor adherence to hypertension treatment.\textsuperscript{149} These are pill bottles with an electronic device in the lid which records the date and time of opening and closing. Researchers can later download this data to a computer. The review found 9 RCTs evaluating electronic monitoring, each of which found that monitoring itself resulted in a reduction in blood pressure, suggesting that this system of monitoring affects patient behaviour.\textsuperscript{149} Additionally, monitoring systems record pill box opening rather than medication taking itself; it will therefore be inaccurate for patients who wish to conceal their non-adherence.

\textbf{Interventions aimed at improving adherence}

Improving adherence is an appealing target for intervention, but to date, there is no strong RCT evidence of the success of any particular intervention.

Nieuwlaat \textit{et al.} updated the Cochrane systematic review looking at interventions to improve adherence to medication in any health condition, with a search date of January 2013.\textsuperscript{148} This review included 182 RCTs (of which 21 RCTs examined adherence to cardiovascular medications) of varying methodological quality, of which only 17 were found to be at low risk of bias. Despite the high volume of research, included trials were highly heterogeneous, both in terms of the clinical condition assessed and the interventions trialled, making it difficult to determine the effectiveness of any particular strategy. In addition, the majority of trials did not use a standard or rigorous outcome measure. The authors conclude that there is no strong evidence that existing interventions improve adherence.\textsuperscript{148} Interventions trialled include education (courses and written materials), motivational interviewing, counselling on the importance of adherence (in person or telephone), reminders, support groups, and direct observation. The trials with the highest methodological quality used complicated multi-faceted interventions which would be difficult to implement in practice, and even these did not result in important
improvements in adherence or clinical outcomes. A key weakness of this review (caused by inadequate intervention descriptions in the source trial reports) was that interventions were not described in sufficient detail to be able to replicate in practice. This problem has been shown to be widespread in reports of RCTs of non-drug interventions.\textsuperscript{150} A subsequent RCT of 303 people found that mobile phone text message reminders significantly improved self-reported medication use at 6 months.\textsuperscript{151}

The link between adherence and shared decision making (SDM) is complex, and although improving patient involvement in decision making has been proposed as a promising route to improve adherence, systematic reviews of the effects of SDM have found insufficient evidence to judge whether this is the case.\textsuperscript{16,152} However, as noted by Sandman \textit{et al.}, although non-adherence is usually described as a problem from a public health perspective, it can alternatively be seen as exercising of patient autonomy and may represent an informed change of judgement over time.\textsuperscript{153} Therefore from the perspective of SDM, it is important to ensure that patients are well informed; whether or not they adhere to the initially agreed treatment plan.\textsuperscript{153}

There is evidence that better involving patients in practical aspects of their care may be a route to improved adherence. A systematic review of home blood pressure monitoring included 11 RCTs, and concluded that home monitoring is likely to improve adherence, particularly when used in combination with other adherence-improving strategies.\textsuperscript{154} Two subsequent RCTs have found that patient self-monitoring together with a protocol for patients to titrate their own medication significantly improved blood pressure control; one of the RCTs examined participants with a prior history of CVD and found the improvement in blood pressure was substantial (450 participants; improvement in blood pressure at 12 months with intervention: 9/3 mmHg, 95\% CI 6/2–13/5 mmHg).\textsuperscript{155,156} Likely factors leading to this improvement include increased titration of mediation, and better adherence to prescribed treatment.

\subsection*{2.2.6 The rule of halves, and subsequent improvements in care quality}

The \textit{rule of halves} was first used to describe the state of hypertension control in the early 1970s in the US,\textsuperscript{157} and has since been found to hold true in many countries world-
The rule states that approximately half of people with hypertension will be diagnosed with the condition, half of those diagnosed will be prescribed treatment, and half of those treated will have good blood pressure control (see Figure 2.4).

Falaschetti and colleagues reviewed data from the Health Survey for England, from 1994 to 2011. They found that by 2011, 37% of people with study diagnosed hypertension were controlled, a dramatic improvement over time, but which still leaves substantial potential for further improvement. They conclude that by 2022, if the trends continue, 80% of those treated for hypertension will be well controlled.

Use of data from the Health Survey for England may risk overestimating the problem of uncontrolled hypertension, since hypertension was diagnosed from three measurements taken on a single occasion, where national guidelines recommend measuring at multiple time points and ideally ambulatory monitoring. Additionally, the group identified as ‘untreated’ may include older people, and people with mild (or stage I) hypertension for whom the evidence supporting aggressive treatment is less strong.

Several other countries have similar (or greater) improvements in control over time, including the US, Canada, and several countries in western Europe. These improvements in risk factor control may partially explain worldwide declining incidence of CVD. However, despite these striking improvements in hypertension detection, treatment, and control in developed countries, most of the world’s population has not
seen such improvements.\textsuperscript{167} Recent reviews have found that the rule of halves still applies across much of Africa, India, the Middle East, and China,\textsuperscript{170–173} and the bulk of hypertension-related morbidity and mortality is in low- and middle-income countries.\textsuperscript{174}

2.3 Informing patients about cardiovascular disease prevention

2.3.1 Education

Patient education has been evaluated in the primary prevention of CVDs in 12 RCTs, which are summarised in table 2.3 on page 46 (individual or group education, rather than population-based campaigns).\textsuperscript{i}

With the exception of the trial by Hennessy \textit{et al.}, most trials had small samples (range from 110 to 453). Eleven of the twelve RCT reports (all except that by Beune \textit{et al.}) provided limited descriptions of development and content of the educational interventions trialled; none of the interventions assessed in these trials were sufficiently well described to allow replication or use in practice. From the descriptions provided, however, the broad content of the interventions appears similar. Most provided information explaining what hypertension is, and recommended that participants make changes to lifestyle; increasing exercise, aiming to lose weight, and reducing salt and alcohol intake were widely advised. Advice was given that attending clinic appointments, and taking medication regularly as prescribed were both important. None of these eleven RCT reports described whether patients were involved in the intervention development. The largest trial was by Hennessy and colleagues, a cluster randomized trial of 10,696 participants.\textsuperscript{177} This trial evaluated a set of leaflets posted to participants on two occasions, together with education to their healthcare providers about their patient control rates. This trial found no significant difference in hypertension control between the intervention and usual care. As with many of the other RCTs, there was little detail provided about the development of the intervention or whether patients were involved. Additionally, the trial did not report on how patients responded to the literature, or indeed whether or not they received, opened, and attempted to read it; given the intervention

\textsuperscript{i}RCTs identified from systematic reviews \textsuperscript{[175], [176] and [20]} plus searches of PubMed. RCTs including > 100 participants reported only; several additional smaller RCTs were identified which are not reported further.
was delivered by post this is a major limitation.

Results of the RCTs were mixed, with eight RCTs finding no significant improvement in their primary outcome, but with four trials (those by Sclar, Marquez-Contreras, Iso, and Hacihasanoğlu) finding that their educational interventions did improve either blood pressure, or adherence to treatment. The lack of detail about the interventions in these trials means it is difficult to draw conclusions about why their results differed; it is possible that the handful of positive trials are due to a small trials bias, where under-powered RCTs have been found to produce false positive results.¹⁷⁹ The vast majority of the trials did not measure patient understanding or satisfaction with decision making as outcomes.

The exception was the RCT by Beune and colleagues¹⁷⁸ which evaluated culturally specific education in Netherlands residents of self-described Surinamese or Ghanaian ethnicity, which described the educational intervention in detail in a linked published protocol with supplemental materials.¹⁸⁰ This trial uniquely based the educational intervention on the results of a linked qualitative study.¹⁸¹ The intervention comprised three educational sessions which focused on eliciting patient understanding and experiences of the causation, symptomatology, and treatments for hypertension. Additionally, the patient’s social circumstances, effects of migration, cultural practices and finances were explored, with an attempt to tailor patient education and setting of goals to these identified needs and circumstances. The trial did not conclusively find the intervention successful: at 6 months there were statistically significant but small improvements in diastolic blood pressure and adherence to planned lifestyle changes. However there was no difference found in systolic blood pressure, or medication adherence scores (improvements in Morisky medication adherence scale (MMAS-8)¹ with education v no education: lifestyle, 0.34, 95% CI 0.12 to 0.55; medication, −0.09, 95% CI −0.65 to 0.46; change in systolic blood pressure (BP) −1.69 mmHg, 95% CI −6.01 to +2.62; diastolic BP −3.01 mmHg, 95% CI −5.73 to −0.30). The trial was small, and did not meet the recruitment target of 246 patients; the inconclusive results may reflect a lack of statistical power.

¹The MMAS-8 is an 8-item, self-reported adherence score where a score of 8 represents complete adherence, and lower values lesser adherence.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Intervention details</th>
<th>Results</th>
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<tbody>
<tr>
<td>Sacket et al 1975(^{19})</td>
<td>230 male steelworkers with essential hypertension (Canada)</td>
<td>Audiotape, booklet, and some contact with a trainer (a high-school graduate with some additional health training); programme included: “facts about hypertension, its effects upon target organs, health, and life expectancy, the benefits of antihypertensive therapy, the need for compliance with medications, and some simple reminders for pill-taking”</td>
<td>No significant difference in medication adherence (defined as &gt;80% of expected pills removed from pill box), but authors state increase in knowledge test scores (factorial ( \text{RCT} ), education comparison only presented here)</td>
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<tr>
<td>Hennessy et al. 2006(^{177})</td>
<td>10,696 people with hypertension (cluster randomized by primary care physician [n=93])</td>
<td>Collection of leaflets sent to patients, some made specifically for the project, others by the US National Institute of Health research. Titles included ‘Your Guide to Lowering Blood Pressure’, ‘What You Can Do About Controlling Your High Blood Pressure’, and ‘What to Ask Your Doctor If You Have High Blood Pressure’. Contents not further specified. Physicians in the intervention group additionally were visited by a pharmacist to audit their performance, and provide feedback comparing individual performance with the group as a whole.</td>
<td>No significant difference in proportion with controlled blood pressure (OR 1.13, 95% CI 0.87 to 1.47);</td>
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<tr>
<td>Kirscht et al 1981</td>
<td>432 adults with hypertension (US)</td>
<td>Information booklet containing either: “a threatening message group, a positive message group, or a control group. Two informational tabloids were developed and delivered to the experimental participants. Each contained material on hypertension, its effects, control measures, and instructions on following a regimen.”</td>
<td>No significant differences in self-reported adherence (expressed as ratio: 0.91 with intervention v 0.90 with control) or pharmacy estimated adherence (ratio of medication collected to expected: 0.68 with intervention v 0.69 with control)</td>
</tr>
<tr>
<td>Pierce et al 1984</td>
<td>119 patients of a primary care clinic found to be uncontrolled (Australia)</td>
<td>4 education sessions, 90 minutes each, groups of 12 patients; session 1: cardiovascular risk factors and the importance of high blood pressure; session 2: importance of exercise; session 3: healthy eating; session 4: coping with stress, and importance of adhering to medication</td>
<td>No significant difference in adherence (by pill count); more in education group had 'reduced' blood pressure (size of reduction unclear): 83% v 67%, P reported as ‘&lt; 0.05’ (factorial rct, education comparison only presented here)</td>
</tr>
<tr>
<td>Sclar et al 1991</td>
<td>453 people with hypertension attending hospital outpatients clinic (US)</td>
<td>Newsletter in pill box, and telephone contact from researcher; Newsletter contained information about hypertension, nutrition, and lifestyle changes. Telephone follow-up asked about experience of treatment and stressed importance of adherence. Newsletter and refill reminder were posted to each patient monthly</td>
<td>Improvement in adherence (mean proportion of prescriptions collected: 0.82 v 0.48 in existing hypertensives, 0.93 v 0.52 in new hypertensives; both comparisons reported as ‘P&lt;0.05’)</td>
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<tr>
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<td>Márquez-Contreras et al 1998&lt;sup&gt;185&lt;/sup&gt;</td>
<td>110 primary care patients with mild to moderate hypertension (Spain)</td>
<td>90 minute small group education session and postal follow-up; session covered: &quot;What is hypertension?, diagnosis of hypertension, why it is important to health; causes of hypertension, symptoms, factors, risk factors, why it is important to address; what treatment will be used.&quot;</td>
<td>Education improved average adherence over 6 months (defined as use of 80–110% expected medication by pill count; 94% with intervention v 89% with usual care; P = 0.007)</td>
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<tr>
<td>Schroeder et al 2005&lt;sup&gt;196&lt;/sup&gt;</td>
<td>245 primary care patients with uncontrolled hypertension (UK)</td>
<td>20 minute ‘adherence support’ session with practice nurse, with 10 minute refresher after 2 months; nurses were encouraged to find individual solutions to adherence problems following a 20–30 minute training session. The areas addressed included: side effects, size or taste of tablets, number of doses a day, non-acceptability of taking tablets, forgetfulness, non-comprehension, total number of different tablets</td>
<td>No significant difference in adherence (measured by electronic pill box monitor); no significant difference in systolic or diastolic blood pressure at 6 months</td>
</tr>
<tr>
<td>Beune et al 2014&lt;sup&gt;78&lt;/sup&gt;</td>
<td>146 primary care patients with hypertension (Netherlands) who self-identified as Ghanaian or Surinamese ethnicity (cluster RCT)</td>
<td>Three 30 minute nurse-led education sessions, with an emphasis on ‘culturally specific education’ designed for the ethnic groups included; topics covered included: what is hypertension? culturally specific barriers to control; individual goal setting</td>
<td>No significant difference in systolic BP, significant reduction in diastolic BP with intervention; systolic: −1.69 mmHg, 95% CI −6.01 to +0.62; diastolic −3.01 mmHg, −5.73 to −0.30; patient adherence to treatment recommendation self-reported on 4 point scale: lifestyle adherence +0.34 with intervention, 95% CI +0.12 to +0.55; medication adherence −0.09, 95% CI −0.65 to +0.46</td>
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<td>Xie et al 1998</td>
<td>169 participants with uncontrolled hypertension; unclear whether primary/secondary care (Beijing)</td>
<td>How education delivered not clearly described; contents included lifestyle advice, relaxation, importance of adherence and keeping appointments</td>
<td>Blood pressure reduction similar in both groups at 3 years (systolic −20 mmHg with intervention v −22 mmHg control; diastolic −13 mmHg in both groups)</td>
</tr>
<tr>
<td>Johnson et al 2011</td>
<td>670 primary care patients with hypertension (US) majority of whom identified as black American</td>
<td>Patient education comprised 30 minute individual education session with a nurse every 6 months, topics included weight loss, low sodium diet, exercise, and importance of adherence to medication and attendance at appointments.</td>
<td>Factorial RCT comparing physician education alone, patient education alone, no intervention, and both interventions; results presented here for all patients receiving education v no education. No significant difference in blood pressure between groups at 6 months (mean 137/82 mmHg with education v 139/82 mmHg with control; P = 0.25 for systolic, P = 0.98 for diastolic)</td>
</tr>
<tr>
<td>Iso et al 1996</td>
<td>111 people with uncontrolled hypertension identified from population-based stroke prevention screening programme (Japan)</td>
<td>Series of half-hour lectures by physicians about stroke prevention, followed by practical sessions with public health nurses covering dietary sodium reduction, increased exercise, maintaining healthy weight, and alcohol moderation</td>
<td>Mean blood pressure at 6 months: 142/83 mmHg with education v 148/82 mmHg with control; P systolic reported as ‘&lt;0.01’, P diastolic = 0.04</td>
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<tr>
<td>Reference</td>
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<tr>
<td>Hachhasanoğlu et al 2011</td>
<td>120 people with hypertension recruited from primary care clinics (Turkey)</td>
<td>Delivery of education not clearly stated—appears was one-to-one interviews with a nurse. Two educational sessions compared with monitoring alone. A. Six sessions covering importance of adherence and attending appointments; B. Same as A plus education about a healthy diet plus reducing sodium in diet; C. blood pressure measurement with no education</td>
<td>Mean blood pressure at 6 months: A. 140/86 mmHg B. 134/84 mmHg C. 156/93 mmHg; P ANOVA systolic &lt;0.001; P ANOVA diastolic &lt;0.001; BMI at 6 months: A. 25.3 B. 25.6 C. 26.1; P ANOVA = 0.56</td>
</tr>
</tbody>
</table>
2.3.2 Motivation for communicating risk

The presentation of risk\(^1\) to patients has become a core part of shared decision making practice.

The theoretical rationale for its adoption has been straightforward: that epidemiological data exists which describes the risk of benefit and harm of medical interventions.\(^2\) Since no medical intervention is universally effective, and all interventions are associated with some risk of harm, communicating these likelihoods is aimed at helping patients make informed decisions. Presenting the results of epidemiological studies to patients to enable them to make decisions was described as ‘the way of the future’ in the original Evidence Based Medicine working paper in 1992;\(^3\) and accounts for a major chapter in the International Patient Decision Aids Standards (IPDAS) guidelines about decision aid development.\(^4\)

A 2014 Cochrane systematic review compared the effects of decision aids containing a risk communication component versus those which did not.\(^5\) Of the 115 decision aids identified, 87% included statistical information.\(^6\) The most frequent outcome assessed by included trials was **accuracy of perceived risk**, defined as the percentage of people whose descriptions of their own risk matched the trial outcomes presented to them. It found that those who received risk information were nearly twice as likely to perceive risk accurately (18 RCTs, 5868 people; RR 1.82, 95% CI 1.52 to 2.16). The included RCTs were found to be of good quality, but there was substantial statistical heterogeneity ($\chi^2 < 0.001; I^2 = 86\%$), likely caused by small trial size and variation in the decision aids and medical conditions assessed. Given that the control group for this comparison did not receive any information on probabilities, it is perhaps not surprising that they were less accurate in their estimates. The review found no evidence on whether risk communication affected decision quality, decisions made, or clinical outcomes.

In CVD in particular, there is evidence of wide variation in how patients value the benefits and downsides of medication. Several questionnaire studies have examined patients’ **required risk reduction** of treatment\(^7\) — in other words, what size of benefit

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\(^1\)The word *risk* is used with here meaning the probability of an outcome occurring, regardless of whether the outcome is good or bad. This is the meaning used widely in health research,\(^8\) and contrasts with the more widespread use meaning the likelihood of an adverse event.
would patients require as a minimum before they consider preventative medication to be worthwhile? In all of these studies, the required risk reduction varied substantially among participants. One of the studies found that larger risk reductions from a hypothetical medication had no effect on patient willingness to use; however, the risk of adverse effects had a much greater impact on decisions.

2.3.3 Strategies for communicating risk

Communicating risk information in a way which is clearly understood is challenging, and the potential to mislead (either deliberately or accidently) is great. There are added practical constraints in the primary care consultation, with limited time, frequent lack of experience of the clinician in shared decision making, and patients who have an expectation of a traditional clinician-led consultation style.

Low levels of numeracy in the general population pose an additional challenge to overcome. Low numeracy affects populations of all education levels; a US study of 463 people with tertiary education found more than two thirds were unable to correctly answer three simple questions which tested understanding of percentages. Presenting probabilities in a clear way may alleviate this problem somewhat, but even with optimal formatting more than half of people may not adequately comprehend simple statistics about treatment benefit and harm. Examples of formats used for communicating CVD risk are shown in Figure 2.5 on Page 54. The following features of risk presentation have been demonstrated to affect understanding:

Relative versus absolute risks

Relative risks have been criticised as liable to exaggerate treatment effects. For example, an intervention which reduces the rate of disease from 5 in 1000, to 4 in 1000 may be said to demonstrate at 20% relative reduction in risk. The absolute treatment benefit, which occurs in this case for 0.1% of people, is typically a much smaller number. Presentation of absolute risks have been shown to lead to increased accuracy of understanding of risk, with relative risk presentations being associated with overestimation of risk. Gigerenzer argues that relative risk presentation de-contextualises the risk, not-
ing it is possible to calculate a relative effect when given an absolute effect, but not the other way around.207

**Natural frequencies versus percentages**

Risk presentation theory has typically preferred the use of natural frequencies (fractions with a common denominator, such as 1 in 1000) due to evidence that many people struggle to perform simple calculations with percentages.207 However, two moderately large RCTs (2,601 participants and 2,944 participants) have found that percentage risks increased the accuracy of understanding compared with natural frequencies,211,212 and one subsequent RCT (2,807 participants) found no difference between formats.209

**Verbal versus numerical description of risk**

The European Commission (EC) Pharmaceutical Commission have developed a plain-language vocabulary of risk to describe the frequency of medication side effects: from “very rare” (less than 0.01%) to “very common” (greater than 10%). A systematic review by Büchter et al. (search date 2012, 10 RCTs) quantified the accuracy of risk understood with the EC vocabulary versus numerical risk. “Very common” led to a 32% point overestimate in perceived risk (95% CI 20% to 43%), “common” to a 35% overestimate (95% CI 31% to 41%), “uncommon” to a 11% overestimate (95% CI 6% to 17%), and “rare” to a 10% overestimate (95% CI 5% to 16%). The included RCTs were not reported sufficiently well to enable a quality assessment, meaning it is not possible to exclude an overestimate in group differences due to bias. Numerical probabilities were associated with a modest improvement in patient satisfaction (mean 0.5 point improvement on 6 point Likert scale, 95% CI 0.3 to 0.6).

**Graphical displays**

Charts and graphics are frequently used as an adjunct to numbers to improve understanding of probabilities.214 In particular, decision aids widely make use of icon arrays (sometimes known as faces charts), which have been demonstrated to increase the accuracy of understanding of treatment effects.215
Although your real age is 59, your heart age is 70.

In a crowd of 100 people with the same risk factors as you, 18 are likely to have a heart attack or stroke within the next 10 years.

Absolute risk as natural frequencies

Your risk of having a heart attack or stroke within the next 10 years is 17.7%.

You have double the risk of having a heart attack or stroke compared with a typical person of your age and ethnic group.

Relative risk

Figure 2.5: Frequently used strategies for communicating CVD risk. Each format depicts the same underlying risk, being an estimate for a hypothetical 59 year old male ex-smoker, of black Caribbean ethnicity, treated hypertension, height of 1.77 m, and body mass index of 30.1 kg/m² Risk estimated using QRISK2 2013.
Framing

Framing describes whether risks are presented as gains, or equivalent losses.\(^{217}\) For example, a 10% chance of developing CVD may be represented equivalently as a 90% chance of remaining free of CVD, but these might be interpreted differently. A factorial RCT by Peters \textit{et al.} (298 participants) compared presenting risk as a percentage versus natural frequencies, and with three different \textit{frames} for presenting an identical risk of an adverse effect from a hypothetical drug.\(^{218}\) The three frames were a negative frame (‘10% of people will develop a blistering rash’), a positive frame (‘90% of people will not develop a blistering rash’), and a combined frame where both pieces of information were presented. The RCT found that negative frame was associated with the highest perception of risk, the positive frame with the lowest, and the combined frame produced a more balanced perception. There was no significant difference in perceived risk between percentages and natural frequencies. An RCT by O’Connor (282 participants, mix of healthy volunteers and people with cancer) presented information about a hypothetical chemotherapy treatment in various formats.\(^{219}\) It found that when survival was presented in a positive frame (probability of surviving), participants were more likely to choose treatment compared with when presented with a negative frame (probability of dying).

2.3.4 Risk communication in cardiovascular disease prevention

Two systematic reviews have been published previously examining the communication of risk for CVD specifically, but were not able to draw robust conclusions. The first by Sheridan and colleagues (search date 2008) evaluated the effects of communicating CVD risk (using any strategy) identified 18 controlled studies (comprised of 14 randomized, and 4 non-randomized).\(^{220}\) No meta-analysis was conducted, likely due to the heterogeneity of study designs included, and only 6/18 included studies were rated as high quality. Three of the RCTs (total of 897 participants) found that communicating a global coronary risk score improved the accuracy with which patients perceived their own risk. Nine studies (6 of which were randomized) found conflicting results about the
effects of communicating CVD risk on risk factors (measured as change in risk scores over time); when limited to good- and fair-quality studies with a one-off intervention, the effect was negligible.

The second systematic review, by Waldron and colleagues (search date 2008) identified fifteen studies (of any quantitative design) which compared different strategies for communicating CVD risk. It included studies which examined the effects of specific CVD risk communication strategies, but concluded that the studies were too heterogeneous and too low in quality to make a firm recommendation for any particular strategy. The authors suggest that risk communicated as percentages or natural frequencies, and using shorter time-frames might be most effective in encouraging behaviour change, but acknowledge that these conclusions are tentative and without robust underlying evidence.

2.3.5 Applying population-based evidence to individuals

External validity describes whether the results of research are generalisable outside of the study setting; i in other words, to whom do the results of the research apply? Clinical trials often recruit populations which are not typical of those for whom the treatments will be used in real life. For example, most clinical trials recruit participants with a single illness—this aims to increase the scientific validity of answering whether an intervention works for a particular condition. However, patients with a single condition are reasonably unusual in practice; trials examining populations with multi-morbidity are lacking. There are further common biases in trial recruitment which may lead to uncertainty about the external validity of research. Clinical trials have been found to favour the recruitment of men over women, recruit few from ethnic minority groups, and are less likely to include older people. Additionally, readers of medical evidence need to consider whether characteristics of the trial setting (for example, country, healthcare system, whether primary or secondary care recruitment) are similar enough to the patient and clinical situation at hand to be applicable.

External validity problems apply to trial interventions in addition to populations. A

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i in contrast with internal validity which describes the scientific integrity of the study.
2008 survey of otherwise well reported clinical trials from highly-cited medical journals found less than half reported sufficient information to be able to reproduce the trial intervention.\textsuperscript{227} This was a particular problem with trials of complex interventions, where considerable detail is often needed for a third party to reproduce. Although drug interventions are in principle easier to replicate, meta-analyses frequently combine results from trials including multiple drugs (for example different drugs in the same class), and at different doses, meaning the best drug to use in practice is often unclear.\textsuperscript{228}

Finally, there are philosophical problems with applying population-based evidence to individuals. Clinical trials report average effects of treatments for populations, but the outcomes for individuals will be distributed around the mean.\textsuperscript{229} Therefore, assuming that an individual would expect the mean improvement in outcome found in a trial is usually misleading. In reality, the outcomes from treatments regarded as effective are more complex, and include the possibility of benefit, no effect, or harm. Figure 2.6 on Page 58 shows this problem schematically for a hypothetical treatment. Ideally, the characteristics of the trial participants who benefited could be sought from the trial report, to allow a judgement about whether a treatment is suitable for an individual patient. However, this approach is also problematic, both statistically (due to the reduced power and increased likelihood of false positive results with subgroup analysis),\textsuperscript{230} and due to the likelihood that differences in treatment response are likely due to the complex, poorly understood, and unquantifiable variation between individuals.\textsuperscript{231}

\section*{2.3.6 External validity in cardiovascular disease prevention trials}

The problem of determining whether clinical trials are externally valid is particularly relevant in CVD prevention.

This can be illustrated by examining analyses of statins for primary prevention, since many of the randomised trials in this area included a proportion of people with established cardiovascular disease.\textsuperscript{232} Those with established cardiovascular disease are more likely to benefit from statins, and therefore including this group may have led to an overestimate of the effect in people with no previous cardiovascular disease (the true primary prevention population). Various teams of reviewers have attempted to miti-
Figure 2.6: Hypothetical example of effects of a treatment (which is effective on average) on a population. In this example, the treatment leads to a mean 0.5 SDs improvement in the outcome, but a substantial minority have no benefit. Adapted from figure in Kravitz et al. 229

gate this problem; the results from four published meta-analyses are summarised in Figure 2.7 on Page 59.

Analysis A was by the Cholesterol Treatment Trialists’ Collaboration, and included all studies, no matter the rate of established cardiovascular disease in participants.90 In fact, 32% of the population described as receiving ‘primary prevention’ in the included studies had a previous MI, and only 46% had no prior history of cardiovascular disease.1

Analysis B was by Brugts et al., and included only studies where less than 20% of the population had existing cardiovascular disease.234 The final analysis C was by Ray et al., and used the most strict criteria: only including studies where they were able to obtain data from the primary prevention population exclusively.235 No data from people with prior cardiovascular disease were included in this analysis. Note that using the more stringent criteria in analysis C, there is no longer a statistically significant reduction in all-cause mortality. This may be due to a reduction in power with the smaller popula-

\footnote{The authors did conduct an individual patient data meta-analysis of the subgroup without prior cardiovascular disease for the outcome of total cardiovascular events. This analysis found that major coronary events and stroke were significantly reduced with statins; however, the key outcome of mortality was not reported. An analysis of this data by a second author team found no significant difference in mortality between statins and placebo in those with <20% estimated CVD risk at baseline.233}
Fig. 2.7: Estimates of the effectiveness of statins on all-cause mortality using four definitions of a primary prevention population. A summarises the analysis of the Cholesterol Treatment Trialists’ Collaboration\textsuperscript{90}, B that by Brugts et al.\textsuperscript{234}, and C by Ray et al.\textsuperscript{235}. In analysis A 54% of the populations of the included studies had some form of established CVD before entering the trial. Analysis B restricted inclusion to trials with <20% people with established CVD, and C included only data from people with no established CVD.

Decisions about how to define a population affect conclusions similarly in ‘mild’ hypertension (known as grade I hypertension, defined as systolic blood pressure of 140–159 mmHg and/or diastolic of 90–99 mmHg). A 2012 Cochrane review restricted inclusion to trials where >80% had grade I hypertension.\textsuperscript{163} This analysis used aggregate data from trials including a total of 8,912 people, but found no significant differences in CVD or mortality rates with drug treatment. A subsequent analysis obtained individual patient data, which enabled the separate analysis of participants with grade I hypertension from additional trials, included 15,266 participants.\textsuperscript{237} This analysis found that drug treatment did significantly reduce stroke (OR 0.72, 95% CI 0.55 to 0.94) and death (OR 0.78, 95% CI 0.67 to 0.92). However, nearly all of the additional participants in this analysis had diabetes. There is therefore uncertainty about whether the positive results of the second analysis are due to increased power (indicating that drug treatment of grade I hypertension is effective), or alternately whether drug treatment of grade I hypertension is effective in people with diabetes only.
A further example of external validity problems in CVD prevention is around ethnicity. RCTs of anticoagulation in AF were conducted overwhelmingly in white populations; only 6% of participants were non-white. Additionally, observational data has shown increased warfarin-related intra-cranial haemorrhage in black compared with white patients. These data hint that the balance of benefit and harm with anticoagulation varies among different ethnic groups, but robust data from RCTs are lacking. In hypertension, ACE inhibitors have been found less effective in black ethnic groups who were under-represented in earlier trials. Therefore, in addition to any statistical uncertainty and the effects of bias, external validity problems are likely to add considerable uncertainty to any individual estimates of treatment effects which are difficult to quantify.

**Individualising results of cardiovascular disease trials**

The two key statistics which are used in CVD decision aids (and decision aids more widely) are the baseline risk of CVD estimated for that individual, and the reduction in risk expected with each of the possible interventions or none that the patient may choose from.

In addition, expected risks of adverse effects of each option are often communicated, particularly where the intervention is associated with a serious adverse event (for example, the risk of haemorrhage when using anticoagulants to prevent stroke in people with AF).

The most straightforward method to determine these values would be to find a clinical trial conducted in a population as similar as possible to the patient. However, trial populations are often diverse, and vary considerably from characteristics of individual patients. One strategy, which provides a partial solution, is to use the results from a subgroup analysis of a trial, identifying the subgroup with characteristics most similar to the patient. Subgroup analyses, however, are highly susceptible to bias; subgroups by definition have smaller sample sizes than full trials, and are frequently associated with the statistically unreliable practice of multiple significance testing.

To work around these issues, a personalised estimate of the likelihood of benefit from
Figure 2.8: Equation for personalising meta-analysis data; IER=intervention event risk; CER=control event risk; RR=relative risk

\[ IER = RR \times CER \]

medication may be obtained by multiplying an estimate of an individuals baseline risk by an estimate of the relative effect of medication, usually obtained from a systematic review and meta-analysis (see Figure 2.8). A confidence interval may be obtained by repeating the calculation using the upper and lower bounds of the 95% CI of the relative risk from a meta-analysis as the intervention event rate, which is the approach used by the Cochrane Collaboration for estimating absolute effects from meta-analyses.

This estimate relies on the assumption that relative effects an intervention are constant among populations with different baseline risks. To illustrate this point, a hypothetical intervention might result in significantly reduced risk of CVD, with a relative risk of 0.8 (i.e. a 20% relative reduction in risk). In a high risk population (in which, say, 30% will go on to develop CVD), the intervention would be expected to prevent CVD in 6%. In a low risk population (in which 10% will go on to develop CVD), the intervention would be expected to prevent CVD in 2%. This is also the theoretical underpinning of why most meta-analyses of health interventions pool outcome statistics by relative results (risk ratio or odds ratio) rather than absolute risk.

This assumption of constant relative effect has been found to hold true empirically in CVDS, particularly in trials of antihypertensive drugs and statins. However, Rothwell re-analysed data from two RCTs in stroke (one of aspirin for the treatment of TIA, and another of carotid endarterectomy) found substantial heterogeneity in relative effect across different populations. Rothwell recommends caution when extrapolating trial results to individuals using this approach, and suggests that careful analysis of the results of subgroups with different risk profiles is needed. However, it should be noted that CVD prevention is one of the few areas where a constancy of treatment relative effect among different population risk strata has been demonstrated; the assumption is held in other clinical domains without empirical proof.
The reference class problem

The risk of any individual in a population can be described as a single-event probability. As an example, consider a population in which 20% will develop CVD in the following 10 years. Any individual in this population will either certainly develop cardiovascular disease, or not (which is testable empirically after 10 years). It is impossible to predict which 20 patients will be affected.

Gigerenzer et al. examined how people respond to single event probabilities. In this study, participants who were told about a ‘30% chance of rain tomorrow’ interpreted this information in various ways. Since the denominator was omitted, participants were confused about whether it would be raining for 30% of the next day, whether 30% of the region would experience rain, or the correct answer, that it would be expected to rain on 30% of similar days.

Individualising risk, (as done in the calculation in Figure 2.8) does not result in the risk for a single target patient, but rather a risk estimate for a hypothetical population. In other words, the calculation adjusts the raw risk data from source clinical trials (which, as discussed above, typically include heterogeneous populations which are imperfectly representative of an individual patient), and providing an estimate in a population with similar risk factors as the target patient. Gifford highlights this issue in an essay about women seeking medical attention for breast symptoms, stating: “epidemiologists speak of risk as a measured property of a group or people, clinicians speak of risk as a specific property of an individual. Risk becomes something that the patient suffers; a sign of future disease that the clinician can diagnose, treat, and manage.”

This concern about whether population risk estimates can ever be applied to individuals is well established, being a example of the reference class problem. The reference class problem refers to the fact that any individual has an unlimited number of attributes. They can therefore be said to belong to potentially infinite classes, each with a different outcome probability.

For example, consider a man aged 51, living in London, who has never smoked. An

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1A more precise definition is ‘30% of times when meteorologists make this prediction, there will be at least a trace of rain the next day’
individualised 10-year risk of CVD could be estimated by examining CVD incidence in other non-smoking men of a similar age, also living in London. But then again, other features could equally chosen: perhaps ethnicity, physical fitness, family history, or occupation among many others. Populations with different combinations of these features would result in different risk estimates. This has been demonstrated empirically in CVD: evaluations of different risk algorithms on the same patients have found substantial differences in groups identified as high risk.\(^{117,261}\)

This causes a philosophical problem for the interpretation of population probabilities for individuals, since risk estimates are highly dependent on the reference class chosen.\(^{262}\) The IPDAS group advise that the reference class is communicated clearly in all risk presentations.\(^{194}\) Following this advice ensures transparency. However, the choice of which features to include in the reference class is not considered in the IPDAS guidelines, and there is a lack of research on this issue in general.

Unanswered questions include how the reference class should be chosen; which characteristics of the reference class are most important to patients; and the use of different reference classes in decision aids affects whether patients judge risks to be relevant, understandability, decision quality, and outcomes. Ultimately, no two people are exactly alike, and the point at which a reference population is judged similar enough is a key question to be answered.\(^{231,260}\)

**Individualised estimates of adverse effect risk**

For some key adverse effects of CVD, efforts have been made to individualise risk. Marcucci & Sinclair have proposed a method for individualising risks of benefits and adverse effects from medication.\(^{263}\) Their model relies on individual baseline risks of harm derived from clinical prediction rules.

Hippisley-Cox et al. created an algorithm to estimate an individuals risk of myopathy, renal failure, and cataract from statin treatment;\(^{264}\) and the HAS-BLED score provides a simple clinical rule to identify people at high risk of bleeding from warfarin.\(^{96}\)

Nonetheless, as discussed earlier, estimates of individual baseline risks and relative risks of adverse effects with treatment are typically difficult to obtain; adverse effect
If you take warfarin, 1 tablet a day, with weekly blood checks to guide the dose, your risk for stroke in the first year will decrease from 6% (6 in 100) to 2.3% (about 2 in 100). Half of strokes caused by atrial fibrillation will be “major”, resulting in permanent disability, and half will be “minor”, allowing the person to function independently. The anticoagulant will also increase your risk for major bleeding from 1% to 8%. If you take aspirin, 1 tablet a day, instead of warfarin, you will have no need for blood tests to monitor the dose concentration and your risk for stroke will decrease from 6% to 4.7%, without an appreciable increase in your risk for major bleeding. By major bleeding, we mean the loss of at least 2 units of blood in 7 days or any life threatening bleeding.

Box 2.1: Example of patient information from the updated EBM framework reproduced from Haynes, Devereaux & Guyatt270 with permission

calculations therefore typically make a simplifying assumption of a constant absolute risk of medication adverse effect in all populations.265

2.3.7 Uncertainty

Although scientific uncertainty is present in all estimates of treatment effects, studies have found that it is rarely communicated to patients in practice.28 However, to date, there is a lack of research into how best to communicate uncertainty and confidence intervals in risk presentations for patients.28,191,266

A study of 75 women receiving information about breast cancer treatment found that including information about uncertainty reduced satisfaction with decisions.267 Additionally, a survey of 1500 primary care doctors found widespread concern that patients are less likely to choose a course of action if information on uncertainty is presented to them.268 These doctors were more likely to think that the doctor should make the decision on the patient’s behalf if there were substantial uncertainty about the research evidence.

The update of the Evidence Based Medicine (EBM) framework paper by Haynes et al. provides an unintended illustration of this problem in their example decision aid (DA), which aims to demonstrate how evidence can be shared with patients deciding about using anticoagulation for AF (see Box 2.1 on Page 64).

1The EBM framework will be discussed in depth in the next Chapter.
Here, a reduction in stroke risk with aspirin is presented with high precision (from 6% to 4.7%). However, subsequent evidence-based guidelines no longer recommend the use of aspirin in any circumstances.\textsuperscript{271,272} The reasons for the change include a more rigorous evaluation of the quality of trials done comparing aspirin with placebo, analysis of additional outcomes, and subsequent trials providing robust evidence of the superiority of anticoagulation.\textsuperscript{271} In fact, the evidence available at the time the EBM framework was written was already equivocal on the matter; more than a quarter of trial participants had existing vascular disease\textsuperscript{95} (compared with the hypothetical patient to whom the information was targeted, who did not), and when the participants of the same trials without existing vascular disease were analysed separately there was no longer a significant reduction in stroke.\textsuperscript{273} Had the EBM group’s example included information about some of the uncertainties about the evidence, the possibility of aspirin having no important effect would not have been surprising.

2.3.8 Sharing decisions with patients—consultation style and decision aids

There is surprisingly little empirical research examining the effects of changing consulting style to share decisions with patients (as opposed to using an intervention such as a decision aid), and that which does exist has not provided strong evidence to support the practice. A 2015 systematic review by Shay & Lafata sought studies of any quantitative design assessing the effects of sharing decisions on patient outcomes. The review found 39 studies, all of which were observational in design, and small to moderate in size (median sample size 189.5, interquartile range 89–635.5); 33 (85%) used patient surveys to determine the degree to which decisions were shared in the consultation. The review authors classified the key outcomes as ‘affective-cognitive’ (e.g. patient satisfaction, and patient trust in the physician), behavioural (e.g. decisions made), and health (e.g. change in blood pressure). Overall, 44% of the studies found that SDM led to a positive change in outcomes; 56% found no significant difference. The review authors found that a positive effect was most likely in the ‘affective-cognitive’ outcomes (54% of study analyses), but least likely in health outcomes. One additional RCT conducted in South London randomised 359 patients to receive a consultation in either a ‘directed’ or ‘shared’
style, by the same GP. It found that the ‘shared’ style led to reduced patient satisfaction in all categories measured compared with the ‘directed’ style.275

Some further evidence is provided by a 2012 Cochrane review by Dwamena et al., which examined evidence on the effects of interventions to encourage patient centred care; defined by the authors here as being care where shared treatment decision-making occurs.276 The review included 43 RCTs, most of which assessed interventions targeted at primary care clinicians. Though these interventions generally improved process outcomes (i.e. patient-centred behaviours did occur in the consultations) and patient satisfaction, the trials reported mixed effects on behavioural and health outcomes (a meta-analysis of these outcomes across all trials was not possible due to heterogeneity of the outcome assessment measures assessed).

Decision aids (DAs) are tools typically designed to be used in a clinician/patient consultation which aim to increase patient participation in decision making.277 The IPDAS group have proposed a standardised development process and content for these tools.18 The group recommend that tools describe the decision to be made, provide education about the options available (including the option of no treatment) together with the type and likelihood of associated benefits and harms, and solicit patients preferences and values. IPDAS-style DAs typically comprise an educational component, worksheets with lists of questions, and statistical information presented as numbers and charts, often presented in the form of a booklet.18

In contrast to the research reviewed above examining changes in consulting style (which has comprised generally small studies, of low quality, and with inconsistent results), substantial RCT evidence exists on the effects of DAs. These trials have have been included in a Cochrane systematic review published in 2014 (search date June 2012), which examined DAs in a range of conditions.16 The review included 115 RCTs which compared DAs about any medical condition to usual care, standard information provision, or simple DAs. It found that DAs significantly improved patient knowledge compared with usual care (5105 participants from 26 RCTs analysed; increase of 13.3 on a 100 point scale, 95% CI 11.2 to 15.5). The review found that DAs significantly reduced Decisional Conflict (see Box 7.1 on page 165); 3960 participants from 19 RCTs analysed;
reduction of 5.7 on a 100 point scale, 95% CI 3.6 to 7.7). It also found some evidence that DAs changed patient decisions compared with usual care, with DAs leading to significantly fewer people choosing invasive surgery instead of conservative management (2507 participants from 11 RCTs analysed; RR 0.80, 95% CI 0.64 to 1.00), and significantly fewer people taking up screening for prostate cancer (2690 participants from 7 RCTs; RR 0.85, 95% CI 0.74 to 0.98).

This review concluded that DAs did not have any substantial effect on health outcomes (from 9 RCTs which measured various outcomes including quality of life, back pain, and urinary symptoms). The review was not able to determine the effects DAs on adherence to medication, patient litigation, or cost-effectiveness, since included trials did not report these outcomes with sufficient robustness. Authors of several of the included studies expressed concerns that DAs may have a negative effect on the doctor-patient relationship, but none of the included studies attempted to measure this. The review authors also note that a change in outcome is not essential for DAs to be useful. They argue that since DAs are used most frequently where there is no obvious best decision, it is more important to assess whether patients experience or avoid the outcomes they prefer. None of the included studies assessed this outcome.

A subsequent systematic review by Durand et al. (search date 2012) examined the same question focussing on disadvantaged groups, which they defined as socio-economically disadvantaged, ethnic minority populations, low education or literacy, or conducted in a geographical area thought to be disadvantaged. The review found that SDM interventions improved knowledge and informed choice and reduced Decisional Conflict in this group, but found no evidence of the effect on adherence, or health outcomes.

### 2.3.9 Decision aids in cardiovascular disease prevention

Six DAs about CVD prevention specifically have been evaluated in RCTs. The contents of these DAs, and the trial results are summarised in Table 2.4 on Page 69. Four of the RCTs examined DAs for drug or lifestyle treatment of hypertension and high cholesterol; two examined antithrombotic treatment for stroke prevention in AF. Three of the DAs are freely available on the internet, two DAs are not currently available at all, one
additional DA was available by emailing the author (who noted in his email reply that the decision aid was now out of date). Two of the DAs were designed as paper booklets, the remaining four were designed to be used interactively and were computer-based.
Table 2.4: Decision aids for CVD prevention; summary of RCTs. Notes: A. not available from internet search and no response from author. B. author responded saying no longer being made available since outdated

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<thead>
<tr>
<th>Author/Year</th>
<th>Decision</th>
<th>Description of decision aid</th>
<th>Trial results</th>
<th>Is decision aid obtainable?</th>
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<tr>
<td>Lalonde 2006&lt;sup&gt;279&lt;/sup&gt;</td>
<td>26 people considering lifestyle change or drug treatment for CVD prevention</td>
<td>‘Making Choices’: 50 page educational booklet; educational information about seriousness of stroke and MI, risk factors (including lipid profiles, blood pressure, and lifestyle), and effects of interventions to reduce risk. Contains personalised page, where estimates of baseline CVD risk, and expected changes with intervention given.</td>
<td>No significant difference between decision aid and control (a personalised risk profile with description of levels of individual risk factors, but no global CVD risk presentation) in knowledge about CVD, or in perceived risk of CVD</td>
<td>yes, PDF available from study website</td>
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<td>Man-Son-Hing 1999&lt;sup&gt;280&lt;/sup&gt;, and McAllister 2005&lt;sup&gt;281&lt;/sup&gt;</td>
<td>287 people with AF considering change from aspirin to warfarin for stroke prevention (Study A); and 434 people considering anticoagulation for AF for stroke prevention (Study B)</td>
<td>29 page educational booklet plus accompanying audio cassette; educational information about consequences of different types of stroke; details about blood test monitoring for those who use warfarin. Non-individualised probabilities of stroke and major haemorrhage with warfarin and aspirin presented as natural frequencies and ‘smiley face’ chart</td>
<td>Study A: No significant difference in Decisional Conflict scores or adherence to chosen treatment between decision aid and usual care; Study B: No significant difference in proportion of people receiving appropriate anticoagulation treatment (according to their stroke risk) at 3 months or 12 months.</td>
<td>yes, booklet available as PDF obtained by emailing the lead author; authors are willing to make audio cassette available also</td>
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<tr>
<td>Author/Year</td>
<td>Decision</td>
<td>Description of decision aid</td>
<td>Trial results</td>
<td>Is decision aid obtainable?</td>
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<td>Mann 2010[^1][^2]</td>
<td>150 people with diabetes considering use of statins for CVD prevention</td>
<td>‘Statin Choice’ decision aid; Web-based risk calculator. Users are asked to input demographic information and levels of risk factors. A personalised estimate of baseline CVD risk, and expected risk with a statin are then presented side-by-side as a percentage, and icon grid. No health education component.</td>
<td>No significant differences between decision aid and no decision aid in Decisional Conflicts scores or accuracy of perceived risk. Authors report significant improvements in secondary analyses with decision aid, with reduced likelihood of risk overestimation and significant improvements in Decisional Conflict sub-scales.</td>
<td>yes, available at study website</td>
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<tr>
<td>Montgomery 2003[^3][^4]</td>
<td>217 people considering drug treatment of hypertension for CVD prevention</td>
<td>Computer-based decision analysis tool. Users are asked to rank various health outcomes</td>
<td>Decision analysis significantly reduced Decisional Conflict scores compared with standard information arms (27.6 v 38.9, P&lt;0.001) No significant difference in treatment decisions made between groups.</td>
<td>no[^5]</td>
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<tr>
<td>Author/Year</td>
<td>Decision</td>
<td>Description of decision aid</td>
<td>Trial results</td>
<td>Is decision aid obtainable?</td>
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<td>Sheridan 2006</td>
<td>75 (Study A) and 87 (Study B) people considering lifestyle change and drug treatment for CVD prevention</td>
<td>'Heart-to-heart', web-based decision aid; Users are asked to input demographic information and levels of risk factors. A personalised estimate of baseline CVD risk, and expected reduction with aspirin, hypertension treatment, or statin (and user-selected combinations of these) are presented as a percentage, and graphically as a 'risk thermometer'. No health education component.</td>
<td>Study A: No significant differences in proportion who discussed CHD with their doctors, or had a specific plan to address CHD between decision aid and usual care. Study B: No significant difference in 10-year CHD risk estimates (absolute reduction with decision aid: −1.3%, 95% CI −3.0% to +0.40%). When adjusted for baseline CHD risk and education level, decision aids resulted in small significant improvement in 10-year CHD risk estimates with decision aid (−1.1%, 95% CI −2.0% to −0.16%)</td>
<td>yes, available at study website</td>
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<tr>
<td>Thomson 2007</td>
<td>109 people considering warfarin or aspirin treatment for AF</td>
<td>Computer-based decision aid which presented personalised estimates of risks of benefit and harm from warfarin and aspirin as a icon array. The control group received a firm decision/recommendation from a doctor based on a decision analysis tool.</td>
<td>The decision aid significantly reduced Decisional Conflict Scores compared with control: mean difference 20.2, 95% CI 20.3 to 20.0. The subgroup of 32 people not already on warfarin were significantly less likely to choose it with the decision aid compared with control (4/16 [25%] v 15/16 [94%], RR 0.27, 95% CI 0.11 to 0.63).</td>
<td>no8</td>
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The trials measured a variety of outcomes, including adherence to treatment, knowledge about CVD, patient perception of their own CVD risk estimate, and patient satisfaction with decisions (using the Decisional Conflict score). These trials mostly showed that DAS were not effective. One RCT (by Lalonde) found that the DA did not improve patient knowledge about CVD. Three RCTs (those by Lalonde, Mann, and Sheridan) assessed patient perception of their own CVD risk, and all found no difference between DAS and control. Two RCTs (those by Man-Son-Hing and Montgomery) found no difference in decisions made between DAS and control. There was some conflicting evidence about the effects on satisfaction with decision-making. Two RCTs (those by Man-Son-Hing and Mann) found no significant improvements in Decisional Conflict with DAS. However, two RCTs (those by Montgomery and Thomson) did find that DAS significantly improved Decisional Conflict (scores out of 100 reduced by approximately 11 and 20 points respectively). It may be that the inconsistent improvements in Decisional Conflict were due to differences in the settings or interventions between the trials (trials evaluated included decisions around starting anticoagulation, antihypertensives, and statins; and the content and format of decision aids varied widely between trials).

2.3.10 Assessing information needs for decision making

In their 2012 evidence review, the IPDAS group did not find strong evidence about how patients’ information needs should be sought; but did highlight two qualitative studies demonstrating that patients with cancer had very different information needs than their doctors expected. The group recommended further research be conducted in this area, and provided some examples of good practice for decision aids about breast cancer, prostate cancer, and hormone replacement therapy, in which qualitative studies were used to identify patient information needs. One decision aid (for patients with diabetes considering whether to take statins) used clinical and non-clinical observers who sat in with patients with diabetes and their doctors during consultations.

The IPDAS group developed a tool for assessing the quality of decision aids. The tool assesses 45 criteria in 10 domains, and three of these criteria are related to patient involvement in the tool development (see Box 2.2).
• The development process included finding out what clients or patients need to prepare them to discuss a specific decision (criterion 1)

• The development process included expert review by clients/patients not involved in producing the decision support technology (criterion 3)

• The decision support technology was field tested with patients who were facing the decision. (criterion 5)

**Box 2.2:** Quality criteria in the IPDASi guidelines for patient involvement in the production of decision aids

The criteria in box 2.2 are binary; a decision aid which had limited patient involvement would score equally to one which used a more rigorous process involving formal qualitative research. They also make up a small part of the total quality score, accounting for three of 47 total points.\(^1\)

Reviews of decision aids have found low patient involvement in development and testing. Of the 84 decision aids included in the Cochrane review, less than half were field tested with patients; and trial reports frequently did not report the development process clearly.\(^2\)

### 2.3.11 Development process of decision aids for cardiovascular disease prevention

This section focuses on the content and development of CVD decision aids in more depth, together with an assessment of the quality of patient involvement using the domains of the IPDAS tool. These are presented in Table 2.5 on Page 77. Since many decision aids have not been evaluated in RCTs, the list of decision aids identified in the previous chapter have been augmented by an internet search.\(^2\)

Twelve decision aids were identified, comprising five focusing on high cholesterol, two on hypertension, two on atrial fibrillation, and three on multiple risk factor management. At least some information on their development and editorial processes was available for all the decision aids. Nine decision aids were interactive and computer-based (8

---

\(^1\)The 47 quality points are scaled to give a final score out of 100.

\(^2\)List collated from PubMed search using terms 'decision aid' AND hypertension, combined with a review of included studies in the Cochrane Systematic Review of decision aids by Stacey et al.\(^1\), and web searches using Google and Google Scholar all conducted August 5th, 2014. Decision aids which are not longer available were not included.
websites, 1 downloadable software). The remaining three were paper-based, and ranged in length from 1 to 33 pages.

Many of these decision aids had similar content types. All twelve presented some form of risk information about the expected effects of treatment options, and ten of the twelve contained educational information about the condition and treatment options. The educational components covered common themes: simple explanations of the physiology of risk factors, and the mechanism of CVD causation; description of types of CVD and their effects; and explanations of what each treatment option entails, particular around how medications are taken, and specific steps which would need to be taken to improve diet, or increase physical activity.

A variety of methods were used to communicate risk information, including percentages, natural frequencies, icon arrays, and imprecise verbal descriptions such as ‘may lower the risk of...’. Risks were communicated variously as absolute risk reductions, and relative risk reductions, and using time-frames of 1 year, 3 years, 5 years, and 10 years.

Risk was communicated inconsistently within most of the DAS; there was often an imbalance between drug and non-drug interventions. None of the six DAS which included a lifestyle change option reported any associated statistical information, whereas five of these six included detailed statistical information about the drug option.

Notably, there was limited patient involvement in the development most of the DAS. None of the DAS explicitly reported whether they investigated patient information needs (IPDAS criterion 1) during the development process (the Statin Choice aid described that observations of consultations, in which patients had limited say in decisions, provided motivation for making a decision aid, but did not directly inform the contents). Four of the twelve DAS had patient representation in the author group, so might have met the criteria; the remaining eight were authored by health professionals without patient involvement in the development process. When included, patient representatives all had a high level of expertise, and included those affiliated at a high level with CVD charities, and a lay member of a CVD guideline committee.

One of the twelve DAS (the Statin Choice DA) was reviewed by patients who were not involved in the development process. Four DAS had at least some field-testing with
patients facing the decision (Arriba-Hertz, Lalonde et al., Heart-to-Heart, and Statin Choice), two of which were tested only in the context of an efficacy trial (Arriba-Hertz, and Lalonde et al.). It seems likely that the DAS would have been finalised by this stage. The remaining two DAS (Heart-to-Heart and Statin Choice) were field tested prior to a final evaluation, thus allowing refinement to the intervention based on patient feedback.

2.3.12 Competing motivations

Motivations for sharing risk information may include a desire to ensure patients are well-informed about the benefits and harms of an intervention, but it may be done in an attempt to increase uptake of interventions, particularly in public health. These motivations are not necessarily aligned. An RCT published in 2010 examined the effects of using a video decision aid for people considering having faecal occult blood testing as a screen for bowel cancer. It found that the decision aid significantly increased participant knowledge about the risks of screening, and led to increased satisfaction with the decision made. However, although the decision aid led to more people viewing screening favourably, it paradoxically led to fewer people actually agreeing to have screening. This aligns with the findings of the Cochrane review of DAS, which found DAS significantly reduced the uptake of screening for several conditions.

This led Bekker to criticise SDM as harmful and misleading in these circumstances, giving too much space to discussion of potential harms, and leading patients to spend more time thinking about the process of doing the test which many found distasteful. Bekker argued that clinicians should adopt informed uptake, where communication tools are designed to increase uptake and adherence to treatments. This tension exists particularly strongly in cardiovascular disease, where there is a strong public health motivation to increase uptake of prevention.

This is illustrated further by the contents of the decision aid by Sheridan et al., which includes both elements aimed at helping patients articulate their preferences, but appears to favour CVD risk reduction. Participants who decide not to act are presented with further information aimed at convincing them otherwise; one example is given in Box 2.3. In this example, patients who felt lifestyle change would spoil their enjoyment
Many people think that taking a medicine or stopping smoking would limit their enjoyment of life. These people often don’t consider how much their enjoyment would be reduced if they had a heart attack.

Box 2.3: Decision aids which promote a particular option: Text given by the Heart-to-heart decision aid\textsuperscript{297} to patients who choose \textit{Intervening will reduce my enjoyment in life} as a reason for not proceeding with CVD risk reduction of life are encouraged to choose medication or smoking cessation nonetheless.

This aligns with the practice of UK GPs interviewed in a qualitative study, which found that many adjusted their style of communicating risk in order to encourage behaviour change.\textsuperscript{298} GPs who considered their patient to be unmotivated, or at high risk would focus the discussion on the high baseline absolute risk estimate, using this as a ‘scare tactic’. GPs who felt their patient was at low risk and motivated would reassure, and emphasise the risk reductions expected with action. Similar clinicians behaviours were seen in the RCT evaluating the Statin Choice decision aid. This trial had an associated observational study which analysed video recordings of the interactions of a small sample of the study clinicians (n = 6) with their patients.\textsuperscript{299} Important problems were noted in 8 out of 22 clinical encounters in how the clinician communicated risk, including non-use of the decision aid at all, providing inaccurate information about the benefits and harms of statins, and advising that patients with diabetes should take a statin.

Improving shared-decision making and risk communication may either reduce CVD rates, or discourage use of primary prevention and increase CVD. This will be examined further in the systematic review presented in Chapter 7.
Table 2.5: Development of decision aids for CVD prevention; IPADSi refers to the International Patient Decision Aids Standards instrument, see Box 2.2 on Page 73 for definitions of criteria; Notes: A. not explicitly stated, but had at least some patient representation on development group; B was field tested as a final evaluation, appears patient feedback did not lead to further changes of decision aid

<table>
<thead>
<tr>
<th>Decision aid</th>
<th>Content overview</th>
<th>Risk information</th>
<th>RCT?</th>
<th>IPDASi1</th>
<th>IPDASi3</th>
<th>IPDASi5</th>
<th>Patient involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>OptionGrid</td>
<td>1 page decision aid, brief explanation of what is involved in having a Mediterranean diet, physical activity, and statin medication. Information on risk of heart attack, stroke, other health problems, and adverse effects.</td>
<td>Mixture of textual risk formats, including relative risk reductions, e.g. 'reduce the risk...by 25 to 30%'. Other outcome risks described narratively, e.g. 'are less common'. Some outcomes with no risk information, e.g. 'helps prevent diabetes'. No time-frames presented.</td>
<td>no</td>
<td>yesA</td>
<td>no</td>
<td>no</td>
<td>Two of the authors were patient representatives</td>
</tr>
<tr>
<td>NHS Patient Decision Aid: High blood pressure</td>
<td>Interactive website. Explanation of hypertension pathophysiology, risk factors, monitoring, and prevalence. Options of no treatment, lifestyle change, and medication presented. Optional 'values clarification' Likert scales.</td>
<td>Mixture of textual risk formats. Medication effects described as natural frequencies out of 1000 over 5 years. No risk information presented for non medication options; authors state that no studies have examined these.</td>
<td>no</td>
<td>yesA</td>
<td>no</td>
<td>no</td>
<td>One of authors was a patient representative</td>
</tr>
<tr>
<td>NHS Patient Decision Aid: Atrial fibrillation</td>
<td>Interactive website. Explanation of normal heart function, AF pathophysiology, symptoms, explanation of stroke, CHADS2 score. Options of anticoagulation, no treatment, and surgery presented. Optional 'values clarification' Likert scales.</td>
<td>Natural frequencies out of 1000. Ranges given to indicate confidence, e.g. 'between 40 and 80 people in every 1,000'. Variable time-frames given, and also as ranges, e.g. 'from 3–5 years'</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>No patient involvement</td>
</tr>
<tr>
<td>Decision aid</td>
<td>Content overview</td>
<td>Risk information</td>
<td>RCT?</td>
<td>IPDASI1</td>
<td>IPDASI3</td>
<td>IPDASI5</td>
<td>Patient involvement</td>
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<tr>
<td>NHS Patient Decision Aid: High Cholesterol</td>
<td>Interactive website. Description of atherosclerosis, difference between HDL and LDL, lifestyle and genetic causes, interpreting cholesterol test results, and prevalence. Options of no treatment, lifestyle change, medication, and food supplements described.</td>
<td>Medication effects reported as natural frequencies out of 1000. No non-medication numerical risks presented; either given narratively as ‘is likely to lower the risk’, in other cases authors state that no studies have examined the effects. Variable time-frames given, and also as ranges, e.g. ‘from 3–5 years’</td>
<td>no</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>One of authors was a patient representative</td>
</tr>
<tr>
<td>NICE Lipid management</td>
<td>23 page booklet; explanation of CVD and motivation for using statins, description of lifestyle measures; presentation of likelihood of CVD reduction and adverse effects of statins versus no treatment</td>
<td>Effects of statins versus no treatment presented as natural frequencies, bar charts, and faces icon arrays, all out of 100 people over 10 years. No risks presented for non-drug intervention.</td>
<td>no</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>Patient trustee of cholesterol charity and patient member of the guideline development group included on panel.</td>
</tr>
<tr>
<td>NICE Atrial Fibrillation</td>
<td>36 page booklet; education about what AF and stroke are, explanation about haemorrhage. Options of no treatment, warfarin, and novel anticoagulants (NOACs) described.</td>
<td>Effects of anticoagulants and NOACs presented as natural frequencies, bar charts, and faces icon arrays, all out of 1000 people over 1 year.</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>States ‘overseen by expert steering group including…patient representatives’. However all named steering group members are health professionals or charity directors.</td>
</tr>
<tr>
<td>Decision aid</td>
<td>Content overview</td>
<td>Risk information</td>
<td>RCT?</td>
<td>IPDASI1</td>
<td>IPDASI3</td>
<td>IPDASI5</td>
<td>Patient involvement</td>
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</tr>
<tr>
<td>Healthwise</td>
<td>Website with hypertension education, and interactive sliders to solicit patient attitudes. Options given are medication, or making lifestyle changes first; no treatment not given as an option</td>
<td>Risk information is imprecise, e.g. ‘medicines...lower your risk of heart attack and stroke.’</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>Includes four ‘personal stories’ described as ‘based on information gathered from health professionals and consumers.’</td>
</tr>
<tr>
<td>Healthwise</td>
<td>Website with cholesterol education, and interactive sliders to solicit patient attitudes. Options given are taking statin, or not taking statin</td>
<td>Risk information is imprecise, e.g. ‘Statins can lower the risk of heart attack and stroke’</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>Includes four ‘personal stories’ described as ‘based on information gathered from health professionals and consumers.’</td>
</tr>
<tr>
<td>Arriba-Herz</td>
<td>Computer based tool which generates charts displaying estimates of CVD risk, and estimates of the effects of various interventions. No background/educational material</td>
<td>Faces icon array out of 100 with percentage risk, both over 10 years</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>yes&lt;sup&gt;B&lt;/sup&gt;</td>
<td>No patient involvement</td>
</tr>
<tr>
<td>Lalonde et al</td>
<td>50 page booklet and personal worksheet; includes education about hypertension and lifestyle changes to reduce risk factors; options given for modifying each individual CVD risk factor, worksheet allows patients to make a personal plan</td>
<td>Faces icon array and natural frequencies, both over 10 years. Booklet in which health care provider calculates personalised estimates of the effects of a wide range of lifestyle and medication options.</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>yes&lt;sup&gt;B&lt;/sup&gt;</td>
<td>Pilot tested with 16 patients with hypertension and dyslipidaemia after creation</td>
</tr>
<tr>
<td>Decision aid</td>
<td>Content overview</td>
<td>Risk information</td>
<td>RCT?</td>
<td>IPDAS1</td>
<td>IPDAS3</td>
<td>IPDAS5</td>
<td>Patient involvement</td>
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</tr>
<tr>
<td>Heart-to-Heart</td>
<td>Computer based tool; includes providing personalised 10 year CVD risk estimate, education around CVD risk factors and reducing them with smoking cessation, aspirin, cholesterol and hypertension medication; coaching element to encourage effective consultation with clinician</td>
<td>Personalised CVD risk presented as percentage and as ‘risk thermometer’, both over 10 years. Static information on benefits of interventions presented as relative risk reductions, some with ranges (e.g. 20–25%).</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>yes</td>
<td>After initial development made available to ‘physicians and patients’ for feedback. Complex medical terminology simplified as a result.</td>
</tr>
<tr>
<td>Statin Choice</td>
<td>Web-based risk calculator; no educational information, baseline CVD risk and benefit from statin presented</td>
<td>Statin benefits presented as natural frequencies and icon array, both out of 100. Information on adverse effects presented as frequencies only, either out of 100 for frequent, or 20,000 for rare outcomes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>Need for decision aid determined by analysing observations of clinical encounters; Decision aid refined following feedback from patients and clinicians.</td>
</tr>
</tbody>
</table>
2.4 Conclusions

Though a large evidence base describing the effects of CVD prevention strategies exists, several areas of scientific uncertainty remain. Established methodologies exist to estimate the CVD risk of an individual, and provide a personalised estimate of their likelihood of benefit from medication using data from RCTs. However, the evidence supporting lifestyle change is largely observational in nature, and there are a lack of proven interventions in this area. The evidence describing adverse effects of medication typically comes from non-randomized studies and informal reporting by clinicians. These lower qualities of evidence are more difficult to translate into personalised estimates of risk.

To date, the evidence of the effects of SDM comes principally from RCTs of DAs, which have found improvements in patient satisfaction with decisions made, and that in many areas DAs lead to changes in the decision made, often towards a less intense or conservative intervention. However, the evidence in CVD specifically is less strong, with most RCTs finding no benefit of SDM. Similarly RCTs of education (which in these trials typically involved a biomedical explanation of hypertension plus emphasising the importance of medication taking) have not provided evidence of improvements in knowledge or adherence. Likewise, although an extensive psychological literature exists around the optimal methods to communicate risk (which favours the absolute risk, presented as natural frequencies, percentages, and icon array charts), recent reviews have found insufficient evidence to recommend a method for communicating CVD risk.
3

Theoretical framework: the patient in evidence-based medicine

3.1 Introduction

Shared decision making (SDM) is defined as the process of patients and clinicians making decisions collaboratively, taking into account the best available research evidence, as well as the patient’s values and preferences. This chapter examines SDM from a critical perspective, arguing that despite SDM being well motivated, interventions to date have had insufficient patient input into their development. This has led patients being presented with simplified versions of the type of information which might be found in a medical text book. By contrast, qualitative research has demonstrated that patient understandings of their illness (known as explanatory models) often differ widely to those of their doctors; this mismatch is a frequent cause of failed communication and unmet
patient expectations. I conclude that incorporating research findings from both quantitative and qualitative studies (known as a mixed-methods approach) in the development of 
SDM interventions would help to address these deficiencies.

3.2 History of, and motivation for, evidence-based medicine

For centuries, medical training was based on the basic sciences of biology, anatomy, and physiology, but the science of clinical epidemiology was not commonplace until the mid-1900s. A book published by French physician Pierre Louis in 1835 is widely cited as one of the first recorded examples of clinical epidemiology. Louis analysed a case series of patients he saw with pneumonia, and determined that blood-letting, a treatment recommended by contemporary experts, had no effect on recovery.

In 1937, the epidemiologist Bradford Hill described frequently-made errors in interpreting statistical data from health research. Bradford Hill argued the measurements of the effects of treatments in clinical trials were often biased due to systematic differences in baseline characteristics between groups. He proposed randomising participants to receive the test intervention or a control to overcome this problem. An additional benefit of randomisation was that it prevented triallists from consciously or subconsciously influencing the allocation participants to intervention or control groups: an important source of bias.

Bradford Hill was part of the Medical Research Council (UK) (MRC) team who in 1948 published the first-ever report of a randomised controlled trial in health, evaluating the use of streptomycin in tuberculosis. The trial was small (102 participants; streptomycin was scarce, and the researchers were not able to obtain enough for a larger trial) but found that streptomycin reduced death compared with control. Streptomycin gradually displaced bedrest, and other commonly used treatments which lacked robust evidence including vitamins, and surgical collapse of the lung.

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¹A term first used by Paul in 1938, who described a desire to bring a individual patient focus to epidemiology, which he felt overly favoured laboratory and large population based studies. Last later defined it more precisely as the process of "consider[ing] the facts derived from population-based studies of clinical conditions before deciding what to do about individual patients."

²Work on an RCT examining the effect of vaccination against whooping cough, also by the MRC team including Bradford Hill, started before the streptomycin trial but was published later, in 1951.
By 1955, 347 RCTs had been published. In 1972, Cochrane published *Effectiveness and efficiency: random reflections on health services*, a key text which expounded what would be the key motivations of the EBM movement. Cochrane argued that the evidence supporting most medical practice was flawed, contending that most decision-making was still based on the personal experience of clinicians or observational data. Cochrane argued that RCTs were the most reliable form of evidence for making health decisions. Cochrane contended that since most treatments were used without robust evaluations, patients were likely being subjected to very many ineffective, or harmful treatments.

In one example, Cochrane described how hypertension treatment was largely based on observational evidence that raised blood pressure was associated with increased mortality; however, it was not clear at the time whether reducing blood pressure with medication would be effective or indeed harmful. At the time, there were only a small number of RCTs which were conducted in the limited population of men aged between 45 and 70 who presented to hospital with severe symptoms relating to hypertension. Cochrane argued that these trials were not in populations representative of the bulk of people with hypertension, and that high-quality RCT evidence was needed to guide hypertension treatment.

RCT methodology has frequently illuminated areas where expert opinion based on observational research and basic sciences was wrong; prominent examples are shown in Table 3.1. Notably, in several of these examples, treatments recommended by contemporary experts and in widespread use were later proven to be ineffective or harmful.

<table>
<thead>
<tr>
<th>treatment</th>
<th>rationale for using/not using</th>
<th>findings of higher quality research</th>
</tr>
</thead>
<tbody>
<tr>
<td>doxazosin</td>
<td>reduces blood pressure in hypertension</td>
<td>found to increase mortality in black ethnic groups</td>
</tr>
<tr>
<td>lidocaine</td>
<td>prevents arrhythmia after myocardial infarction</td>
<td>found to increase mortality</td>
</tr>
<tr>
<td>arthroscopic surgery for knee osteoarthritis</td>
<td>improved appearance of cartilage after debride-ment</td>
<td>no improvement in function or symptoms at 1 year</td>
</tr>
</tbody>
</table>

*Table 3.1:* Changes in practice due to Evidence Based Medicine: examples of where expert opinion has been found incorrect by high quality research evidence; adapted from Ebell *et al.* with permission.
beta-blockers believed to reduce cardiac output in heart failure found to reduce mortality

vitamin E in heart disease reduces levels of free radicals no effect on any clinical outcome

hormone replacement therapy improves lipid profile no change in cvd mortality, and increase in cvd events in women aged > 60

3.2.1 The Evidence Based Medicine framework

The first version of the Evidence Based Medicine (EBM) framework was published in 1992, and described a framework for integrating the results from the best available clinical research in practice. In an early editorial, EBM was been defined as ‘a process of turning clinical problems into questions and then systematically locating, appraising, and using contemporaneous research findings as the basis for clinical decisions.’ The original EBM model described five steps for integrating evidence into practice, which are shown in Box 3.1.

1. Convert these information needs into answerable questions
2. Track down, with maximum efficiency, the best evidence with which to answer them (and making increasing use of secondary sources of the best evidence)
3. Critically appraise that evidence for its validity (closeness to the truth) and usefulness (clinical applicability)
4. Integrate the appraisal with clinical expertise and apply the results in clinical practice
5. Evaluate one’s own performance

Box 3.1: Five steps for practising evidence-based medicine, from the original model, reproduced from Sackett.

The EBM framework recommended that clinicians should develop the skills to consult and critically appraise original research as the primary basis for decision-making. The EBM framework called for the use of highest quality of evidence, and following the
work by Bradford Hill, identified RCTs as the gold standard test for evaluating the effects of interventions. Systematic reviews, which synthesised data from all available RCTs for a particular clinical question, therefore comprised the highest quality of evidence (see Figure 3.1 on Page 86).

Figure 3.1: Hierarchy of evidence quality; reproduced from Akobeng.

The authors provided an example of “the way of the future” describing a clinician discussion with a patient after a first seizure who wanted to know the risk of a future seizure. In this example, rather than relying on experience, the clinician conducted a computer database search for literature, critically appraised the most likely paper, and was able to provide a reasonably precise estimate (which was between 43% and 51% by 1 year).

The EBM framework emphasised the teaching of search and critical appraisal skills, and the availability of time and resources to search MEDLINE. Though the framework does not provide practical guidance on how clinicians should incorporate the EBM steps into their daily work, the authors themselves (who were hospital physicians) included a copy of key research papers in patient records, and discussed these regularly at ward rounds. Later, they developed an ‘evidence cart’: a trolley taken on ward rounds which contained evidence-based text books, a computer and CD-ROMs of evidence synopses and databases (including the Cochrane Library, the JAMA Rational Clinical Examination series, and MEDLINE). Staff on the ward round were encouraged
to ask one or two answerable questions for each patient, and answers sought while at the bedside. Using ward rounds as a platform for the teaching and practice of EBM has been described widely by EBM proponents.316,322,323

3.2.2 Evidence Based Medicine as a social movement

Pope has argued that EBM seeded a social movement.302 These are defined by the sociologist Blumer as ‘collective enterprises to establish a new order of life’. Pope describes EBM as a power struggle, where groups of clinicians moved away from a medicine based on tradition and experience, causing conflict with the medical establishment. From this viewpoint EBM was most important as a rallying call for political change, rather than the principles it espoused which had been in existence for many decades.302,324

This is illustrated by Sackett, who as one of the leaders of the EBM group visited a series of hospitals in the UK to spread EBM methods. An important part of these visits was leading a ward round of patients admitted the previous night; young physicians were encouraged to challenge their seniors by demanding empirical evidence for decisions, where previously they might have been expected to defer to their seniors’ experience and expertise.325

Despite the enormous impact of EBM, it has been controversial, and was met (and continues to be met) by substantial criticism. At least some criticism has come from those who were at risk of losing authority or power. The main editorial in the September 1995 issue of the Lancet was titled, “Evidence based medicine, in its place”, and called the EBM group “elitist”.326 The editor appeared particularly offended by the implication that critical appraisal summaries published by the EBM group might be better than the Lancet’s long-established editorial processes. The editorial was highly negative, but other than general attacks on the perceived arrogance of the EBM group, the Lancet had few specific criticisms of the EBM philosophy itself.

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3This term is widely used in the literature on Evidence-Based Medicine, meaning a precise question structured in such a way that an empirical answer might be sought; an example might be: is warfarin effective at reducing stroke in people with atrial fibrillation?
The lack of the patient in Evidence Based Medicine

The original framework described that patients would benefit from having access to treatments which worked, and higher quality of information. However, other than making decisions in physical proximity to the patient (the EBM group aimed to use evidence at the bedside of patients in hospital), the EBM framework does not describe whether patients were in any way actively involved in the process.

The original EBM papers (by the admission of one of the authors) did not contain much reference to patient values; the primary focus was on encouraging change in clinicians’ behaviours and attitudes. Note that none of the key steps described in Box 3.1 referred to patient interaction. The group did call for ‘randomized trials using different strategies for interacting with patients’, but this was not explained in any further detail.

This deficiency was recognised in an update to the framework, published in 2002, which formalised the inclusion of ‘patient preferences and actions’ into EBM. This update aimed to address criticisms that evidence-based medicine promoted a formulaic or rule-book approach to medicine. The updated framework is shown schematically in Figure 3.2 on Page 89. In this model, the clinician’s role is to integrate information about the patient’s clinical circumstances, their values and preferences, and research evidence to inform health decisions.

This updated paper recommended that patient preferences should take precedence over clinician preferences wherever possible. The authors noted that individual patients differed in important ways, including having different access to resources, and different attitudes towards taking medication. They conclude that patients treatment preferences are likely to differ often from what clinicians expect.

The authors provided an example of how patients could be involved in decision making, providing a patient summary of RCTs of warfarin for stroke prevention in people with AF (presented in the previous chapter; in Box 2.1 on Page 64). This example used an approach that the majority of decision aids would later take: using statistical information from clinical trial reports or systematic reviews, adjusting this information to take
Figure 3.2: Schematic showing the updated model for evidence-based decision reproduced from Haynes, Devereaux & Guyatt\textsuperscript{270} with permission
into account an individual patient’s baseline risk, and communicating this information in an easy-to-understand way.

### 3.4 Why involve patients? — the Shared Decision Making movement

Shared decision making (SDM) can be defined as the process of patients and their clinicians discussing evidence about treatment options and coming to a joint decision which takes into account patient preferences. SDM is related to, and a key method for delivering *patient centred care*, which has been defined as care which is ‘responsive to the needs, values, and expressed preferences of each individual patient’.

Although SDM is related to the EBM movement, it has different philosophical underpinnings. The term ‘Shared Decision Making’ was first used by Wennberg as a result of his 1973 research, *the Dartmouth Atlas*, an epidemiological study which aimed to investigate variation in health care provision, uptake, and outcomes across geographic areas in the USA.

The Atlas found unexpectedly large variation in the use of medical interventions: one example being use of tonsillectomy in Vermont children, where although the overall rate was 19%, rates in individual neighbourhoods ranged from 16% to 66%. Similar variation in practice occurred for many operations including cholecystectomy, hysterectomy, and varicose vein surgery. The variation was not explained by differences in patient characteristics, disease severity, or research evidence, leading Wennberg to conclude that idiosyncratic practice by individual clinicians or hospitals was responsible. Wennberg defined *unwanted variation* as “variation in the utilization of health care services that cannot be explained by variation in patient illness or patient preferences”.

Unwanted variation occurred most strongly in conditions where there a range of treatment options with finely balanced benefits and harms, or where there was a lack of professional consensus. Wennberg described these as *preference sensitive decisions*, concluding that these ought to reflect a patient’s individual values and preferences, but were instead being decided by physicians. In 1987, Graboys et al. examined the effect of giving a second opinion to 88 patients whose cardiologists had recommended they have coronary artery bypass surgery. A second cardiologist, after reviewing all
88, gave 77 the option of conservative management. 60 of these patients decided not to have surgery. This early research gave promise that increasing patient involvement in decision making could not only reduce unwanted variation, but also reduce costs, and prevent harm to patients through avoiding interventions which would not lead to the outcomes which were important to them.332

In addition to the motivation to reduce population-wide harm and reduce costs, there are also ethical arguments for SDM. Personal autonomy, the ability of individuals to shape their own lives, is a long-standing tenet of biomedical ethics.338 In 1972, Veatch described the moral difficulties of doctors taking a paternalistic approach, and recommended a ‘contractual’ model, where health decision making is shared in a way which emphasises individual patient values.339

Beauchamp and Childress, in their widely cited book, ‘Principles of Biomedical Ethics’ describe how patient involvement in decision-making is key in preserving autonomy, and define autonomous decisions as ‘those made with substantial understanding and freedom from controlling influences’.340 The authors set out a framework of consent, describing a process involving the disclosure of ‘the nature and purpose..., alternatives, [and] risks and benefits’ of any intervention before its use.340

These ethical imperatives have been codified. In the UK, the General Medical Council’s (GMC) ethical code on consent since 2008 explicitly states that doctors must empower patients to make their own decisions, by communicating the likelihood of benefit and harm from treatments, and how these compare with not treating.341

In January 2009, the UK Government created a NHS constitution, which set out legal rights for NHS patients. This established a right for patients to be involved in healthcare decisions, and obliges clinicians to provide patients with relevant information to help them in decision.342 Similar legal requirements to give patients the information needed to actively participate in health decision making have been enacted in several other countries, including Germany, the Netherlands, and Canada.343–345

Despite strong moral and practical arguments (and legal obligations) for SDM, there is evidence that it is not done widely in practice. The right to be involved in health decisions was enacted in France in 2002, but authors of a 2011 report claimed that no ma-
Robust evaluations of the uptake of SDM making are lacking, but some lower quality evidence suggests that it doesn’t happen in most cases. In a UK telephone survey of 4,733 randomly sampled people, 42% reported that their doctor had involved them at least somewhat in a recent health decision. Multiple expert analyses of large series of recordings of doctor/patient consultations conducted in the US, Spain, and Peru have consistently found very low rates of SDM in practice.

### 3.5 How should decisions be shared in practice

Sharing health decisions has been identified as a difficult task for clinicians. Although DAs have attracted much research attention; comparatively little has been written about how to share decisions in the clinical consultation in practice. For example, Charles et al. reviewed the literature on SDM, and described what they considered to be the critical components:

1. that at least two participants—physician and patient be involved
2. that both parties share information
3. that both parties take steps to build a consensus about the preferred treatment; and
4. that an agreement is reached on the treatment to implement

This description is useful as a conceptual framework, but lacks practical guidance for clinicians on how to accomplish these steps. Elwyn et al. noted this deficiency in 2012, publishing a model for SDM in the consultation. They recommend a three-step process for decision making (see Figure 3.3).

Each of these steps are presented alongside practical examples of questions and prompts to encourage the patient to make a decision based on their own values and preferences. Choice talk (stage 1) describes discussion that there is a choice to make; clinicians might use phrases such as “There is good information about how these treatments differ that I’d like to discuss with you.” During the option talk stage, the model suggests that clinicians describe the available options, alongside statistical information on the benefits
and harms of each. It is at this stage that decision support tools may be used. Finally, \textit{decision talk} describes the stage of eliciting patient values and preferences, and asking if they are ready to decide.

### 3.5.1 Patient explanatory models of illness

The evidence supporting educational interventions and DAs for CVD prevention was reviewed in the previous chapter. The interventions reviewed had much in common. The educational components were typically the sort of information which might be found in a medical textbook targeted at clinicians. Typically this included information on the patho-physiology, prevalence, and health consequences of a risk factor if uncontrolled, albeit using plain language and avoiding medical jargon. Risk information was widely used, but presented inconsistently, often with multiple formats used in the same decision aid.

Patient involvement at all stages of development was limited; none robustly identified what patients facing the decision would want or need to know. Likewise, review and field-testing with patients was extremely limited, with little evidence that this process led to changes in the DA.

Though it is possible that this combination of biomedical education and risk data as presented in these DAs \textit{might} be useful to patients, the empirical evidence reviewed in the last Chapter does not show substantial or consistent improvement in outcomes with this approach. Furthermore, there is substantial social science research indicating that these approaches may be overly simplistic.

Medical anthropology draws a distinction between the concepts of \textit{illness} and \textit{disease}.\textsuperscript{357} Disease may be defined as a pathological abnormality in a body organ or system.
Illness, by contrast, can be defined by the patient’s experience: encompassing pain, distress, and changes in social function.\textsuperscript{358}

In their seminal analysis of studies in medical anthropology, Kleinman \textit{et al.} describe illness and disease as \textit{explanatory models}, being the way in which patients and physicians understand sickness respectively.\textsuperscript{359} The authors described how disease and illness do not have a one-to-one relationship. They note that the same severity of disease may produce vastly differing levels of pain and distress in different individuals, and also that a substantial proportion of healthcare consultations involve pain or distress without a identifiable biological cause.\textsuperscript{359}

The authors argue that understanding disease or illness alone is not sufficient to be able to resolve problems in health care, and that a negotiated, shared understanding of sickness between patients and physicians is essential.\textsuperscript{359} Kleinman \textit{et al.} provide a series of case studies from their anthropological research which demonstrate the point. In one extreme example, physicians were puzzled by the behaviour of a woman with pulmonary oedema, who self-induced vomiting and repeatedly urinated in her bed. When they challenged her, she became angry. The patient later revealed that she was attempting to remove fluid from her lungs; her understanding was that fluid would drain from the lungs through the mouth and the urethra (further reinforced by her doctors’ description of ‘water tablets’ to treat her condition). Once the physicians understood the patient’s explanatory model they were able to address her concerns, and the behaviours which appeared odd to the physicians stopped.

\textbf{3.5.2 Patient explanatory models in cardiovascular disease prevention}

In 1991, Davison \textit{et al.} described their ethnographic research in South Wales which examined perspectives on heart disease in order to improve cardiovascular prevention programmes.\textsuperscript{360,361} The authors collected data from semi-structured interviews with 180 urban and rural residents together with notes from observations and informal interactions. They coined the term \textit{lay epidemiology}, describing lay perspectives on disease causation and risk.\textsuperscript{360}

Many participants had firm ideas about the sort of person likely to develop a heart
attack, described by the authors as *coronary candidates*. This is illustrated by a quote from one participant:\textsuperscript{360}

*Interviewer: And you say that your uncle had a heart attack...*

*Informant: Well, with him, frankly he was a walking heart attack waiting to happen! (laughter)*

People described as coronary candidates had typical features, including being overweight, smokers, red-faced people or people with a grey complexion, those who were unfit, people who eat too much rich food, and people under stress.\textsuperscript{360} Many of the lay ideas of heart disease causation mirrored those found in epidemiological research.\textsuperscript{362}

These findings had several implications for health promotion. First, the authors draw parallels between lay perceptions of risk and Rose’s prevention paradox. Participants perceived that heart disease was highly predictable, and those who did not see themselves as coronary candidates were therefore not motivated to take preventative action.\textsuperscript{360,361} The descriptions of coronary candidates were often caricatures, often those with extremely high weight, or poor fitness. However, as described by Rose, the bulk of disease will occur in those low and moderate levels of risk factors (since they vastly outnumber those at high risk).\textsuperscript{108}

Second, health promotion campaigns tended to involve educating about single risk factors, for example advice to stop smoking, or to lose weight. Davison and colleagues hypothesised that such messages were incorporated into patients’ ideas of a coronary candidate. The authors conclude that this strategy may have unintended negative consequences for health promotion.\textsuperscript{362,363} Those with no experience of \textit{CVD} might be less likely to engage in healthy behaviours, since they did not identify as being a coronary candidate personally. However, \textit{CVD} is common, and statistically more likely to occur in those who do not fit the coronary candidate caricature. The authors suggested that contact with friends or family with \textit{CVD} who did not fit the candidate model might lead to a concept that \textit{CVD} is random, and inherently unpreventable, thus hindering health promotion further.

A qualitative study (61 semi-structured interviews) looking at the lay epidemiology
of heart disease in Glasgow added to these lay models.\textsuperscript{364,365} This study described lay concepts of the impact of family history, and also widespread understanding that heart disease manifests as an instantly fatal heart attack, and was therefore an attractive mode of death compared with other illnesses.\textsuperscript{365}

In their 2001 review, Vermeire and colleagues criticised much research on why patients adhere or don’t adhere to treatment.\textsuperscript{366} They found much adherence research centred on studies of statistical association between patient characteristics and adherence; they found studies of nearly 200 such variables examined in this manner, and few had any important implications for practice (associations between poor adherence and complex, frequent dosing, and high medication cost being the exceptions). They found fault with the theoretical perspectives of such studies, since they assumed that patients passively accepted doctors’ treatment decisions. The implication being that poor adherence was due to patient failings, whether in remembering or knowledge. The review authors hypothesised that patient perspectives on medication taking, and the possibility that patients actively chose not to adhere could be responsible, and recommended the use of qualitative research to take the field forward.\textsuperscript{366}

There is substantial empirical evidence to support this point. More than 30 cross-sectional studies have examined the relationship between knowledge levels and adherence in other medical conditions; the majority of those, which also comprised the highest quality studies, have found no significant association.\textsuperscript{10}

An early qualitative study in this area was conducted by Conrad in 1985.\textsuperscript{367} This paper reported the results of 80 semi-structured interviews with people epilepsy who took anti-convulsant medication. The authors describe participants medication-taking practice as self-regulation, since many self-adjusted the dose depending on side-effects and the frequency of seizures they were experiencing at any particular time. Pound \textit{et al.} conducted a systematic review and meta-ethnography\textsuperscript{1} including 37 qualitative studies (from 1992 to 2001) examining medication adherence in chronic diseases, including four studies in hypertension.\textsuperscript{368} This review found widespread patient concerns about the medicines they were prescribed. Study participants commonly tested out new treat-

\textsuperscript{1}The meta-ethnography method will be described in more detail in Chapter 4 on Page 109
ments, and persisted only if they didn’t notice any adverse effects. Participants widely feared dependence on medicine taking, and had fears of becoming tolerant to them, or addicted. These concerns led many participants to reduce, or stop their medicine altogether. The authors conclude that rather than failings in doctors or health systems (on which much adherence research had focused), much non-adherence was due to patients actively deciding not to take medication.

The effects of hypertension vary in people of different ethnic groups; in particular, black populations in the US and UK have a high prevalence and low control rates.\textsuperscript{369,370} Much research has sought cultural explanations for these differences in hypertension rates and control.\textsuperscript{371} Qualitative studies have found that cultural understandings about hypertension prevalent in ethnic minority populations might explain low rates of treatment use and adherence in these groups; and that immigrant populations continue to use traditional remedies as an alternative to pharmaceutical treatment.\textsuperscript{181,372} US qualitative studies of African Americans have found that many attribute poor hypertension control to racism: both through experiences of racism increasing stress, and feeling unable to trust doctors they feel are prejudiced.\textsuperscript{373–375} The authors of many qualitative studies in ethnic minority populations have concluded that educational interventions should be culturally specific, and take account of traditional beliefs.\textsuperscript{376–378} However, there are other possible explanations for poor blood pressure control in these groups, including genetic predisposition, and ethnic variation in response to medication.\textsuperscript{369} Ethnic minority populations may also be more likely to live in deprived areas, and have poorer access to health care; both of which may further confound apparent ethnic differences.\textsuperscript{379} The importance of cultural beliefs and practices on health behaviours and hence hypertension control compared with these other factors is unclear. This question will be addressed in the systematic review and synthesis of qualitative studies in Chapter 6.

The qualitative studies reviewed above provide evidence that an inadequate understanding of patient perspectives could lead to the failure of health interventions, and have demonstrated this particularly in CVD prevention. The study by Davison and colleagues found that health education campaigns which were insensitive to lay health understandings might have been paradoxically leading people to decide against healthier
lifestyles.

As described previously, the IPDAS guidelines do highlight the use of qualitative research as being good practice; but the group’s quality score (Box 2.2 on Page 73) does not require it. Indeed, decision aids which had a single patient member in the authorship team (as with two of the examples reviewed on Page 77) could meet the quality point, ‘finding out what clients or patients need to prepare them to discuss a specific decision’. This problem was particularly evident in the CVD DAS reviewed, where patient involvement was not well described, and typically involved having a single lay member of the authorship team. In two of the cases, the lay members had roles with CVD organisations, and might be expected to have high levels of medical knowledge in the area. However, such a development process does not seem likely to uncover important information about patient understanding about health. Importantly, a large number of qualitative studies have already been conducted in this area, including those reviewed above and others which will be described in more detail in Chapters 6 and 7. These studies specifically seek to understand patient perspectives on CVD prevention, and the importance they hold for decision making and health behaviours. However, the results of these studies have not been systematically incorporated into the development of existing educational and decision support interventions.

3.5.3 Incorporating qualitative research into the development of decision aids—using a mixed methods approach

The term mixed methods usually describes a process of combining qualitative and quantitative methods to answer a research question\(^1\).\(^{380}\)

Leech & Onwuegbuzie categorised the very wide range of methods for integrating qualitative and quantitative data, based on three key design decisions.\(^{381}\) First, they categorised study designs as ‘partially’ or ‘fully’ mixed; where partially mixed studies conducted the qualitative and quantitative parts of the studies independently in their entirety before integrating the results in the data interpretation part (typically the discussion section). Fully mixed studies would integrate qualitative and quantitative

\(^1\)This is the most common usage of the term, although it may be used to refer to a study design which uses multiple methodologies of any type.
methodologies in multiple parts of the study, for example in the objective setting and data analysis. Second, they describe mixed methods designs as being either sequentially or concurrently in time. Third, they describe that either the qualitative or quantitative parts may be described as dominant, or may have equal status in the study.

This thesis uses the following pragmatic approach. The studies described in Chapters 5, 6, and 8 (the first using a purely quantitative approach, the latter two purely qualitative) were undertaken independently. The main integration of the findings together is in the Discussion (Chapter 9), which aligns with Leech’s ‘partially mixed’ category.

The exception is the systematic review in Chapter 7, which considered both RCT and qualitative data. This was done since a key aim of the chapter is to examine patient perspectives on specific risk communication tools tested in trials, and hence investigate reasons for their success or failure.

The studies in the thesis were conducted concurrently, though this allowed the interview schedule from the qualitative review in Chapter 8 to be informed by initial reading of the papers retrieved from both systematic reviews (Chapters 6 and 7).

The qualitative and quantitative methods will be of roughly equal status, and the Discussion chapter aims to bring together the results of the individual studies, and draw conclusions for best practices for future interventions (Chapter 9).

3.6 Conclusions

Evidence based medicine has revolutionised clinical practice over the past 25 years. Despite the EBM framework emphasising the importance of incorporating patient preferences into health decisions, it did not define methods of doing so. The current state-of-the-art for SDM is the decision aid, which combines health education with an individualised estimate of the probability of good and bad outcome from different treatment options. However, currently available educational interventions and decision aids have had limited or often no patient involvement in their development; RCTS of these interventions have not demonstrated substantial changes in either decision making quality or clinical outcomes.

Kleinman and colleagues described how the failure of physicians to understand pa-
tient explanatory models of illness was an important factor hindering the success of treatments. Davison et al. found that this was particularly true in CVD, where unexpected lay explanations of CVD causation might have contributed to reduced uptake of prevention. Paradoxically, educational campaigns at the time appeared to exacerbate the situation, by caricaturing ‘coronary candidates’ as those with extreme levels of risk factors. A possible contributor to the lack of success of current interventions is their failure to adequately incorporate these patient perspectives. Incorporating both qualitative and quantitative research in the development of SDM interventions is therefore likely to be helpful in overcoming these issues.
This chapter reviews methods for incorporating qualitative research in systematic reviews, and introduces the methods which are used in Chapters 6 and 7.

4.1 Introduction to systematic reviews

Systematic review methodology has been motivated by the deficiencies in expert-led reviews (alternatively called traditional, narrative, journalistic, authoritative, or non-systematic reviews). These reviews are unstructured, and rely heavily on the literature picked by an individual expert, and are therefore susceptible to bias. Such
reviews tend to provide information on a broad clinical area, in contrast to systematic reviews, which aim to answer a highly specific question.386

Literature selection in expert-led reviews has been described as “vague and even eccentric” in one guide to scientific writing.387 Experts have been found often to hold strong and mutually contradictory views about research results (and disagree substantially more than non topic-experts),384 a phenomenon which may be caused by well-established cognitive biases.388 Finally, expert recommendations tend to be outdated, and have been found to lag behind the meta-analyses of clinical trials in systematic reviews.389 Two notable examples of the problem of non-systematic approaches to the literature are the use of maternal steroids for pre-term birth, and thrombolysis for myocardial infarction. These interventions were both eventually found to be life-saving by systematic reviews, but previous failure to evaluate already published RCTs in a systematic way may have delayed their use by several decades.390–392

Systematic reviews aim to overcome these problems, by using a pre-defined protocol to systematically identify all research relevant to a particular question, and using well-established, reproducible methods for data synthesis.393 Systematic reviews aim to be transparent, rigorous, and up-to-date.394 Systematic reviews and meta-analyses of RCTs are regarded as the highest quality of evidence, and have thus become core tools for practising evidence-based medicine.318

Systematic reviews follow a well-established methodology to identify, appraise, and synthesize the available evidence.395 These steps are depicted in Figure 4.1 and are described as follows. (1) One first generates clear and answerable questions, which describe the populations, interventions, comparators, outcomes and study designs of interest. (2) Subsequently, one identifies candidate studies via sensitive database searches. (3) One then screens the titles and abstracts identified by the searches to select those likely to meet the criteria for inclusion (dictated by the key questions and the review protocol). The full-texts of the selected studies are then retrieved, and assessed against the inclusion criteria. (4) Information of interest is extracted from each included paper. This includes predefined data elements that describe the study population, the intervention(s) and control, outcomes and corresponding statistical information, and high-
level assessments concerning study conduct and risks of bias. (5) One then synthesizes the extracted information, narratively and sometimes via meta-analysis. (6) Findings of the review are reported to consumers (physicians, researchers, patients, and other decision makers).

These methods are well established for systematic reviews and syntheses of quantitative data, which account for the overwhelming majority of published systematic reviews. This chapter examines the adaptations necessary to conventional systematic review methodology when incorporating qualitative research.

![Figure 4.1: Schematic outlining the methodological steps used in a typical systematic review; from Wallace et al. with permission.](image)

4.2 Motivation for including qualitative research in systematic reviews

Systematic reviews of quantitative data are well placed to answer questions about the magnitude of benefit and harm from an intervention. Qualitative research can provide information about why, and how interventions work or don’t work. It also provides a way for clinicians to gain an insight into the experiences of patients and their families.

The volume of published qualitative research has been growing rapidly, with the number of published articles growing more than three-fold in the ten years from 1998–2007, and by 2007 reaching 4% of all research articles published in 67 of the most highly cited journals of primary medical research. Readers of qualitative research are therefore facing the same problems of information overload which have been well documented in clinical trial publications.

The Cochrane Library, in 2013, published its first ever systematic review and synthe-

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"The most recent survey of published qualitative systematic reviews was conducted in 2004, and found only 42 published examples. By contrast, several thousand reviews of clinical trials had been published by the same date, and there has been exponential growth in this number ever since. Qualitative systematic reviews continue to grow in number, a search of PubMed using the query 'systematic review'[ti] qualitative[ti] at the time of writing retrieved 297 articles."
sis of qualitative studies, examining barriers and facilitators to using lay health workers. It provided a qualitative counterpart to an earlier systematic review of RCTs on the topic, which demonstrated the effectiveness of lay health workers on several important health outcomes, including increasing breast feeding, immunisation rates, tuberculosis treatment success, and reducing infant mortality. In this case the qualitative review made recommendations which aim to help the successful implementation of a complex, evidence-based intervention.

4.3 Identifying studies

A key component of a systematic review, is conducting highly sensitive database searches, aimed at identifying all relevant research to the review question. For a traditional systematic review of RCTs, there are several factors which facilitate this process. First, it is increasingly difficult for trialists to avoid pre-registering their trials with public registries. Pressure to do so has increased since 2005, when journals belonging to the International Committee of Medical Journal Editors (ICMJE) adopted a policy that they would not publish any clinical trial which was not pre-registered. Legislation has been enacted in several countries, including the US, which compels trialists to pre-register drug trials.

Second, conventions exist for the naming of RCTs: the CONSORT group recommend that the words “Randomized Trial” are included in all RCT titles. RCTs published after 1996 may therefore accurately be identified by using this as a search term in electronic databases.

Finally, researchers have developed and validated search filters (combinations of search terms aimed at narrowing the search scope to the study design of interest) for RCTs. These have near perfect sensitivity, and thus can considerably narrow the search scope. By contrast, qualitative research often lacks any of these features, making identifying all pertinent studies difficult.

\(^1\)CONSORT is the international consensus group for RCT reporting, and adherence to their guidelines is a requirement for publication in most medical journals.

\(^2\)At the time of writing, PubMed contains over 23,000,000 entries. By contrast, a search conducted using the RCT search filter yielded only 368,000 entries. Thus, by using this filter 98.4% of the database may be safely excluded from further consideration.
Qualitative research is often found in places other than journal articles; it may be published as book chapters, and a large proportion is unpublished, and disseminated at conference presentations, or as part of doctoral or masters theses. These sources are not easily searchable at present.

Even qualitative research which is published in journals may be difficult to find due to poor indexing. The MeSH term for “Qualitative research” was introduced in 2003, but has been found to lack sufficient accuracy for use in systematic reviews. From the point of view of retrievability, qualitative research suffers from inconsistent descriptions (including, but not limited to: ethnography, grounded theory, thematic analysis, content analysis, observational methods, and constant comparative method).

**Precision** is the term used in the information retrieval literature to describe the proportion of retrieved articles which are relevant. Precision and sensitivity are linked, and a strategy which aims for increased sensitivity will generally result in reduced precision. Since systematic reviews aim to retrieve all relevant literature, high sensitivity is paramount. An ideal study design filter would therefore balance perfect sensitivity, with precision high enough to safely exclude enough irrelevant articles to ensure the number of documents finally retrieved is manageable for manual review.

There has been increasing work on producing search filters for qualitative research, and several now exist for frequently used databases. However, their sensitivity is substantially lower than the equivalent RCT filters. One qualitative filter achieved 52.7% sensitivity, which compares poorly with the RCT filter used by the Cochrane Collaboration’s RCT filter which was 100% sensitive. Thus, if used alone, qualitative filters are likely to incorrectly exclude a large proportion of relevant literature.

Even relying on systematically obtained published literature alone may be unreliable due to publication bias. This refers to the fact that many studies are conducted, but never generate a publication (also known as grey literature). The increased difficulty in finding and analysing grey literature produces a bias, since studies with a posi-

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1 MeSH (Medical Subject Headings) is the controlled vocabulary used by PubMed to index included papers; these terms are widely used to perform thesaurus searching for systematic reviews; http://www.ncbi.nlm.nih.gov/mesh

2 Precision is synonymous with Positive Predictive Value as used in the diagnostic test literature; likewise information retrieval papers often use the term recall which has identical meaning to sensitivity.
tive result are more likely to lead to publication than those with a negative result\textsuperscript{421–424}.

Although publication bias has not been studied to the same extent in qualitative research, one study examined 224 qualitative research abstracts presented at the 1998 and 1998 British Sociological Association conferences and found that only 44\% had been published 3.5–4.5 years later.\textsuperscript{425} Importantly, abstracts with high quality reporting of methods were more likely to lead to publication than those with quality problems. The authors suggest that reviewers could attempt to include unpublished data in their reviews, and also make sure to account for this potential bias in their analyses and conclusions.\textsuperscript{425} However, even if conference abstracts were sought and scrutinised, there is unlikely to be sufficient detail in these to include in a synthesis.

In her examination of qualitative synthesis, Doyle argues that an exhaustive search, which is necessary for quantitative synthesis to reduce statistical bias, is not appropriate in qualitative research.\textsuperscript{426} Since qualitative synthesis is designed to uncover themes rather than make statistical inferences, use of qualitative sampling methods (such as adding studies until \textit{conceptual saturation}\textsuperscript{1} is reached) might be more appropriate. This approach also has also been used to make very large search retrievals more practical to process.\textsuperscript{428} However, although the presence of a theme in multiple studies may not increase its statistical importance, it would increase confidence of the existence of such themes, and additionally allow the geographic and cultural spread of themes in a systematic way.\textsuperscript{429}

For these reasons the following methods are adopted in the thesis, which aim to pragmatically balance obtaining as much relevant qualitative research as possible, with a search retrieval for which manual review is feasible. In view of issues described above, a high sensitivity, low precision strategy was designed for the search. This was designed to minimise false negatives (relevant papers in the databases which would be missed), but at the expense of much greater numbers of articles retrieved by the search, which then require manual checking.

To deal with this high search yield, I added a \textit{title screen} stage to the study selection

\textsuperscript{1}A concept in qualitative research defined as ‘data adequacy’: the point where no new ideas are being generated by studying additional participants (or adding additional primary studies in the case of systematic reviews).\textsuperscript{427}
process. Figure 4.2 shows how this fits into the study identification schematically. Using a list of titles only, this stage aims to exclude only studies which are clearly irrelevant (which accounts for the vast majority at this stage).

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**Figure 4.2:** PREFERRED REPORTING ITEMS FOR SYSTEMATIC REVIEWS AND META-ANALYSES (PRISMA)-style flowchart of filtering steps in a systematic review together with illustrative estimates of numbers which might be expected at each stage when using qualitative research. A systematic review of RCTs might retrieve several hundred articles from the search (stage 2), a sensitive qualitative strategy might retrieve tens of thousands which would not be feasible to conduct a formal double title and abstract screen. Adding in the additional screen of titles overcomes this problem. *Sources: PubMed contains 24 million entries at time of writing (http://www.ncbi.nlm.nih.gov/pubmed), stages 2, 3, and 4 based on figures from Methley et al.*

Since the clinical terms used in the first review (Chapter 6) were broad, the search filters developed by Shaw and colleagues were used. To mitigate for poor sensitivity, a snowball sampling technique was used, in which papers cited by the included studies,
and also subsequent studies in which the included studies were cited were assessed for inclusion.\textsuperscript{1}

Since the clinical terms in the second review (Chapter 7) had a lower search yield, and since this review included two study types (RCTs and qualitative studies), it was not necessary to use a search filter for the database searches. Irrelevant study designs were screened out at the manual title screen and abstract screen stages. In both systematic reviews in the thesis, the initial search yielded a high volume of potentially relevant papers (>7,000 for the first review, and >15,000 for the second), so a manual screen of titles was conducted as an extra filtering step before abstract assessment. At this stage, only articles which were clearly irrelevant were excluded.

This approach is supported by a validation study of qualitative search strategies published after both the reviews in the thesis were completed.\textsuperscript{430} This study compared the performance of three strategies: a conventional search (PICO-style\textsuperscript{ii}) including a study design filter, the same search without a study design filter, and a novel strategy which incorporated elements found in qualitative questions (including elements named phenomenon of interest and evaluation type). The PICO-style search with no study design filter (similar to the approach adopted here) achieved the best sensitivity, with the other strategies missing a substantial number of relevant articles.

For pragmatic reasons, I have chosen to include only qualitative research which is published in journals. This strategy aims to retrieve higher quality evidence, and ensure a search and synthesis is feasible within practical resource constraints. However, it is probable that there is relevant unpublished research which was not included in these reviews.

\subsection*{4.4 Data extraction}

Systematic reviews of clinical trials require the extraction of a well defined set of variables, and as such the data extraction phase of a review typically involves recording de-
1. Getting started
2. Deciding what is relevant to the initial interest
3. Reading the studies
4. Determining how the studies are related
5. Translating the studies into one another
6. Synthesising translations
7. Expressing the synthesis

Box 4.1: Seven steps of meta-ethnography

tails about study design and conduct, potential biases, and statistical outcome data using a standard extraction template. Since qualitative results are descriptive rather than statistical, they lend themselves less well to this type of summary. In practice, I developed a structured template of summary information and notes using a database, using these notes as an aide-memoire together with the full text papers when conducting the synthesis.

4.5 Synthesis

In 1988, Noblit and Hare described a method for synthesising the results of ethnographic studies, termed meta-ethnography. They describe a key limitation of ethnographic studies: that they study a specific group of people, in a specific location, and at a specific time. It is, therefore, difficult to generalise from these studies. They propose methods for synthesising the results of multiple related ethnographic studies in different populations, and describe that combining multiple accounts can enable researchers to infer new information about social and cultural phenomena which generalise across populations. The steps defined by Noblit and Hare are outlined in Box 4.1.

Steps 1–3 are analogous to tasks in a conventional systematic review and are described above. Key to the synthesis task in meta-ethnography is the concept of translation, which covers steps 4 and 5 from Box 4.1. Translation, here, is used to refer to the process of
finding links between different qualitative studies, which will often describe the same phenomenon using different terminology.\textsuperscript{435} Reviewers group together related concepts across different studies to create \textit{higher order constructs} during this process.

A worked example of meta-ethnography, published by Britten and colleagues (looking at experiences of medication taking in patients with chronic diseases), further clarifies the concept of translation. In this paper, the reviewers grouped the phenomena dislike of taking drugs, fear of side-effects, aversion to medicines, and harmful effects of drugs under the higher order construct of medication aversion.\textsuperscript{436} Since the publication of this key paper, meta-ethnography has been used to synthesise the results of qualitative studies more widely, and not limited to ethnographic studies.\textsuperscript{429}

4.5.1 Third order constructs

Schutz proposed the concept of \textit{ordered constructs} for considering sociological research, which is of particular relevance and widely used in systematic reviews.\textsuperscript{437} First order constructs are defined as the understandings of study participants; second order constructs refer to the interpretations of the primary study authors. Third order constructs, therefore, refer to the interpretations of a researcher synthesising multiple studies based on first and second order constructs.\textsuperscript{436}

Third order analysis has been alternately described as the process of \textit{going beyond} the source papers;\textsuperscript{429,435} that is, considering whether the findings from a collection of studies allow new conclusions to be drawn which may not be evident from any one study in isolation. In this way, it is analogous to meta-analysis in quantitative systematic reviews, in which the increased statistical power gained by pooling data from multiple studies may demonstrate a significant treatment effect which would not be obvious from simple tabular summarisation of the trial results.\textsuperscript{438}

One example of a third order analysis is from a qualitative synthesis by Thomas and colleagues, who synthesised qualitative research examining children’s perspectives on healthy eating.\textsuperscript{439} Several source studies reported that children were attracted by food which tasted good; others found that children did not perceive health to be of particular concern to them. The reviewers were able to conclude that marketing fruit and vegeta-
bles as tasty might be expected to be more effective than describing them as healthy, a conclusion not found in any source paper individually.

A large number of alternate methods for synthesising qualitative data have been proposed, among others meta-synthesis\textsuperscript{440}, meta-summaries\textsuperscript{441}, thematic synthesis\textsuperscript{429}, and critical interpretive synthesis.\textsuperscript{428} Despite the disparate names, these methodologies have much overlap, and are largely based on the principles of meta-ethnography.\textsuperscript{442}

The systematic reviews in this thesis used thematic synthesis, a variant of meta-ethnography, based on the approach described in the Economic and Social Research Council (UK) (\textsc{esrc}) Narrative Synthesis guidelines,\textsuperscript{443} and by Thomas and colleagues.\textsuperscript{429} Thematic synthesis was chosen since it encourages a systematic search, though in practice it has much overlap with meta-ethnography.\textsuperscript{429} Additionally, a strict interpretation of meta-ethnography involves drawing conclusions only from the second order constructs (that is, the reviewers synthesise only the conclusions of the original authors, and ignore other material such as quotes).\textsuperscript{444} This risks producing theoretically dense and abstract conclusions, whereas the aim of the reviews in this thesis are to produce practical conclusions for clinical practice.\textsuperscript{435} Thematic synthesis, by contrast, includes both the analysis of the original study authors plus original quotations and other primary descriptions of the interview; the method has been used for synthesis in several previous reviews with a clinical focus.\textsuperscript{445–447} The synthesis was carried out as follows.

As a first stage of synthesis, I coded the included studies line-by-line. An example of this coding is shown in Figure 4.3 on Page 117. Codes at this stage are somewhat arbitrary, and created as needed from the themes described in the qualitative papers.

The second stage involved listing all the themes, and grouping them by concept (equivalent to the translation task of meta-ethnography). An excerpt of the groupings is shown in Figure 4.4 on Page 118.

As a third stage, analytical themes (equivalent to third-order themes) were generated using this concept map, plus with reference to original papers. This was done using the \textit{one sheet of paper} method,\textsuperscript{449} where concepts were linked in a hierarchical tree structure. Since this stage is somewhat more subjective than the other stages,\textsuperscript{450} one supervisor (Chris McKevitt) and I each conducted this stage independently, then met to resolve
differences and produce a joint agreed version of the synthesis.

4.6 Integrating qualitative and quantitative data

In practice a spectrum of approaches have been described for producing a synthesis of qualitative and quantitative data, ranging from treating each data type separately to some papers which describe various forms of integrating qualitative and quantitative results.\textsuperscript{451,452} The review in Chapter 7, which examines the effects of different strategies for CVD risk, is incorporating qualitative research to find explanations for the success or failure of different strategies. Therefore, this review took a pragmatic approach, conducting a conventional systematic review and meta-analyses of RCTs, followed by a thematic synthesis of qualitative research aiming to explore whether patient perspectives may help explain the quantitative results.

4.7 Quality assessment—assessing bias

In systematic reviews of quantitative studies, there is widespread consensus that quality appraisal is important.\textsuperscript{453} This typically takes the form of one of a number of well-established checklists,\textsuperscript{454} with key sources of bias having been established empirically for clinical trials.\textsuperscript{455} By contrast, there is no current consensus among qualitative researchers whether quality assessment is even desirable, particularly done by checklist.\textsuperscript{456} Dixon-Woods described some of the issues around such quality assessments, and in particular that the large number and heterogeneity of qualitative methods used in practice in particular makes application of a standardised checklist difficult.\textsuperscript{457} Dixon-Woods proposed a core set of prompts (see Box 4.2) for markers of good quality which should apply across different qualitative methodologies. The author stresses that these should be seen as a minimal set of criteria, and that assessment of quality additionally requires assessment of problems which may be idiosyncratic for different methodologies and research questions.
1. Are the research questions clear?

2. Are the research questions suited to qualitative inquiry?

3. Are the following clearly described?
   - sampling
   - data collection
   - analysis

4. Are the following appropriate to the research question?
   - sampling
   - data collection
   - analysis

5. Are the claims made supported by sufficient evidence?

6. Are the data, interpretations, and conclusions clearly integrated?

7. Does the paper make a useful contribution?

**Box 4.2:** Prompts for appraising qualitative research; reproduced with permission from Dixon-Woods.457
4.7.1 Theoretical appraisal

Hannes and colleagues, in their guidance written for the Cochrane Collaboration, describe how assessing quality with a technical checklist alone is not sufficient, and recommends the following three stage approach to quality appraisal:

1. Filtering (selection of studies to include)

2. Technical appraisal (use of a critical appraisal checklist)

3. Theoretical appraisal

Stages 1 and 2 are part of a conventional systematic review. Stage 3 refers to a critical appraisal of the theoretical approach the study has taken, and considering whether it is likely to give valid answers to the study question. Specifically, this stage appraises the quality and reasoning for the decisions made by the researcher in the data collection and analysis. Hannes suggests that this stage requires in depth and nuanced consideration and is idiosyncratic to the review question, and is also therefore best not incorporated into a simple checklist.

Some specific examples of this stage are particularly relevant to the first review in the thesis, (Chapter 6). A study which is theoretically weak may, for example, assume patients mean the same thing as doctors when they use the word ‘hypertension’. If they mean different things, the researcher will misunderstand the patient’s views and experiences. Likewise, when examining medication taking, a theoretically weak study may ask about reminders and routines only, and gain only a superficial understanding of their experiences with medication. A stronger study would aim to have a more in depth understanding of a patient’s day-to-day life, and how their illness and treatment fits in. One further example is that participants have been found to respond differently in qualitative research to interviewers who identify themselves as doctors compared to those who identify as researchers. Interviews conducted by the patient’s own doctor, therefore, may risk participants withholding information they might more readily disclose to an unknown researcher (for example, about not taking medication regularly, or...
lifestyle issues they would prefer their own doctor not to know about). These examples, and others like them, would not be easily evident from any standardised checklist.

In this thesis, in addition to a technical checklist, the theoretical approaches used by qualitative studies is considered in the results sections, and their impact on synthesis results considered in the discussion sections. Qualitative studies were included regardless of quality. All studies were assessed using a quality checklist, and the impact of both theoretical issues and checklist scores on the robustness of conclusions are considered in the results sections.

After the completion of the systematic review in Chapter 6, the Cochrane Collaboration has proposed an alternative approach for assessing biases from qualitative studies. This approach is based upon many of the same points as the Dixon-Woods checklist, and includes identical questions on sampling, data collection, analysis, and providing evidence for the study interpretation. It differs in the following ways, particularly designed for use in systematic reviews. First there are additional points added for whether the study is genuinely qualitative, and whether the context (in other words the setting and recruitment frame) is clearly described. This is particularly pertinent for systematic reviews, where the researcher may be analysing the reasons for similarities and differences between different studies. Finally, the Cochrane approach has adopted some features of the scoring system used by the Cochrane Risk of Bias tool for RCTs: studies are marked as being at high, low, or unclear risk of bias for each quality point. The results are not summed per study, but presented for each quality domain as a matrix which can be displayed graphically. This has a key advantage for evidence syntheses, since ideally information on the strengths and weaknesses of individual studies should inform the synthesis and analysis. The likely effects of different biases on the final results is more difficult to judge from a numerical score alone.

The consensus among systematic reviewers about quality assessment in qualitative studies is very rapidly evolving, and a new framework called CERQUAL was published in October 2015 (after the reviews in this thesis were completed). CERQUAL provides a formal method for bringing together study-level quality data to determine whether overall review conclusions are of ‘high’, ‘moderate’, ‘low’, or ‘very low’ confidence.
4.8 Conclusions

Systematic reviewing, a methodology which to-date is predominantly used for quantitative studies, also has utility for reviewing qualitative research. Qualitative systematic reviews face particular challenges, including the difficulty in identifying qualitative studies, lack of standardisation of qualitative methods, and a lack of agreement among researchers whether and how quality should be assessed. Some of these problems can be overcome by adapting conventional systematic review methods. When successful, qualitative research syntheses permit a critical overview of all pertinent evidence, an assessment of the spread and validity of themes from individual studies, and may permit new conclusions to be drawn would not have been possible from the source studies taken individually.
Figure 4.3: Example of line-by-line coding in qualitative synthesis (from the systematic review in Chapter 6) of an excerpt of a qualitative study by Ogedegbe et al. New codes were created as needed throughout this process.
Medication beliefs

Expectations of what treatment will do/ consequences of untreated hypertension

  - rupture of blood vessels: Kjellgren-N-9-SW, Lee-N-9-SK, Panpakdee-N-11-TH
  - thinning blood: Lukoshek-Y-11-US
  - suicide: Peres-N-9-BR

Figure 4.4: Example of the thematic groupings from the systematic review in Chapter 6. For convenience the study labels incorporate information about whether they targeted a specific ethnic group (Yes/No), the quality score, and the country the interviews were conducted in. For example, Firmo-N-10-BR describes the study by Firmo and colleagues, which did not restrict to a particular ethnic group, scored 10/11 on the quality score, and was conducted in Brazil.
Trends in risk factor prevalence and management before stroke – the South London Stroke Register

5.1 Introduction

Chapter 2 described results from the INTERHEART and INTERSTROKE studies, which (in line with many other studies) found that 90% of CVD could be attributed to modifiable risk factors (Page 25). This has led to major national and international public health and primary care campaigns to identify and treat CVD risk factors. However, as reviewed on Page 43, despite improving trends in risk factor management over time in many countries in Europe and North America, large proportions remain unaware, untreated, or uncontrolled.
Several studies have found ethnic differences in stroke risk factors in particular. A US case–control study (1156 participants) found that hypertension and diabetes mellitus were significantly more prevalent among black than white patients with stroke, whereas AF was significantly more prevalent in white stroke patients.\textsuperscript{464} This pattern was reported similarly by the South London Stroke Register (\textit{sLSR}) from 1995 to 1998.\textsuperscript{465} Analyses of routinely collected primary care data in the UK has found that black ethnic participants with hypertension were significantly less likely to have good control than white participants; though both ethnic groups had their blood pressures monitored and recorded with similar frequency.\textsuperscript{466} A US cross-sectional study found that apparent ethnic differences in stroke risk factors were explained by differences in income.\textsuperscript{467}

Authors of a number qualitative studies have suggested that ethnic minority groups might be less likely to use prescription medication to treat CVD risk factors; explanations suggested by the authors include prevalent cultural concerns about medication side effects, and widespread use of traditional remedies.\textsuperscript{22,181,372,468–470} These factors meant this group were both less likely to agree to treatment, and less likely to adhere to treatment.

Two of these studies (those by Morgan, and Connell \textit{et al.}) are of particular relevance to this Chapter, since they recruited from GP practices based within the South London Stroke Register (\textit{sLSR}) area.\textsuperscript{22,372,468} These studies, conducted ten years apart (by Morgan in 1995, and Connell \textit{et al.} in 2005), examined patient perspectives on hypertension and its treatment.\textsuperscript{22,372,468} Both studies recruited black African and black Caribbean participants; the study by Morgan additionally recruited white ethnic participants. These studies found that black African and black Caribbean participants frequently did not use medication as prescribed, often adjusting in response to symptoms, or if hypertension was perceived to be cured. There was widespread use of traditional ‘bush’ remedies found in both studies. The study by Morgan found that white participants tended to report high levels of adherence to prescribed treatments, and did not describe widespread use of alternative medication. This Chapter will present quantitative data on risk factors and their treatment in stroke patients from the same geographic area, and including the time period of these qualitative studies.
This Chapter seeks to analyse trends over time from 1995–2010 in key risk factors and their treatment using data from the SLSR: a prospective population-based register of people with first-in-a-lifetime stroke based in a Lambeth and Southwark in south London. This chapter will focus on CVD risk factors which may be treated by medication, namely hypertension, hypercholesterolaemia, diabetes, AF, and prior CVD (MI or TIA). The association between socio-demographic factors (particularly: age, ethnicity, sex, and socio-economic status) and appropriate primary prevention prescribing will be examined.

This study was published in the journal Stroke (see Appendix A on Page 327).

5.2 Methods

5.2.1 South London Stroke Register

The South London Stroke Register (SLSR) is an ongoing, population-based register of people with a first-ever stroke, which started in 1995. The SLSR aims to recruit all people with first stroke who are ordinarily resident in a defined area of south London covering 22 electoral wards across Lambeth and Southwark (see Figure 5.1). Participants are interviewed at the time of stroke, and visited by a researcher for a follow up interview at 3 months and 1 year post-stroke, then annually thereafter.

The source population of this area was 271,817 according to the 2001 census, which reported the ethnic make-up of the population as 63% white, 28% black (9% black Caribbean, 15% black African, and 4% black other), and 9% of other ethnic group. By the 2011 census, the source population had increased to 357,308, with ethnic make-up being 56% white, 25% black (7% black Caribbean, 14% black African, 4% black other), and 18% other. The largest increase was in those aged 49 to 59 (49% increase between 2001–11) years; the population aged >65 years reduced by 10%.

\footnote{The qualitative study reported later in the thesis (in Chapter 8 on Page 207) recruited participants from two contrasting GP practices situated within the SLSR recruitment area.}
5.2.2 Ethics

Ethical approval for the SLSR was given by the Research Ethics Committees at St Thomas’ Hospital, Kings College Hospital, St Georges Hospital, University College London Hospital and Lewisham Hospital when the register commenced in 1995 and has regularly been renewed since. Written informed consent is obtained from all living patients before participation in the register. If a patient is not able to give consent, assent from the patient’s carer or next of kin is requested instead.

5.2.3 Case ascertainment

Multiple overlapping sources of notification are used to maximise case ascertainment. Researchers make daily visits to local hospitals, where ward records of stroke units and neurosurgical units, electronic patient records, brain imaging requests, and accident and emergency records are scrutinised. GP practices within and bordering the study area are regularly contacted and encouraged to notify new cases of stroke, particularly where the stroke occurs out of the study area, or where the person is not admitted to hospital. Study staff also make scheduled contact with nursing homes and other outlying hospitals. Community therapists are contacted on a 3-monthly basis. Records from the Coroner’s office, the Bereavement office, and death certificates are sought monthly. Deaths due to stroke are notified to the research team annually by the Office for National Statistics (UK).

Stroke diagnosis was defined using the criteria set out by the WHO, and confirmed by a study clinician. In brief, stroke was defined as rapid onset focal neurological deficit lasting more than 24 hours or leading to death, where no cause other than a vascular origin was evident. This definition includes strokes of ischaemic aetiology, intracerebral haemorrhage (ICH), and sub-arachnoid haemorrhage.

A capture-recapture study conducted in 2001 estimated the completeness of case ascertainment of the SLSR to be 88%; recruitment methods have not changed substantially since 2001 other than minor changes over time to the frequency and location of

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1 Global neurological impairment was acceptable in cases of reduced consciousness; sub-arachnoid haemorrhage was included regardless of clinical focal neurological deficit where history and investigations (brain imaging or lumbar puncture results) indicated the diagnosis.
site visits in order to adapt to changes in acute stroke services.

**Figure 5.1:** Recruitment area for the SLSR; the orange shaded area is the core area used for recruitment from 1995–date in Lambeth (left part), and Southwark (right part). From November 2004 to December 2007 the recruitment area was temporarily expanded to additionally include the yellow area as part of a clinical trial.

### 5.2.4 Data collection

The data for this analysis is primarily collected from the initial patient contact with the SLSR research clinician. A study clinician aims to meet with eligible patients as soon as possible after the acute stroke. This meeting will typically take place in hospital, but would occur in the patient’s own home for those not admitted to hospital or who
were notified late. A standardised interview is conducted with the patient, where the researcher gathers data including on socio-demographics, past medical history, vascular risk factors, and regular medication use. Patients are asked to describe their ethnic group using criteria from the 1991 UK Census question on ethnicity.

Risk factors which had been diagnosed before the stroke (hypertension, AF, diabetes mellitus, and prior CVD [MI or TIA]) and usual prescribed medication (antiplatelets, anticoagulants, antihypertensive drugs, and cholesterol-lowering drugs) were obtained by contacting patients’ usual general practitioners and from their hospital records. Data on hypercholesterolaemia were collected from 2001 onwards.

Strokes were classified by pathological subtype by a senior study clinician with reference to patient records and CT or MRI images and reports where available. Stroke was classified as ischaemic, ICH, sub-arachnoid haemorrhage (SAH), or undefined.

Socio-economic status was estimated using Carstairs scores, which combine male unemployment, overcrowding, car ownership, and proportion in social classes IV and V in a small area.475 The resultant score is a continuous variable obtained by weighting and standardising the variables, then summing the result.476 For England and Wales as a whole in 2001, the mean Carstairs score was 0, with standard deviation (SD) 3.41 and range from −5.71 to 16.50 (with census ward as the unit of analysis; higher scores indicate higher socio-economic deprivation).477 The recruitment area is substantially more deprived than the national average, and in 2001 had a mean Carstairs score 5.5, SD 4.3, and range −1.47 to 15.47.477

For each participant in the SLSR, the Carstairs scores was derived from the 2001 census data per Lower Layer Super Output area.1 Scores were obtained from patients’ home postcodes at the time of stroke. Socio-economic status was therefore assessed by area, rather than for individuals.

1Lower Layer Super Output areas are geographical small areas covering an average population of 1,500 residents or 600 households designed by the Office for National Statistics (UK) (ONS) to aid the presentation and analysis of census results.478
5.2.5 Statistical methods

Data were grouped into 4-year spans to increase numbers per group. The statistical significance of trends over time in socio-demographics was assessed using the $\chi^2$ test for trends. The statistical significance of trends over time in risk factors and primary prevention prescribing was assessed in multi-variable logistic regression models which included age group, sex, ethnicity, stroke subtype, and Carstairs scores as co-variates.

The strength of associations between socio-demographics and risk factors and prescribed medication were assessed in multi-variable logistic regression models which included sex, age, ethnicity, stroke subtype, deprivation, and year of stroke as co-variates. For time trends, the year of stroke was transformed to produce odds ratios describing the relative change in outcome with each 5 year advance in time. Presenting the results of logistic regression analyses as odds ratios may lead to an exaggerated estimate of effect size where the frequency of the outcome is high. Since the outcomes in this study (risk factors and prescription rates) all occurred in $>$10% of the population, I used the method of Zhang & Yu to convert odds ratios and their confidence intervals to an equivalent risk ratio. P values <0.05 were regarded as statistically significant. Analyses and charts were produced using the statistical package R.

5.3 Results

5.3.1 Description of participants

Between January 1995 and 2011, a total of 4,416 patients were registered. Their characteristics are described in Table 5.1 on page 127. Patient median age was 72.4 years (inter-quartile range, 61.2–81.1); ethnicities were white (70.5%), black (21.3%; 13.0% black Caribbean, 7.6% black African, and 0.6% black other), and other (5.7%). Stroke subtypes were ischaemic (73.8%), ICH (12.7%), sub-arachnoid haemorrhage (SAH) (5%), and undefined (8.4%). Carstairs scores indicated that a substantial proportion of recruited patients lived in socio-economically deprived areas (mean 9.52, SD 3.71; higher = more deprived). Patients with white and black ethnicities had significantly lower Carstairs scores than other ethnicities, but the absolute differences were small (mean score by
ethnicity grouping: white 9.42, black 9.66, other 10.2; P = 0.006). Data completeness was high for all variables (ethnicity, 97%; stroke subtype, 96%; risk factors, 95%–97%; prescribed medication, 96%–97%).

5.3.2 Trends in diagnosed risk factors over time

Trends over time from 1995–2010 in risk factors diagnosed before stroke are reported in Figure 5.2 (see page 128) and Table 5.1 (see page 127). Seventy-two percent of patients had one or more risk factors diagnosed before stroke. Overall risk factor prevalences were: hypertension, 64%; hypercholesterolemia, 24%; AF, 16%; diabetes mellitus, 19%; previous MI, 11%; and previous TIA, 12%. Hypercholesterolemia significantly increased over time (10.5%–31.7%; P <0.001); before-stroke MI and TIA significantly reduced (MI, 7.7%–2.7%; P <0.001 and TIA, 16.3%–8.9%; P <0.001). Hypertension, AF, and diabetes mellitus did not change significantly over time.
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<td>209 (19.5%)</td>
<td>221 (22.2%)</td>
<td>225 (25.7%)</td>
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<td>19 (2.2%)</td>
<td>19 (2.2%)</td>
<td>0.058</td>
</tr>
<tr>
<td><strong>White</strong></td>
<td>1028 (78.8%)</td>
<td>753 (70.1%)</td>
<td>671 (67.5%)</td>
<td>576 (65.7%)</td>
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<td>221 (20.2%)</td>
<td>225 (25.7%)</td>
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<td>&lt;0.001</td>
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<tr>
<td><strong>Under 65</strong></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ischaemic stroke</td>
<td>916 (70.2%)</td>
<td>786 (73.2%)</td>
<td>776 (78.1%)</td>
<td>699 (79.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICH</td>
<td>177 (13.6%)</td>
<td>163 (15.2%)</td>
<td>124 (12.5%)</td>
<td>88 (10%)</td>
<td>0.009</td>
</tr>
<tr>
<td>Sub-arachnoid haemorrhage</td>
<td>71 (5.4%)</td>
<td>71 (6.6%)</td>
<td>51 (5.1%)</td>
<td>20 (2.3%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Undefined</td>
<td>141 (10.8%)</td>
<td>54 (5.8%)</td>
<td>43 (4.3%)</td>
<td>70 (8%)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>845 (69.2%)</td>
<td>555 (49.6%)</td>
<td>630 (65.1%)</td>
<td>545 (63.4%)</td>
<td>0.091</td>
</tr>
<tr>
<td>Raised cholesterol</td>
<td>-</td>
<td>97 (10.5%)</td>
<td>226 (23.7%)</td>
<td>272 (31.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>209 (17%)</td>
<td>178 (18%)</td>
<td>194 (20.3%)</td>
<td>180 (20.7%)</td>
<td>0.13</td>
</tr>
<tr>
<td>AF</td>
<td>252 (20.6%)</td>
<td>138 (13.9%)</td>
<td>148 (15.3%)</td>
<td>127 (14.9%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Prior MI</td>
<td>90 (7.7%)</td>
<td>37 (4%)</td>
<td>48 (5%)</td>
<td>23 (2.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior TIA</td>
<td>196 (15.2%)</td>
<td>105 (10.6%)</td>
<td>111 (11.5%)</td>
<td>76 (8.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 1 untreated risk factor</td>
<td>524 (40.2%)</td>
<td>184 (17.1%)</td>
<td>236 (23.7%)</td>
<td>311 (35.5%)</td>
<td>0.513</td>
</tr>
<tr>
<td>Treated hypertension (n=2590)</td>
<td>433/827 (52.4%)</td>
<td>373/507 (73.6%)</td>
<td>460/618 (74.4%)</td>
<td>297/540 (55%)</td>
<td>0.502</td>
</tr>
<tr>
<td>Treated cholesterol (n=634)</td>
<td>-</td>
<td>54/81 (66.7%)</td>
<td>175/223 (78.5%)</td>
<td>210/270 (77.8%)</td>
<td>0.001</td>
</tr>
<tr>
<td>AF on antplatelet (n=628)</td>
<td>86/232 (37.1%)</td>
<td>52/101 (51.5%)</td>
<td>84/147 (57.1%)</td>
<td>64/125 (51.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AF on anticoagulant (n=664)</td>
<td>30/245 (12.2%)</td>
<td>21/124 (16.9%)</td>
<td>30/147 (20.4%)</td>
<td>29/125 (23.2%)</td>
<td>0.059</td>
</tr>
<tr>
<td>MI on antplatelet (n=416)</td>
<td>75/155 (48.4%)</td>
<td>55/77 (71.4%)</td>
<td>74/96 (77.1%)</td>
<td>45/75 (60%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TIA on antplatelet (n=449)</td>
<td>86/174 (49.4%)</td>
<td>56/82 (68.3%)</td>
<td>71/111 (64%)</td>
<td>46/75 (61.3%)</td>
<td>0.015</td>
</tr>
<tr>
<td>TIA on anticoagulant (n=468)</td>
<td>6/192 (3.1%)</td>
<td>5/83 (6%)</td>
<td>4/111 (3.6%)</td>
<td>5/75 (6.7%)</td>
<td>0.349</td>
</tr>
</tbody>
</table>

**Table 5.1:** Trends in demographics and vascular risk factors diagnosed prior-to-stroke. AF indicates atrial fibrillation; ICH, intracerebral haemorrhage; MI, myocardial infarction; SAH, sub-arachnoid haemorrhage; and TIA, transient ischaemic attack.
**Figure 5.2:** Trends in risk factors prior to stroke, overall and by ethnic group (red line with circles represents white ethnic groups; blue line with crosses represents black African and black Caribbean ethnic groups)
5.3.3 Factors associated with risk factors diagnosed before stroke

The results from the multi-variable analyses are reported in Table 5.2 on page 132. Hypertension, diabetes mellitus, AF, previous M1, and TIA were significantly more likely to be diagnosed in older people. Hypercholesterolemia was the highest in those aged 65 to 74 years. Hypertension and M1 were significantly more prevalent in men; other risk factors were not significantly differ between men and women.

Black African and black Caribbean ethnicity was associated with significantly greater risk of hypertension and diabetes mellitus than white patients (adjusted RRS: hypertension, 1.22; 95% CI 1.17–1.27 and diabetes mellitus, 2.15; 95% CI 1.91–2.39) and significantly lower AF, M1, and TIA (adjusted RRS: AF, 0.47, 95% CI 0.35–0.60; M1, 0.58, 95% CI 0.43–0.77; TIA 0.76, 95% CI 0.59–0.96). Hypertension prevalence was similar in ischaemic stroke and ICH, but significantly lower in SAH (adjusted RR for SAH vs ischaemic stroke, 0.63; 95% CI, 0.52–0.75). There was a significantly lower risk of hypercholesterolemia, diabetes mellitus, previous M1, and AF with ICH and SAH compared with ischaemic stroke. There was no significant association between Carstairs score and any risk factor.
5.3.4 **Trends in primary prevention medication prescribed to patients**

Trends in prescribed medication are reported in Table 5.1 (see Page 127) and in Figure 5.3 (see Page 131). Twenty-six percent of patients had a single untreated risk factor, 13% had 2 or more risk factors. The proportions of those with risk factors prescribed appropriate treatment were hypertension, 62%; hypercholesterolemia, 75%; M1 (antiplatelets), 62%; AF, 64% (anticoagulants, 17%; antiplatelets, 48%; [1% were prescribed combined antiplatelet and anticoagulant]); TIA (antiplatelets), 58%. Prescribed treatment for hypercholesterolemia increased over time (70%–77%; P = 0.004). Antiplatelet prescription for AF significantly increased (37%–51%; P < 0.001); anticoagulant prescription increased, but was this was not statistically significant (12%–23%; P = 0.059). Antiplatelet prescription in M1 and TIA significantly increased over time (M1, 48%–60%; P < 0.001 and TIA, 49%–61%; P = 0.015). Antihypertensive prescription did not change significantly over time.

5.3.5 **Factors associated with the prescription of preventative treatments**

The multi-variable analyses are reported in Table 5.3 on page 133. Anticoagulant prescription in AF for older patients was low and was the least in those aged ≥85 years (compared with those aged <65 years; 65–74 years, adjusted RR 0.41; 75–84 years, adjusted RR 0.77; ≥85 years, adjusted RR 0.19). Significantly more women with hypertension were treated than men; there were no significant differences for other risk factor treatments between sexes.

Black patients with hypertension were significantly more likely to be prescribed treatment than white patients (adjusted RR, 1.17; 95% CI, 1.10–1.15). There was no significant association between other risk factor treatments and ethnicity, or between deprivation and any risk factor treatment. ICH and SAH were associated with significantly higher anticoagulant prescription (adjusted RR v ischaemic stroke: ICH, 3.14; 95% CI, 2.21–4.04 and SAH, 4.64; 95% CI, 2.40–5.72).
Figure 5.3: Trends in prescribed medication before stroke in those with known risk factors, overall and by ethnic group (red line with circles represents white ethnic groups; blue line with crosses represents combined black African and black Caribbean ethnic groups)
<table>
<thead>
<tr>
<th></th>
<th>hypertension</th>
<th>high cholesterol</th>
<th>diabetes</th>
<th>AF</th>
<th>prior MI</th>
<th>prior TIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>under 65*</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>65–74</td>
<td>1.16 (1.1 to 1.21)</td>
<td>1.39 (1.17 to 1.63)</td>
<td>1.55 (1.33 to 1.79)</td>
<td>1.59 (1.27 to 1.96)</td>
<td>1.7 (1.34 to 2.15)</td>
<td>1.21 (0.96 to 1.52)</td>
</tr>
<tr>
<td>75–84</td>
<td>1.19 (1.14 to 1.24)</td>
<td>1.11 (0.92 to 1.33)</td>
<td>1.23 (1.03 to 1.45)</td>
<td>2.35 (1.98 to 2.75)</td>
<td>1.69 (1.33 to 2.13)</td>
<td>1.16 (0.92 to 1.45)</td>
</tr>
<tr>
<td>85 and over</td>
<td>1.16 (1.1 to 1.23)</td>
<td>0.78 (0.59 to 1.01)</td>
<td>0.85 (0.65 to 1.09)</td>
<td>3.04 (2.6 to 3.49)</td>
<td>1.76 (1.32 to 2.3)</td>
<td>1.21 (0.91 to 1.58)</td>
</tr>
<tr>
<td>male*</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>female</td>
<td>1.05 (1 to 1.09)</td>
<td>0.99 (0.85 to 1.14)</td>
<td>0.95 (0.83 to 1.08)</td>
<td>1.1 (0.95 to 1.27)</td>
<td>0.66 (0.54 to 0.8)</td>
<td>1.07 (0.9 to 1.27)</td>
</tr>
<tr>
<td>white*</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>black</td>
<td>1.22 (1.17 to 1.27)</td>
<td>0.85 (0.7 to 1.01)</td>
<td>2.15 (1.91 to 2.39)</td>
<td>0.47 (0.35 to 0.6)</td>
<td>0.58 (0.43 to 0.77)</td>
<td>0.76 (0.59 to 0.96)</td>
</tr>
<tr>
<td>other</td>
<td>1.06 (0.96 to 1.15)</td>
<td>1.06 (0.78 to 1.38)</td>
<td>2.35 (1.96 to 2.74)</td>
<td>0.39 (0.22 to 0.63)</td>
<td>0.77 (0.48 to 1.15)</td>
<td>0.86 (0.56 to 1.25)</td>
</tr>
<tr>
<td>unknown</td>
<td>0.89 (0.72 to 1.05)</td>
<td>0.7 (0.37 to 1.14)</td>
<td>1.75 (1.2 to 2.36)</td>
<td>1.13 (0.88 to 2.17)</td>
<td>1.46 (0.84 to 2.3)</td>
<td>0.71 (0.31 to 1.33)</td>
</tr>
<tr>
<td>ischaemic stroke*</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>ICH</td>
<td>0.95 (0.88 to 1.02)</td>
<td>0.51 (0.36 to 0.68)</td>
<td>0.55 (0.43 to 0.7)</td>
<td>0.65 (0.49 to 0.85)</td>
<td>0.58 (0.4 to 0.8)</td>
<td>0.58 (0.41 to 0.78)</td>
</tr>
<tr>
<td>sub-arachnoid haemorrhage</td>
<td>0.63 (0.52 to 0.75)</td>
<td>0.27 (0.12 to 0.52)</td>
<td>0.23 (0.12 to 0.41)</td>
<td>0.33 (0.14 to 0.63)</td>
<td>0.45 (0.2 to 0.83)</td>
<td>0.08 (0.01 to 0.24)</td>
</tr>
<tr>
<td>undefined</td>
<td>0.96 (0.87 to 1.04)</td>
<td>0.95 (0.72 to 1.21)</td>
<td>1.12 (0.89 to 1.38)</td>
<td>0.91 (0.7 to 1.17)</td>
<td>1.23 (0.91 to 1.61)</td>
<td>0.74 (0.51 to 1.02)</td>
</tr>
<tr>
<td>per 5 years advance in time</td>
<td>0.97 (0.95 to 1)</td>
<td>1.51 (1.36 to 1.66)</td>
<td>1.04 (0.97 to 1.11)</td>
<td>0.93 (0.86 to 1)</td>
<td>0.87 (0.79 to 0.96)</td>
<td>0.76 (0.69 to 0.84)</td>
</tr>
<tr>
<td>Carstairs score (per 1 point increase)</td>
<td>1.01 (1 to 1.01)</td>
<td>1.09 (1.02 to 1.07)</td>
<td>0.99 (0.97 to 1.01)</td>
<td>0.99 (0.97 to 1.01)</td>
<td>1.03 (1.05 to 1.07)</td>
<td>1.02 (1.01 to 1.04)</td>
</tr>
</tbody>
</table>

Table 5.2: Association of socio-demographics and stroke subtype with risk factors. Risk ratios with 95% CI; columns show results from a logistic regression model with the risk factor as the dependent variable. AF indicates atrial fibrillation; ICH, intracerebral haemorrhage; MI, myocardial infarction; SAH, sub-arachnoid haemorrhage; and TIA, transient ischaemic attack. *indicates reference category.
<table>
<thead>
<tr>
<th>Hypertension</th>
<th>High Cholesterol</th>
<th>MI - Antiplatelet</th>
<th>AF - Anticoagulant</th>
<th>AF - Antiplatelet</th>
<th>TIA - Antiplatelet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 65*</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>65–74</td>
<td>1.1 (1.02 to 1.17)</td>
<td>1.12 (1.03 to 1.19)</td>
<td>1.04 (0.79 to 1.24)</td>
<td>0.41 (0.2 to 0.82)</td>
<td>1.12 (0.81 to 1.42)</td>
</tr>
<tr>
<td>75–84</td>
<td>1.05 (0.97 to 1.13)</td>
<td>1.18 (1.1 to 1.24)</td>
<td>1.05 (0.81 to 1.25)</td>
<td>0.77 (0.44 to 1.3)</td>
<td>1.16 (0.87 to 1.43)</td>
</tr>
<tr>
<td>85 and over</td>
<td>0.95 (0.84 to 1.05)</td>
<td>1.21 (1.1 to 1.28)</td>
<td>0.89 (0.6 to 1.16)</td>
<td>0.19 (0.08 to 0.41)</td>
<td>1.26 (0.96 to 1.53)</td>
</tr>
<tr>
<td>Male*</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>1.09 (1.03 to 1.15)</td>
<td>0.89 (0.76 to 0.99)</td>
<td>0.88 (0.71 to 1.05)</td>
<td>1.35 (0.93 to 1.91)</td>
<td>0.92 (0.75 to 1.1)</td>
</tr>
<tr>
<td>White*</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Black</td>
<td>1.17 (1.1 to 1.23)</td>
<td>0.93 (0.8 to 1.05)</td>
<td>0.92 (0.66 to 1.16)</td>
<td>0.8 (0.37 to 1.49)</td>
<td>0.94 (0.65 to 1.25)</td>
</tr>
<tr>
<td>Other</td>
<td>1.06 (0.92 to 1.18)</td>
<td>1 (0.8 to 1.15)</td>
<td>0.7 (0.35 to 1.11)</td>
<td>1.17 (0.29 to 2.77)</td>
<td>0.87 (0.37 to 1.46)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.76 to 1.22)</td>
<td>not estimable</td>
<td>1.07 (0.6 to 1.43)</td>
<td>1.5 (0.47 to 3.11)</td>
<td>0.97 (0.48 to 1.48)</td>
</tr>
<tr>
<td>Ischaemic Stroke*</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>ICH</td>
<td>0.79 (0.69 to 0.89)</td>
<td>1.03 (0.82 to 1.18)</td>
<td>0.68 (0.4 to 0.99)</td>
<td>3.14 (2.21 to 4.04)</td>
<td>0.45 (0.24 to 0.74)</td>
</tr>
<tr>
<td>Sub-arachnoid Haemorrhage</td>
<td>0.74 (0.55 to 0.93)</td>
<td>0.85 (0.37 to 1.21)</td>
<td>0.45 (0.08 to 1.11)</td>
<td>4.64 (2.4 to 5.72)</td>
<td>0.3 (0.02 to 1.06)</td>
</tr>
<tr>
<td>Undefined</td>
<td>0.83 (0.72 to 0.95)</td>
<td>1.08 (0.91 to 1.21)</td>
<td>1.04 (0.78 to 1.26)</td>
<td>0.71 (0.28 to 1.41)</td>
<td>1.19 (0.9 to 1.46)</td>
</tr>
<tr>
<td>Per 5 years advance in time*</td>
<td>1.01 (0.98 to 1.04)</td>
<td>1.09 (1.03 to 1.15)</td>
<td>1.15 (1.07 to 1.22)</td>
<td>1.21 (1.01 to 1.45)</td>
<td>1.18 (1.09 to 1.26)</td>
</tr>
<tr>
<td>Carstairs score (per 1 point increase)*</td>
<td>1 (0.99 to 1.01)</td>
<td>1 (0.99 to 1.02)</td>
<td>1 (0.98 to 1.02)</td>
<td>0.98 (0.94 to 1.03)</td>
<td>1 (0.98 to 1.02)</td>
</tr>
</tbody>
</table>

**Table 5.3:** Association of demographics and stroke subtype with prescribed preventative pedication. Risk ratios with 95% CI; columns show results from a logistic regression model with the risk factor as the dependent variable. AF indicates atrial fibrillation; ICH, intra-cerebral haemorrhage; MI, myocardial infarction; SAH, sub-arachnoid haemorrhage; and TIA, transient ischaemic attack. *indicates reference category.
5.4 Discussion

This study analysed trends in the prevalence and treatment of risk factors before stroke over a 15-year period, in a defined geographical area of south London. Hypercholesterolemia increased significantly over time, and previous MI and TIA fell. Prescribing of antiplatelets and cholesterol-lowering treatments significantly increased during the study period. A minority of patients with AF was prescribed anticoagulants; this did not significantly improve over time and was least likely in older people. Overall, one third of first strokes occurred in people who were not prescribed treatment for one or more previously diagnosed risk factor.

Anticoagulants are effective for the prevention of AF-related stroke; a 2007 meta-analysis found that anticoagulation was substantially more effective than aspirin. It is notable that the vast majority of AF-related stroke in the SLSR occurred in people not receiving anticoagulation.

Guidelines recommending anticoagulation for AF were published in the early 1990s. A UK consensus statement published after the SLSR data were collected recommended that aspirin is no longer used for stroke prevention in AF. Anticoagulant prescribing for AF remained low throughout the study period, and was the lowest in older patients, among whom AF was most prevalent. Notably, there is evidence from a randomised controlled trial in 973 people aged >75 which found warfarin was more effective than aspirin in preventing stroke, with no difference in haemorrhage between treatments.

The findings from the SLSR aligns with that from other studies; a study of medical records (41,250 participants) in the UK west Midlands found significantly lower primary prevention use among older people, despite advancing age being the most important risk factor for vascular disease. The SLSR did not record contraindications to the use of anticoagulation; not all of those not prescribed anticoagulants would have been eligible to receive them. Additionally, current guidelines recommend that anticoagulation is indicated only for people identified as having a high stroke risk, defined as a CHA2DS2-VASc score ≥2 for women, or ≥1 for men. Although the SLSR did not

\footnote{CHA2DS2-VASc is a score for assessing the risk of stroke in people with AF. A score is obtained by summing the following points: Congestive heart failure (1 point), Hypertension (1 point), Age (≥75=2 points), Diabetes (1 point), Vascular disease (1 point), Age (≥65=1 point), Sex (female=1 point).}
record data on all of the composite parts of this score; given the very high prevalences of those risks which were collected in the stroke population (68% were aged over 65, 50% were women, 61% had hypertension, and 18% had diabetes), it seems likely that many would be eligible for treatment by these criteria.

Research conducted in the US has found low warfarin use even among those with no contraindications.485 Barriers to anticoagulant use have been examined in three qualitative studies conducted in the US and UK; these studies suggest that clinicians attitudes play an important role in under-use of this treatment.486–488 Clinicians perceived that warfarin was associated with high rates of bleeding, particularly in the elderly, and many felt that patients would not agree to treatment. One of the studies found that very few patients took part in the decision-making process themselves, or had any understanding of the magnitude of benefits or harms.488

5.4.1 Strengths and weaknesses of this study

This study focused on risk factors in the group of people who went on to have stroke, and not risk factor prevalences in the general population. The stroke population are more likely than those without stroke to include those with inadequately managed risk factors. The results can not, therefore, be used to determine how well risk factors are managed in the population. It does, however, provide an estimate of the burden of potentially preventable disease.

All participants were asked to self-report ethnic group; this is a major strength when compared with the use of routinely collected ethnicity data from patient records, which have found to mis-classify a substantial proportion of people.489 Grouping of ethnicities was necessary in order to achieve adequate statistical power, however the size of associations found could be considered an average across the component ethnic groups. If the groups are very heterogenous, then this average may not reflect individuals well.490

This study used the Carstairs score as a proxy for socio-economic group. This is a well established metric for socio-economic status, and incorporates multiple variables. One weakness is that it is susceptible to the ecological fallacy; in other words individuals

points, 65-74=1 point), Diabetes (1 point), prior Stroke/TIA/thrombo-embolism (2 points), Vascular disease (1 point), and Female Sex (1 point)
with high socio-economic status may live in areas with low average socio-economic indicators and vice-versa. The Carstairs score, however, has the advantages of allowing very high levels of data completeness (since it is postcode based, scores were calculable for 100% of the study population), and that it encompasses multiple components of socio-economic status.

This study was population-based, with multiple notification sources, including hospitalized and community patients with stroke. Risk factor diagnoses were confirmed by reference to patient medical records in all cases. Although bias may occur through changes in documentation practice during the time period, this was mitigated by using both hospital and primary care records. This study did not collect individual blood pressure or serum cholesterol values; therefore, the results represent rates of detected risk factors and omit those who were unaware. Risk factor prevalences are susceptible to changes in diagnostic cut-offs and the idiosyncratic behaviours of individual doctors over time. UK hypertension guidelines have recommended similar cut-offs during the study period (>160/100 or >140/90 mm Hg with other risk factors)\textsuperscript{492}; diagnostic criteria for diabetes mellitus were lowered in 1999 from a fasting blood glucose ≥7.8 to ≥7.0 mmol/L. European guidelines on hypercholesterolemia were published in 1998, recommending a diagnostic cut-off of total cholesterol ≥5, or LDL cholesterol ≥3\textsuperscript{493}; subsequent revisions recommend treatment based on overall cardiovascular risk.\textsuperscript{494} The large increase in hypercholesterolemia is likely to be explained by increased detection.

5.4.2 Implications for decision-making

From a population perspective, this study indicates that a substantial proportion of stroke occurs in people with known risk factors who are not having optimal treatment prescribed. There appears to be no substantial differences associated with lower socio-economic status, ethnicity, or sex (with the exception of a small difference in hypertension treatment in black ethnic groups). Although risk factors different by ethnic group (with black ethnic groups having higher prevalence of hypertension and diabetes, and white ethnic groups having higher prevalence of prior CVD and AF), likelihood of treatment did not significantly differ by ethnicity except for hypertension, where black eth-
nic groups were modestly more likely to be prescribed treatment. These results therefore do not provide any evidence to suggest that prevention treatment decisions are being made differently in ethnic minority groups.
6

Lay perspectives on hypertension and medication taking

6.1 Introduction

Chapter 3 (Pages 93–98) described how patients frequently have an understanding of health and illness which differs substantially from the conventional biomedical description. These *lay explanatory models* were found in research by Kleinman to profoundly affect health behaviours, and often provided explanations for patient behaviours which physicians otherwise found difficult to understand.\(^{358}\) Davison and colleagues described the impact of lay explanatory models in CVD prevention in a large qualitative study in Wales; the authors concluded that the failure to take patient perspectives adequately into account had led to public health educational campaigns which were making patients less likely to engage in healthy behaviours.\(^{361}\)
In 2005, Pound and colleagues reviewed the 37 qualitative studies on medication taking in a wide range of chronic medical problems (including four studies of CVD prevention, all relating to hypertension), and found that patients often actively decided not to take medication (intentional non-adherence), rather than unintentionally omitting it. Frequent reasons for medication avoidance were concern about dependency, and a desire to avoid the feeling of having an illness. Even those who did adhere to prescribed treatment frequently self-regulated medication taking, for example, taking medication only at time of symptoms, amending the dosage to reduce side effects, or omitting doses for convenience. Most did not discuss these changes with their doctors.

As discussed in the Literature Review chapter (see Pages 44 and 67), a large number of educational interventions and decision aids have been trialled; but the effects on the quality of decision-making, adherence to treatment, and clinical outcomes have been found to be minimal. In their development, few involved patients in any way, and those which did typically used one or two expert patient authors: a process which seems unlikely to elucidate the type of information on lay explanatory models described by qualitative research.

A better understanding of patient perspectives, through qualitative research, is therefore critical: to provide an explanation of the low rates of treatment, adherence, and control, why educational interventions and decision aids have so far failed, and to inform the development of evidence-based interventions to improve management. Indeed, authors of studies of lay epidemiology suggest that clinicians’ failure to recognise how people understand disease causation and risk is one of the key obstacles to the success of public health programmes.

This chapter presents a systematic review and narrative synthesis of qualitative studies on hypertension. Specifically, I aimed to examine lay understandings about hypertension aetiology and perspectives on medication-taking. I also aimed to investigate how patient perspectives varied among different cultures and ethnic groups.

A version of this study was published in the BMJ (see Appendix A on Page 310).
6.2 Methods

6.2.1 Data sources and searches

I conducted searches of electronic databases (Medline, Embase, the British Nursing Index, Social Policy and Practice, and PsycInfo) from the database start until October 2011, and hand-searched reference lists of relevant papers. The search strategy combined established methodological terms for qualitative research, with specific terms for hypertension (see Appendix E on Page 349).

6.2.2 Study selection

I included reports of face-to-face qualitative interviews and focus groups looking at patient perspectives on hypertension and medication-taking, telephone interviews and quantitative questionnaire analyses were excluded. Studies of people with uncomplicated hypertension were included, and studies principally (over 50%) of people with existing CVD, diabetes or pregnancy were excluded. Studies were included regardless of quality.

I conducted the search and performed an initial screen of titles (as described in Chapter 4 on Page 106. Clearly irrelevant titles were excluded at this stage. The remaining abstracts were independently considered for inclusion by me, and one of my supervisors (Chris McKevitt [CMcK]). We then met to agree the final included studies, disagreements were resolved by discussion. There was no language limitation for inclusion, and translations were obtained for non-English language papers. Figure 6.1 shows a PRISMA flowchart depicting the inclusion and exclusion of papers.

6.2.3 Data synthesis and analysis

I conducted a narrative synthesis following the steps recommended by the Economic and Social Research Council (UK) (ESRC) Research Methods Programme guidance. This guidance was developed to encourage systematic and reproducible approaches to narrative synthesis and promotes transparent reporting and assessing of the robustness of the results. The guidance provides a toolbox of different methods for reviewers. Tex-
Figure 6.1: PRISMA flowchart: flow of studies through the systematic review of qualitative studies
tual summary, tabulation, and thematic analysis were used to synthesise the results, as discussed in Chapter 4. The main components of the guidance are described below.

### 6.2.4 Developing a theoretical model

The narrative synthesis guidance recommends developing a hypothesis before collecting data.\(^{443}\) The hypothesis for this study is that patient understanding and experiences of hypertension might contribute to low rates of medication adherence and blood pressure control.

### 6.2.5 Developing a preliminary synthesis, and exploring relationships in the data

A textual summary of the populations, research question, and results of the included studies was extracted using a standard template. To ensure reliability, a sample of these was checked by CMcK. Relationships in the data were and organised emerging themes using the One Sheet of Paper (osop) method,\(^{449}\) using the textual summaries and the full text of papers when needed. This thematic synthesis was conducted in duplicate and independently by me and CMcK. A final list of themes and the relationships between them was agreed by discussion and consensus. The full-text papers were then coded according to the presence or absence of themes. I tabulated these codes by country to examine similarities and variation across cultures. Qualitative research does not permit statistical inferences: the occurrence of a theme in more than one paper does not imply that it is important or frequent in the population studied. It may, however, provide a greater degree of certainty that the theme is valid, even if in a small minority of people. For this reason, I have reported the number of studies where a particular theme was found.

### 6.2.6 Assessing the robustness of the synthesis

The quality of the included papers was assessed using the checklist by Dixon-Woods presented in the earlier Methodology Chapter (see Box 4.2 on Page 4.2). I judged whether a study met each of these criteria, and summed to give a score out of 11. The use of quality assessment when reviewing qualitative research has been debated, due to the lack of
agreement among researchers about what criteria should be used, the multitude of possible qualitative methods, and the role of subjective judgement in analysis. I therefore did not exclude papers with low quality scores, but instead used the scores to provide one indicator of the robustness of the synthesis.

Two sensitivity analyses were then conducted by re-analysing the data after removing groups of studies thought to be possible sources of bias. First, I examined whether study quality affected the conclusions by assessing only the highest quality studies (excluding those scoring <9/11 from the synthesis). Second, to find if the large number of studies in ethnic minority groups had led to unrepresentative conclusions, I conducted a sensitivity analysis looking only at studies which did not focus on a specific ethnic minority groups.

6.3 Results

59 papers describing 52 qualitative studies were finally included in the review (see the PRISMA flowchart in Figure 6.1 on Page 141). The characteristics of the included studies are described in Table 6.1 on Page 144. Studies reported interviews conducted in the US (20), the UK (8), Brazil (7), Sweden (2), Canada (2), the Netherlands (2), New Zealand (2), Denmark (1), Finland (1), Ghana (1), Iran (1), Israel (1), South Korea (1), Spain (1), Tanzania (1), and Thailand (1). Forty-two studies used one-to-one qualitative interviews, nine studies used focus groups, and one used a mixture of these methods. Twenty-four of the 52 studies included people only from ethnic minority groups. Areas covered by study interviews included: patient understanding of the aetiology, effects, exacerbating factors, and consequences of hypertension, attitudes towards medication, and the perceived influences of stress, diet, and racism.
Table 6.1: Description of included studies (Lay perspectives on hypertension and medication taking; NS=Not stated)

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Study type</th>
<th>Population</th>
<th>Recruitment site</th>
<th>Targeting specific ethnic groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bane et al. 497</td>
<td>Northern Ireland</td>
<td>Focus groups</td>
<td>25 men and women aged 37–70; each prescribed 1-5 hypertension drugs</td>
<td>Six general practices</td>
<td>NS</td>
</tr>
<tr>
<td>Benson &amp; Britten 498, 499</td>
<td>England</td>
<td>Individual interviews</td>
<td>28 men and women (62% women), wide age range (reported as frequency table); 50% prescribed 1 hypertension drug, 11% prescribed 3 or more hypertension drugs</td>
<td>Urban general practice</td>
<td>NS</td>
</tr>
<tr>
<td>Beune et al. 500</td>
<td>Netherlands</td>
<td>Individual interviews</td>
<td>15 men and women (75% women) aged 35–65; all prescribed 1 or more hypertension drug in past year; range not reported</td>
<td>Inner city general practices</td>
<td>African-Surinamese</td>
</tr>
<tr>
<td>Beune et al. 181, 501</td>
<td>Netherlands</td>
<td>Individual interviews</td>
<td>46 men and women aged 35–65; all prescribed 1 or more hypertension drug, range not reported</td>
<td>Inner city general practices</td>
<td>Ghanaian, African-Surinamese, and white European</td>
</tr>
<tr>
<td>Blumhagen 502 USA</td>
<td>Individual interviews</td>
<td>117 men and women (98% men), all formerly in armed forces, aged 22–79; drug use not described</td>
<td>Primary care centre for military veterans</td>
<td>Majority white US</td>
<td></td>
</tr>
<tr>
<td>Boutain et al. 21</td>
<td>USA</td>
<td>Individual interviews</td>
<td>37 men and women aged 43–88; 89% prescribed 1 or more hypertension drug</td>
<td>Community social events and word of mouth</td>
<td>African-American</td>
</tr>
<tr>
<td>Boutain 503</td>
<td>USA</td>
<td>Individual interviews</td>
<td>30 men and women, median age 55; 83% prescribed 1 or more hypertension drug</td>
<td>Rural parish church in south Louisiana</td>
<td>African-American</td>
</tr>
<tr>
<td>Boutin-Foster et al. 504</td>
<td>USA</td>
<td>Individual interviews</td>
<td>60 men and women (92% women) aged 29–84 with poorly controlled hypertension; prescribed drugs not reported</td>
<td>General practice</td>
<td>African American</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Study type</td>
<td>Population</td>
<td>Recruitment site</td>
<td>Targeting specific ethnic groups</td>
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</tr>
<tr>
<td>Connell <em>et al.</em> 22</td>
<td>UK</td>
<td>Individual interviews</td>
<td>19 men and women aged 40–75; prescribed drugs not reported</td>
<td>Inner-city general practice</td>
<td>Black Caribbean from Jamaica, Guyana, and Trinidad</td>
</tr>
<tr>
<td>Costa &amp; Nogueira <em>505</em></td>
<td>Brazil</td>
<td>Individual interviews</td>
<td>21 people; ages and prescribed drugs not reported</td>
<td>Hypertension register from primary care clinic</td>
<td>NS</td>
</tr>
<tr>
<td>Costae <em>et al.</em> 506</td>
<td>Brazil</td>
<td>Focus groups</td>
<td>25 women; ages and prescribed drugs not reported</td>
<td>Hypertension register from primary care clinic</td>
<td>NS</td>
</tr>
<tr>
<td>Costa &amp; Nogueira <em>505</em></td>
<td>Brazil</td>
<td>Individual interviews</td>
<td>21 people; ages and prescribed drugs not reported</td>
<td>Hypertension register from primary care clinic</td>
<td>NS</td>
</tr>
<tr>
<td>dela Cruz &amp; Galang 23</td>
<td>US</td>
<td>Focus groups</td>
<td>27 men and women, ages not reported; all prescribed 1 or more hypertension drugs</td>
<td>Four health maintenance organisation primary care clinics</td>
<td>Filipino-American</td>
</tr>
<tr>
<td>Fermo <em>et al.</em> 507</td>
<td>Brazil</td>
<td>Individual interviews</td>
<td>30 men and women aged 60 and over; prescribed drugs not reported</td>
<td>Subsample of those taking part in hypertension clinical trial</td>
<td>NS</td>
</tr>
<tr>
<td>Fongwa <em>et al.</em> 376</td>
<td>USA</td>
<td>Focus groups</td>
<td>20 women aged 35–68; all prescribed 1 or more hypertension drugs</td>
<td>Inner-city free primary care clinic</td>
<td>African-American</td>
</tr>
<tr>
<td>Ford <em>et al.</em> 470</td>
<td>USA</td>
<td>Focus groups</td>
<td>25 women aged 40–74; prescribed drugs not reported</td>
<td>12 rural African methodist episcopal churches</td>
<td>African-American</td>
</tr>
<tr>
<td>Garro 508, 509</td>
<td>Canada</td>
<td>Individual interviews</td>
<td>29 men and women aged 28–79; prescribed drug not reported</td>
<td>Chronic disease register at local health centre and word of mouth</td>
<td>Ojibwe</td>
</tr>
<tr>
<td>Gascon <em>et al.</em> 510</td>
<td>Spain</td>
<td>Focus groups</td>
<td>44 men and women, ages not reported; all prescribed one or more hypertension medications</td>
<td>Patients of primary care centres, telephone screened to find non-adherent patients</td>
<td>NS</td>
</tr>
<tr>
<td>Greenfield <em>et al.</em> 511</td>
<td>USA</td>
<td>Focus groups</td>
<td>37 men and women aged 25–68, 27 of whom were prescribed 1 or more hypertension drug</td>
<td>Outpatient clinic with 21% patients uninsured, 25% covered by Medicaid</td>
<td>African-American</td>
</tr>
<tr>
<td>Greenfield <em>et al.</em> 511</td>
<td>Israel</td>
<td>Interviews</td>
<td>22 men and women aged 39–75; drug prescription not reported</td>
<td>Primary care clinic</td>
<td>Moroccan Jewish</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Study type</td>
<td>Population</td>
<td>Recruitment site</td>
<td>Targeting specific ethnic groups</td>
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<tr>
<td>Heurtin-Roberts&lt;sup&gt;512,513&lt;/sup&gt;</td>
<td>USA</td>
<td>Individual interviews</td>
<td>60 women aged 45–70; all prescribed 1 or more hypertension drugs</td>
<td>Outpatient general medical and hypertension clinics of large public hospital</td>
<td>African-American</td>
</tr>
<tr>
<td>Higgin-bottom&lt;sup&gt;273,514&lt;/sup&gt;</td>
<td>UK</td>
<td>Focus groups and interviews</td>
<td>36 men and women aged 37–82; prescribed drugs not reported</td>
<td>13 general practices with high ethnic minority populations in Midlands and north of England</td>
<td>Black caribbean</td>
</tr>
<tr>
<td>Horowitz et al.&lt;sup&gt;515&lt;/sup&gt;</td>
<td>USA</td>
<td>Focus groups</td>
<td>88 men and women, 34% aged &gt;65; prescribed drugs not reported; 36% reported to be uncontrolled</td>
<td>Outpatient clinics in four hospitals in east and central Harlem</td>
<td>African-American and Latino-American</td>
</tr>
<tr>
<td>Johnson&lt;sup&gt;516&lt;/sup&gt;</td>
<td>USA</td>
<td>Individual interviews</td>
<td>21 men and women aged 65–92 identified by their physicians as non-adherent to hypertension drugs</td>
<td>Emergency department (free blood pressure check service), and from physician’s patient lists</td>
<td>African-American</td>
</tr>
<tr>
<td>Kjellgren et al.&lt;sup&gt;517,518&lt;/sup&gt;</td>
<td>Sweden</td>
<td>Individual interviews</td>
<td>33 men and women aged 35–83; all with experience of taking 1 or more hypertension drugs at time of interview or in the past</td>
<td>Half from rural general practice; half from hypertension specialist clinic in city hospital</td>
<td>NS</td>
</tr>
<tr>
<td>Lahdenpera &amp; Kyngas&lt;sup&gt;519&lt;/sup&gt;</td>
<td>Finland</td>
<td>Individual interviews</td>
<td>21 men and women aged 32–63 engaged in trial of educational intervention, 2 of whom were prescribed 1 or more hypertension drugs</td>
<td>Participants from clinical trial of long term hypertension educational intervention</td>
<td>NS</td>
</tr>
<tr>
<td>Lee et al.&lt;sup&gt;520&lt;/sup&gt;</td>
<td>South Korea</td>
<td>Individual interviews</td>
<td>26 men and women, all reported to be non-compliant, aged from 31 to &gt;65</td>
<td>Public health centre taking part of in national hypertension initiative; private medical practices, and medical practices looking after employees of various companies</td>
<td>NS</td>
</tr>
<tr>
<td>Lewis et al.&lt;sup&gt;378&lt;/sup&gt;</td>
<td>USA</td>
<td>Focus groups</td>
<td>40 men and women aged 21–82, all prescribed 1 or more hypertension drugs</td>
<td>Through word of mouth via respected professionals and community leaders</td>
<td>African-American</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Study type</td>
<td>Population</td>
<td>Recruitment site</td>
<td>Targeting specific ethnic groups</td>
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</tr>
<tr>
<td>Lewis</td>
<td>USA</td>
<td>Individual interviews</td>
<td>21 women aged 57–86, each prescribed 1–3 hypertension drugs</td>
<td>Urban multidisciplinary care centre for elderly people principally serving low income, frail, elderly people</td>
<td>African-American</td>
</tr>
<tr>
<td>Lisper et al.</td>
<td>Sweden</td>
<td>Individual interviews</td>
<td>21 men and women, ages not reported; all prescribed 1 or more hypertension drugs</td>
<td>One urban primary health care centre</td>
<td>NS</td>
</tr>
<tr>
<td>Lukoschek</td>
<td>USA</td>
<td>Focus groups</td>
<td>42 men and women aged 33–63; separate groups for participants identified as adherent and non-adherent to drugs</td>
<td>Primary care clinic at municipal hospital serving mostly uninsured or Medicaid insured patients with low education levels</td>
<td>African-American</td>
</tr>
<tr>
<td>Machado &amp; Ca.</td>
<td>Brazil</td>
<td>Individual interviews</td>
<td>11 men and women, ages not reported; all prescribed 1 or more hypertension drug</td>
<td>Primary care</td>
<td>NS</td>
</tr>
<tr>
<td>Mohammadi et al.</td>
<td>Iran</td>
<td>Individual interviews</td>
<td>Number of people and ages unclear; all prescribed 1 or more hypertension drug</td>
<td>Recruitment site unclear</td>
<td>NS</td>
</tr>
<tr>
<td>Morecroft et al.</td>
<td>UK</td>
<td>Individual interviews</td>
<td>28 men and women aged 20–78, all prescribed 1 or more hypertension drug</td>
<td>Five general practices in East Midlands</td>
<td>NS</td>
</tr>
<tr>
<td>Morgan</td>
<td>UK</td>
<td>Individual interviews</td>
<td>60 men and women aged 35–55; 58 prescribed 1 or more hypertension drug</td>
<td>15 inner-city general practices</td>
<td>Black Caribbean and white British</td>
</tr>
<tr>
<td>Ogedegbe et al.</td>
<td>USA</td>
<td>Individual interviews</td>
<td>93 men and women, mean age 58, prescribed mean of 2 hypertension drugs, 60% reported as uncontrolled</td>
<td>Primary care practice in New York university hospital</td>
<td>African-American</td>
</tr>
<tr>
<td>Ogedegbe et al.</td>
<td>USA</td>
<td>Individual interviews (some via telephone)</td>
<td>106 men and women, mean age 56 (±13) years, prescribed mean of 2 hypertension drugs</td>
<td>Two primary care practices in New York, first with diverse population, second predominantly serving people with low income</td>
<td>African-American</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Study type</td>
<td>Population</td>
<td>Recruitment site</td>
<td>Targeting specific ethnic groups</td>
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</tr>
<tr>
<td>Panpakdee et al.</td>
<td>Thailand</td>
<td>Individual interviews</td>
<td>16 men and women aged 34–75; 96% prescribed 1 or more hypertension drug</td>
<td>University hospital outpatient clinic</td>
<td>NS</td>
</tr>
<tr>
<td>Peres et al.</td>
<td>Brazil</td>
<td>Individual interviews</td>
<td>32 men and women aged 37–81; prescribed drugs not reported</td>
<td>2 inner-city primary care clinics</td>
<td>NS</td>
</tr>
<tr>
<td>Proulx et al.</td>
<td>Canada</td>
<td>Individual interviews</td>
<td>27 man and women recruited from adherence study, each prescribed 1 hypertension drug</td>
<td>Subsample of larger clinical trial of people identified as being non-adherent</td>
<td>NS</td>
</tr>
<tr>
<td>Rose et al.</td>
<td>USA</td>
<td>Individual interviews</td>
<td>19 men aged 33–49 recruited from hypertension clinical trial</td>
<td>Subsample of larger clinical trial</td>
<td>African-American</td>
</tr>
<tr>
<td>Araujo &amp; Sadala &amp; Messias</td>
<td>Brazil</td>
<td>Individual interviews</td>
<td>21 men and women; ages and prescribed drugs not reported</td>
<td>Those attending an adult health programme</td>
<td>NS</td>
</tr>
<tr>
<td>Sångren et al.</td>
<td>Denmark</td>
<td>Individual interviews</td>
<td>17 men and women aged 34–50; prescribed 1–3 hypertension drugs</td>
<td>Four general practices</td>
<td>NS</td>
</tr>
<tr>
<td>Schoenberg et al.</td>
<td>USA</td>
<td>Individual interviews</td>
<td>41 men and women aged &gt;65; prescribed drugs not reported</td>
<td>Several local churches and local public health department clinic</td>
<td>African-American</td>
</tr>
<tr>
<td>Silva et al.</td>
<td>Brazil</td>
<td>Individual interviews</td>
<td>8 men and women; ages and prescribed drugs not reported</td>
<td>Those attending an adult health programme</td>
<td>NS</td>
</tr>
<tr>
<td>Sims</td>
<td>UK</td>
<td>Individual interviews</td>
<td>49 men and women aged 38–84; 45 of whom were prescribed 1 or more hypertension drugs</td>
<td>General practice in south of England with nurse-led hypertension clinic</td>
<td>NS</td>
</tr>
<tr>
<td>Spencer et al.</td>
<td>Ghana</td>
<td>Individual interviews</td>
<td>100 men and women; ages reported as categories from 18 to &gt;75; prescribed drugs not reported</td>
<td>Monthly hypertension clinic at Ghana Health Mission</td>
<td>MS</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Study type</td>
<td>Population</td>
<td>Recruitment site</td>
<td>Targeting specific ethnic groups</td>
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</tr>
<tr>
<td>Strahi\textsuperscript{536}</td>
<td>Tanzania</td>
<td>Focus groups and interviews</td>
<td>33 men and women in focus groups, 11 of whom were interviewed individually; prescribed drugs not reported</td>
<td>Small hypertension and diabetes clinic in city suburb</td>
<td>NS</td>
</tr>
<tr>
<td>van Wissen et al.\textsuperscript{537}</td>
<td>New Zealand</td>
<td>Individual interviews</td>
<td>19 men and women (79% women) aged 41-67; all prescribed 1 or more hypertension drug</td>
<td>Register of previous research participants from Wellington School of Medicine</td>
<td>2 Maori, rest white European</td>
</tr>
<tr>
<td>Viswanathan et al.\textsuperscript{538}</td>
<td>USA</td>
<td>Individual interviews</td>
<td>20 women, ages presented as categories from 25 to &gt;75; all prescribed 1 or more hypertension drug</td>
<td>Community health centre, Chicago</td>
<td>African-American</td>
</tr>
<tr>
<td>Wai et al.\textsuperscript{539}</td>
<td>New Zealand</td>
<td>Individual interviews</td>
<td>20 men and women; 10 reported to have poor adherence aged 41-81, all prescribed 1 or more hypertension drugs; patients with good and poor adherence identified for interview</td>
<td>Auckland general practice</td>
<td>Samoan</td>
</tr>
<tr>
<td>Weaver et al.\textsuperscript{540}</td>
<td>UK</td>
<td>Individual interviews</td>
<td>11 men and women aged 41-82 with diagnosis of hypertension in past 6 months; prescribed drugs not reported</td>
<td>2 general practices</td>
<td>NS</td>
</tr>
<tr>
<td>Wexler et al.\textsuperscript{469}</td>
<td>USA</td>
<td>Focus groups</td>
<td>26 men and women (77% women) aged 32-71; prescribed drugs not reported</td>
<td>Patients of Ohio State University primary care research centre</td>
<td>African-American</td>
</tr>
</tbody>
</table>
6.3.1 Narrative synthesis

Causes of hypertension, and the role of stress  Stress, food, being overweight, family history and alcohol were the main causes of hypertension reported by participants (see Table 6.2).

Table 6.2: Lay concepts of hypertension causation by country

<table>
<thead>
<tr>
<th>Perceived causes of hypertension</th>
<th>Countries (references)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>Brazil (^{507,527,530,533}); Canada (^{509,528}); Denmark (^{531}); Ghana (^{535}); Israel (^{511}); Netherlands (^{581},500,501) (2 studies); South Korea (^{520}); Tanzania (^{536}); Thailand (^{526}); UK (^{468,497,534}); US (^{376-378,459,469,502-504,541})</td>
</tr>
<tr>
<td>Food</td>
<td>Brazil (^{507,527,530,533}); Canada (^{509}); Israel (^{511}); Netherlands (^{500,501}); US (^{376,377,459,469,470,502,515,541}); UK (^{372,534})</td>
</tr>
<tr>
<td>Being overweight</td>
<td>Brazil (^{530,533}); Netherlands (^{501}); South Korea (^{520}); Tanzania (^{536}); UK (^{372,534}); US (^{549})</td>
</tr>
<tr>
<td>Family history</td>
<td>Canada (^{509}); Netherlands (^{500,501}); US (^{376,459,504}; Brazil (^{507,533}); South Korea (^{520}); UK (^{372})</td>
</tr>
<tr>
<td>Lack of exercise</td>
<td>Brazil (^{533}); Netherlands (^{501}); South Korea (^{520}); US (^{469,541})</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Brazil (^{533}); Canada (^{509}); Netherlands (^{501}); UK (^{468,534}; US (^{502})</td>
</tr>
<tr>
<td>Heat</td>
<td>Brazil (^{507}, Israel (^{511}); Thailand (^{520}); US (^{502})</td>
</tr>
<tr>
<td>Smoking</td>
<td>Canada (^{509}); UK (^{372} Us (^{502})</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Canada (^{509}); Tanzania (^{536})</td>
</tr>
<tr>
<td>Exposure to cold</td>
<td>Canada (^{509})</td>
</tr>
<tr>
<td>Too much water</td>
<td>US (^{502})</td>
</tr>
<tr>
<td>Over-exertion</td>
<td>Canada (^{509})</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>Canada (^{509})</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Canada (^{509})</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>Canada (^{509})</td>
</tr>
<tr>
<td>Exposure to farm chemicals</td>
<td>Canada (^{509})</td>
</tr>
<tr>
<td>Eye strain</td>
<td>Canada (^{509})</td>
</tr>
<tr>
<td>Nightmares</td>
<td>Canada (^{509})</td>
</tr>
<tr>
<td>Thick blood</td>
<td>US (^{513})</td>
</tr>
<tr>
<td>Blood rising</td>
<td>US (^{502,513})</td>
</tr>
<tr>
<td>Bad climate</td>
<td>Netherlands (^{581})</td>
</tr>
<tr>
<td>Kidneys</td>
<td>US (^{504})</td>
</tr>
<tr>
<td>Resistance to blood flow</td>
<td>US (^{504})</td>
</tr>
<tr>
<td>Heart pumping harder</td>
<td>US (^{376})</td>
</tr>
<tr>
<td>Too much blood</td>
<td>Israel (^{511})</td>
</tr>
<tr>
<td>Witchcraft/Spirits</td>
<td>Canada (^{508}; Israel (^{511})</td>
</tr>
</tbody>
</table>
Participants widely and strongly connected stress and worries with hypertension, as a cause, an exacerbating factor, and a consequence (see Table 6.2). A participant from a Dutch study appears to regard worry and blood pressure as synonymous:\textsuperscript{181}

It is the burden of my family. BP [blood pressure] is a sort of...eh. Actually it doesn’t make a difference how you call it: BP or worrying too much, it seems to be the same thing

Stress from work, unemployment, finances, and family matters were frequently mentioned as impediments to blood pressure control, both directly and indirectly. Most participants reported that stress led directly to increased blood pressure, but leading a stressful life also caused difficulties in finding time to take medication, eat well, and attend clinic appointments.

Participants from ten studies (Brazil, Iran, Sweden, US, and UK) described reducing or avoiding stress as a consequence of their diagnosis: including by relaxing, trying to avoid arguments, and changing job.\textsuperscript{181,372,377,448,459,468,507,517,523,530,534}

A difficult life with previous long-term stresses was thought to be responsible for hypertension in three studies (Ghana, and US).\textsuperscript{502,503,535} People in three US studies of African Americans, and one UK study of Black Caribbean people felt the stress of experiencing racism increased their high blood pressure.\textsuperscript{21,377,502,503,514}

A significant stressful event in the past was thought to be responsible for later hypertension by a minority of participants from four studies (Ghana, Tanzania, UK, and US),\textsuperscript{502,514,535,536} as illustrated by a UK study participant:\textsuperscript{514}

I was going through a lot of issues at work and I was going through a lot of issues around race and victimisation I was under extreme stress. So, I went to my doctor and that’s when I was diagnosed with high blood pressure.

Hypertension was seen by some participants in seven studies as a temporary or curable condition, which would not require long-term treatment (Canada, Netherlands, Thailand, US, and UK).\textsuperscript{22,181,377,448,501,526,528}
In five studies (Tanzania, UK, and US), some participants perceived hypertension to be a distinct condition from high blood pressure, highlighted by this US study participant:

"My blood just boils, and you don’t know what’s making it happen. You can’t help it. I can’t control it, I’m the kind of person who just can’t keep my mouth shut for nothing. That pertension can hit you at any time. It’s higher and stronger than with pressure. If you have pressure your blood is up, but not as high as with pertension."

Most participants understood that hypertension caused serious complications, including stroke (18 studies: Brazil, Sweden, South Korea, Thailand, UK, US), death (13 studies: Brazil, Canada, Denmark, Netherlands, Sweden, UK, and US), and heart disease (14 studies: Brazil, Sweden, UK, and US). Less widely reported complications included kidney disease (3 studies: Brazil, UK, and US), paralysis (3 studies: Canada and US), suicide (1 study, Brazil), and thinning blood (1 study, US). Awareness of possible complications was often a source of fear, as illustrated by a participant in the study from Tanzania:

"I am afraid because I have seen a friend of mine die suddenly. She was overweight and we were living with her in the same house. She woke up in the morning with no problems, ready to leave for work, we talked until the last minute. Suddenly, she fell and died on the spot."

People from five studies (South Korea, Sweden, UK, and US) described that taking medication reduced anxiety or worries. This was often thought to be both a direct physiological action of medication, but in some cases was due to feeling protected from hypertension complications. However, participants in 2 studies (Sweden and US) negatively perceived medication to function as a sedative, as illustrated by a Swedish participant:

"Well, that depends basically—no one kind of medication—some doctors give us like the—oh, sedatives out there to make you relax and go to sleep..."
that you can become addicted to. But other than that, I don’t think it’s much of a dandy, but you have to watch it once you get that sedative type.

**Symptoms and their meaning** Participants commonly (13 countries, 27 studies) reported symptoms which they connected with hypertension, particularly headache and dizziness (see Table 6.3 on Page 153). Participants in 16 of the studies reported that hypertension caused them no symptoms.

**Table 6.3: Symptoms most widely associated with hypertension**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Countries (Number of studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Brazil (4), Canada (1), Denmark (1), Ghana (1), Netherlands (2), South Korea (1), Sweden (2), UK (2), USA (8)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Brazil (3), Canada (1), Denmark (1), Ghana (1), Netherlands (1), New Zealand (1), South Korea (1), Sweden (1), Tanzania (1), Thailand (1), UK (3), USA (9)</td>
</tr>
<tr>
<td>Palpitations/racing heart</td>
<td>Brazil (3), Canada (1), Netherlands (1), Sweden (1), Tanzania (1), USA (3)</td>
</tr>
<tr>
<td>Sweating</td>
<td>Brazil (1), Canada (1), Netherlands (1), Tanzania (1), USA (3)</td>
</tr>
<tr>
<td>Tiredness</td>
<td>Brazil (3), Canada (1), Denmark (1), Ghana (1), Sweden (2), UK (1), USA (2)</td>
</tr>
<tr>
<td>Neck pain</td>
<td>Brazil (3), South Korea (1), Spain (1), USA (2)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>Brazil (2), Spain (1), Thailand (1), USA (1)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Brazil (2), Canada (1), UK (1), USA (1)</td>
</tr>
<tr>
<td>Visual changes</td>
<td>Brazil (1), Canada (1), UK (1), USA (4)</td>
</tr>
<tr>
<td>Feeling nervous/irritable</td>
<td>Brazil (2), USA (2)</td>
</tr>
</tbody>
</table>

Eleven studies (Brazil, Denmark, the Netherlands, New Zealand, Spain, Thailand, UK, and US) found a large number of participants used the presence or absence of symptoms to indicate whether their blood pressure was raised,\(^{22,181,448,468,500,504,507,510,525,531,537}\) as illustrated by a Danish participant:\(^{531}\)

When I got on medication I felt a change for the better in 14 days…the headache lifted and I felt 95 percent well…and that’s where it’s at. It hasn’t changed since then. It’s not headache, it’s a heaviness which makes you constantly aware of the fact that there is something wrong. It’s like a chunk of lead swimming around inside the head and I can feel in the teeth and in my gums and when I’m sitting quietly in a chair I can feel the pumping pressure.
Attitudes to medication-taking  Participants in nine studies, (Brazil, the Netherlands, Thailand, UK, and US), reported taking medication regularly according to the prescription.\textsuperscript{22,372,376,459,501,507,526,530,538} A belief that medication is essential is illustrated by a participant in one of the Brazilian studies:\textsuperscript{530}

It is effective if I take it every day, I can’t miss a single day.

A participant in one of the US studies described how she planned to ensure she never ran out of tablets:\textsuperscript{376}

I have to make sure I do it like two weeks in advance to make sure I get there... I let the medication get to a certain number of pills and then I’ll call them... get my medication and there won’t be a break in between me taking it.

Intentional non-adherence: Link between hypertension, stress, and symptoms
Deliberately choosing to avoid or reduce medication (intentional non-adherence\textsuperscript{368}) was a theme recurring in many of the studies. People from the Netherlands, the UK, and the US, (11 studies) reported that symptoms made them more likely to take medication, and lack of symptoms less likely to do so.\textsuperscript{22,181,372,448,500,504} People from Brazil, Denmark, the Netherlands, Thailand, UK, and the US (10 studies) reported they only took medication exclusively when symptoms were present.\textsuperscript{22,181,372,448,500,507,510,525,526,530,531}

A participant from the Thai study describes how he came to restart treatment after a period of feeling well:\textsuperscript{526}

At that period, I did not visit the doctor because I did not have any symptoms. Then I had symptoms again. I had severe headaches, so I went to a hospital ... after I took medication, my headaches were gone. I recognized that my high blood pressure had not disappeared.

A participant in the Canadian study stopped medication as he preferred to control blood pressure by reducing stress instead:\textsuperscript{528}
I dropped them. I didn’t last long with them. I said to myself, I’ll try to fix my pressure myself…I worked with doctors. They told me that I would end up having to take them but I didn’t want to…I’m not a big pill-taker.

Studies from the Netherlands, Sweden, and the UK, reported that participants perceived medication was not needed at times of reduced stress with one participant reporting that he didn’t take medication in his home country, where he felt more relaxed. A quote from the Swedish study illustrates this:

I use my blood pressure pill after how I feel. So when I’m relaxed and not under any stress like in summer when it’s nice weather and vacation, I’ve never taken any blood pressure pills.

**Intentional non-adherence: dislike of side-effects, fear of addiction**  People widely reported intentionally missing occasional doses (Canada, the Netherlands, Thailand, UK, and US) or stopping medication altogether for a period of time without informing their doctor (Canada, Denmark, Spain, Netherlands, Thailand, UK, US). Participants from Spain, the UK, and the US experimented with stopping medication, to see how they felt without it. Participants from Brazil, Canada, Spain, the UK, and the US reported that they self-adjusted their medication dose, often due to a desire to avoid side effects, or a perception that their blood pressure was controlled. A few participants in two studies (UK, and US) omitted medication when using alcohol or recreational drugs due to a fear of a harmful interaction between the two. Participants from Canada, Thailand, the UK and the US (in 10 studies) reported a fear of long term problems from taking medication. These were described as a “build up” of medication in the body, or developing a tolerance or addiction to them. A participant from a UK study describes his reluctance to take medication:

I prefer to let nature take its course as far as my body is concerned. I’m not one to introduce anything to it if I’m feeling alright. If I’m feeling ill I will take any medication that will make me better or even cure me, but if I feel
better I don’t see why I should take it, because I don’t want to be addicted to nothing other than food and water

Other adverse effects were frequently reported, including ankle swelling, lethargy, and urinary frequency. Impotence was mentioned widely by men (the Netherlands, Thailand, UK, and US) as a troublesome side-effect of treatment.23,181,372,468,499,525,526,538

**Intentional non-adherence: Alternative medicines** Participants from six countries (twelve studies) reported supplementing or replacing medication with a wide range of traditional and alternative medicines (see Table 6.4). Traditional treatments were widely perceived to be safer and more natural than pharmaceuticals.

<table>
<thead>
<tr>
<th>Country (references)</th>
<th>Alternative treatments reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil507,527</td>
<td>Avocado leaf tea, boldo tea, garlic, lemon balm, passion fruit juice, rosemary, sugar water, tea leaf chayote, water</td>
</tr>
<tr>
<td>Netherlands181,500</td>
<td>Acupuncture, bush-suporo, blanched celery, coconut bark, cucumber, garlic, garlic tea, homeopathy, neem, papaya leaf, perekese, red cotton, tamarind, prayer</td>
</tr>
<tr>
<td>Spain510</td>
<td>Lemons, nettle tea</td>
</tr>
<tr>
<td>Thailand520</td>
<td>Jorn, hed lin cheu, khin chai, meditation, pha talai</td>
</tr>
<tr>
<td>UK22,372,373,468</td>
<td>Aloe vera, banana leaf, “bitters”, “blood toner”, breadfruit leaf, cerasee, ginseng, green papaya, medina, royal jelly, sorocce tea</td>
</tr>
<tr>
<td>USA376,377,459,541</td>
<td>Acupuncture, coconut oil, garlic, ginger, guava, guava leaves, herbal teas, home brewed mango leaves, lemons, lime, lemon grass, massage, noni juice, pito-pito, poltices, prayer</td>
</tr>
</tbody>
</table>

**Non-intentional non-adherence** Participants described various external factors which limited their ability to adhere to medication (non-intentional non-adherence10) Participants from 8 studies (New Zealand, South Korea, and US) reported that other commitments meant that they were too busy to take medication or attend medical appointments.23,375,378,470,520,525,529,539 Participants from two Brazilian studies, and seven of the US studies reported they found hypertension treatment difficult to afford: the costs of medication, healthy food, and visiting doctors were all reported as barriers.375,376,459,469,470,507,515,525,529,530 Participants in three of the US studies reported that not having health insurance hindered them from accessing medical care.375,507,539
Robustness of findings  The studies were generally well reported (mean quality score 9.8/11). Sensitivity analyses were performed for the key themes (connecting hypertension with stress, having symptoms, using symptoms to judge blood pressure levels, taking medication only when symptoms present). These showed that the principal results were robust when limiting the analysis to the highest quality studies (excluding those <9/11 on the quality score), the studies not conducted in an ethnic minority group, and the studies conducted outside the US (see Table 6.5).

<table>
<thead>
<tr>
<th>Theme (group excluded)</th>
<th>Countries, studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress as cause of hypertension: Excluding studies in specific ethnic groups</td>
<td>Brazil507, 527, 530, 533; Canada528; Denmark531; Ghana535; Tanzania536; USA502</td>
</tr>
<tr>
<td>Excluding lower quality studies</td>
<td>Brazil507, 527; Canada509, 528; Denmark531; Israel511; Netherlands181, 501 (1 study); Thailand526; UK468; USA21, 376, 378, 459, 502, 503, 543</td>
</tr>
<tr>
<td>Hypertension causes symptoms: Excluding studies in specific ethnic groups</td>
<td>Brazil507, 527, 530, 533; Denmark531; Ghana535; New Zealand537; South Korea520; Spain510; Sweden517, 518; Tanzania536; Thailand526; UK499</td>
</tr>
<tr>
<td>Excluding lower quality studies</td>
<td>Brazil507, 527; Canada509; Denmark531; Netherlands181, 501 (1 study); New Zealand537; South Korea520; Spain510; Sweden517, 518 (1 study); Thailand520; UK376, 377, 448, 470, 499, 513, 529, 532</td>
</tr>
</tbody>
</table>

6.4 Discussion

This review aimed to synthesise findings from individual studies about patient perspectives on hypertension and medication-taking, and to examine whether variation exists between cultures and ethnic groups. Many participants perceived stress to be the primary cause and exacerbating factor of hypertension. Participants widely described symptoms they perceived to be caused by hypertension, particularly headache, palpitations, and dizziness. Contrary to the conclusions of individual studies, these symptoms were remarkably consistent among different ethnic and geographic groups. It is notable that these symptoms are also commonly reported as being caused by anxiety in the biomedical literature.544

Participants intentionally adjusted their medication dose, took medication sporadically and stopped altogether, often without consulting their doctor. Reasons given by participants for reducing medication included: a perception that their blood pressure
had improved because of reduced symptoms, that medication was unnecessary when under less stress, a dislike of taking medication, and a fear of addiction or tolerance, side-effects.

6.4.1 Comparison with qualitative studies in other medical conditions

A systematic review by Pound and colleagues in 2005 included 37 qualitative studies looking at medication taking in any medical condition (including four hypertension studies also reported in this review). That review also found medication was seen as undesirable, and that many participants feared dependence and tolerance. Participants frequently tested new medications for a time to check for adverse effects and whether symptoms were reduced. Our review provides confirmatory evidence from a larger number of studies that these themes are important in hypertension, and adds further themes important in hypertension specifically, particularly around stress and symptoms.

6.4.2 Comparison with the biomedical literature

Stress and symptoms The nature of the connection between hypertension and stress has been researched extensively. Acute stress has been shown to temporarily increase blood pressure levels. There is also evidence from observational studies that chronic stress can be associated with a sustained high blood pressure rise. In the medical literature, however, stress is considered in the context of other important risk factors for hypertension, both modifiable and non-modifiable: age, ethnicity, family history, obesity, a sedentary lifestyle, alcohol and salt intake. While participants in our review widely reported avoiding stressful situations, a meta-analysis of RCTs of relaxation interventions for people with hypertension found they did not substantially improve blood pressure levels. From the medical perspective, stress plays a small role in hypertension, whereas a recurring theme in the studies presented here was that stress was by far the most important cause. Likewise, the biomedical literature suggests that symptoms are more likely to be connected with anxiety and stress than blood pressure itself. Although people with hypertension have been found to report symptoms in observational
studies, these studies also found that symptoms did not coincide with periods of raised blood pressure when measured clinically. They also found that these symptoms were significantly more likely in anxious people. A larger study in the general population found the same association with nervousness, but also found no link with periods of high blood pressure.

**Adverse effects** Side-effects were a widely reported reason for self-adjusting or stopping medication. Participants in these studies described a range of adverse effects of treatment, many of which are listed in the medical literature, including leg swelling, urinary frequency, fatigue, and impotence. Other longer-term fears about the drugs including the perception of addiction, “building up” over time, or acting as sedatives, are not present in the medical literature. It is interesting that a fear of addiction is not exclusive to hypertension: qualitative studies have found that participants with other chronic medical problems reported identical views.

**Similarities among cultural, ethnic, and geographical groups** Previous studies have examined the health beliefs of specific ethnic groups; in particular, many studies have been conducted in African-American people, to explore cultural factors influencing low rates of hypertension control. The authors of many of the studies in this review conclude that specific culturally-appropriate education is needed, implying that their findings are unique in the particular population studied. However, the principal themes identified here were remarkably similar across geographic and ethnic groups. Hypertension was perceived as a symptomatic illness associated principally with stress by participants in most studies; this was confirmed in the sensitivity analyses looking at studies which were not restricted to minority ethnic groups, and in the non-US studies.

**Differences between cultural, ethnic, and geographical groups** Racism was frequently reported by participants from minority ethnic groups. The stress caused by racism was reported to exacerbate hypertension in several studies from the US of African Americans and one of Filipino Americans, and one study of people in the UK of black Caribbean ethnicity. Migrant populations also perceived that they were more likely to
have low paying jobs, and suffer greater economic hardship. African American participants from two US studies reported a lack of trust of their white doctors, perceiving them to be prejudiced against them. The UK study by Morgan and Watkins which compared the reports from Black Caribbean and White British participants, found that a large number of Black Caribbean participants reported self-adjusting and stopping medication, whereas all but one White British participant reported taking medication regularly. Although a traditional diet was mentioned as an exacerbating factor for hypertension in many studies, this did not appear to be unique to any particular group. The Dutch study by Beune and colleagues found that people of Surinamese, Ghanaian, and white European ethnicity equally felt their traditional diet worsened their blood pressure.

**Implications for clinicians and hypertension education**  The evidence presented here adds weight to the criticism of educational interventions that assume poor adherence is due to patients’ failings, either in understanding or remembering to take medication. In order to address these issues, clinicians and educational interventions must acknowledge and incorporate patient concerns and perspectives, rather than simply informing about the conventional medical view. Specifically, patients should be given an honest and accurate representation of the likelihood of adverse effects with treatment. The evidence of safety of long-term use of medication should be discussed, including that medication is not thought to ‘build up’ in the body or cause a physical dependence. Fears about addiction could be further addressed by informing patients that they are unlikely to suffer from adverse effects if they decided to stop, no matter how long they took treatment for. This is in stark contrast to existing educational interventions which emphasise the importance of continuous tablet taking. Rather than denying the possibility of symptoms, patient experiences should be acknowledged. Patients could be informed that people with hypertension often report symptoms, but they have not been found to be a reliable indication of blood pressure level fluctuations. Patients could be informed, that their risk of CVD is increased no matter if they have symptoms or not, and that treatment can effectively prevent CVD regardless of whether symptoms are
present. Stress should be placed in the context of other modifiable and non-modifiable risk factors for hypertension and CVD; it should be noted that relieving stress alone is not likely to normalise blood pressure, and that medication is recommended at times of high and low stress. Finally, there was not strong evidence that educational interventions need to be tailored to a particular cultural or ethnic group in hypertension; the consistency of the results presented here suggests that it is more important to take account of common understandings and experiences across the world. Self adjustment, titration, and stopping of medication was widespread in the qualitative studies. Though this might be interpreted as non-adherence, it might alternately be interpreted as a desire to participate in treatment decisions. Participants used cues were not aligned with the biomedical understanding of hypertension, but better clinician engagement with patient desire to self-manage might provide one route to improve hypertension control.

**Strengths and weaknesses** This study used a systematic strategy for identifying, reporting, and synthesising qualitative research. Several features suggest the results are robust. First, a large number of studies were identified, which were largely judged to be of high quality. Second, many of the themes we identified were reported repeatedly in a large number of papers. These themes did not vary substantially across different countries. Third, the results of sensitivity analyses, when the groups of papers thought possible to cause bias were removed, did not change the conclusions of the main analysis. I chose to use the ESRC guidance on narrative synthesis both as it encourages transparent reporting, and places a strong emphasis on assessing the robustness of results; the lack of both has been a criticism of other methods of synthesising qualitative research. ⁴⁵⁷ Although there has been no formal test of different synthesis methods versus each other,⁴⁵⁷ the strong evidence of themes found here and the large degree of overlap between narrative synthesis and other qualitative synthesis methodologies suggest that other the methods would have produced similar results. I made a pragmatic decision to include studies from peer-reviewed journals only, to retrieve the highest quality research. It seems likely that a body of qualitative research also exists in book chapters, university theses, and conference presentations, which was not included by
this review. Though we used no language restriction for inclusion and included some non-English language papers, those not listed on English language databases would have been missed. Certain groups were represented in the research disproportionately: nearly half of the studies looked at an ethnic minority population, and nearly half were conducted in the US. Although a potential source of bias, we did not find the themes in these papers differed substantially from those from other countries, and from studies without restriction to an ethnic group.

Conclusions for practice Lay perspectives on hypertension are often different from the medical view: people worldwide widely perceive that hypertension is principally a stress-related condition with symptoms, and fear addiction or dependence on treatment. These commonly caused people to reduce or stop medication. If they are to be successful at meeting patients’ information needs, clinicians and future educational interventions must acknowledge and address these widespread perspectives and experiences.
7

Effects of different strategies for communicating cardiovascular risk—a systematic review of randomized controlled trials and qualitative studies

7.1 Introduction

Deciding whether or not to start drug treatment to reduce the risk of CVD is an excellent example of a health decision with clinical equipoise. For a whole population, medications to reduce blood pressure and cholesterol levels are highly effective at reducing CVD rates. However, a large number of people have to be treated in order to pre-
vent each individual CVD event.\textsuperscript{554} Therefore, for most individuals, medication will not improve their health, frequently causes side effects, and changes them from a ‘healthy’ person to one who requires tablets every day, usually lifelong.\textsuperscript{368,555}

Making a decision will depend highly on the patient’s values and preferences, and depends upon how they feel about the likelihood and type of side-effects expected, their thoughts about medication taking, and the importance they attribute to the expected reduction in CVD risk.

Much of this information is statistical, but such information is notoriously difficult to communicate accurately\textsuperscript{207}. Chapter 2 reviewed the psychological literature on risk communications (Page 52); strategies shown to be effective in general include \textit{natural frequencies} with a common denominator, and charts showing risk pictorially. CVD prevention, however, has some particular challenges, including weighing risks of benefit and harm, and looking at risks which may take decades to manifest.\textsuperscript{26} Additionally, strategies unique for CVD prevention such as \textit{heart age} have been proposed and merit consideration.\textsuperscript{29}

This chapter therefore aims to systematically examine the published evidence on communicating cardiovascular risk and potential benefit from treatment. I aimed to identify RCTs examining specific risk communication strategies, and find out what their effects on patients’ satisfaction with their decisions (Decisional Conflict Scale,\textsuperscript{556}, see Box 7.1 on page 165), and on clinical outcomes including CVD rates, and level of risk factors. As patient perspectives have been shown to be particularly important influences on the success of CVD prevention strategies, I also searched for qualitative studies looking at experiences of using the strategies identified.

Two key related reviews were discussed in detail in the Literature Review chapter (Page 55), being those by Sheridan et al.\textsuperscript{220} and Waldron et al.\textsuperscript{557} Both reviews completed their searches in 2008 and were hampered by the low quality of included studies: neither was able to draw firm conclusions about how CVD risk should be communicated. This chapter seeks to benefit both from the publication of relevant RCTs published after the previous reviews, plus with the inclusion of qualitative research in order to gain insights into the reasons for the success or failure of risk communication strategies.
Decisional conflict refers to the extent someone is feeling uncertain about which course of action to take. The Decisional Conflict Scale is a validated score by O’Connor and colleagues which measures Decisional Conflict in the following domains:

1. How well informed does the participant feel?
2. How clear is the participant about which benefits and harms are most important to them?
3. How well supported does the participant feel in making the decision?
4. How uncertain does the participant feel about the decision?
5. How satisfied is the participant with the decision made?

The scale comprises 16 questions across these domains, each with a Likert scale response. The total is usually scaled to give a result from 0 to 100, though some studies use a result from 1 to 5.

Box 7.1: Description of the Decisional Conflict Scale

7.2 Methods

The protocol for the review presented in this chapter was registered at PROSPERO, registration number CRD42013005395.

7.2.1 Identifying papers

Electronic databases (Pubmed, EMBASE, Web of Science, Cochrane CENTRAL, Google Scholar) were searched from inception to October 2014 using a sensitive search strategy (see Appendix E).

As described in Chapter 4, existing qualitative search filters have poor specificity. For this reason, and since this review included both RCTs and qualitative studies, a study design filter was not used in the search. Instead, irrelevant designs were excluded manually.

Additional papers were obtained by hand searches of the bibliographies of included and other relevant papers, and searching for citing and cited papers (known as snowball

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PROSPERO is a prospective registry for systematic review protocols available at http://www.crd.york.ac.uk/PROSPERO/. The protocol of the review in chapter 6 was not registered since PROSPERO accepted registrations only after a substantial amount of work was already under way on this chapter.
sampling) using Web of Knowledge.

As a first stage, to deal with the high search yield, I performed a screen using the titles only. At this stage, I excluded only titles which were clearly irrelevant. The titles and abstracts of remaining studies were assessed against the inclusion and exclusion criteria using a standard template. To minimise error, this was done in duplicate by me and one of my supervisors (Chris McKeivitt [CMcK]). Differences were resolved by discussion. Finally, the full text papers were retrieved for relevant studies, and considered for inclusion.

7.2.2 Inclusion criteria—RCTs

Randomised controlled trials which compared cardiovascular risk communication versus usual care, and those comparing risk communication strategies versus each other were eligible for inclusion.

Trials in participants with or without prior vascular disease, and those in participants presented with individualised or hypothetical risk estimates were both included.

Eligible interventions were tools or strategies which presented the likelihood of a future vascular event. Interventions which also presented the effects of a treatment on future risk, or presented the likelihood of adverse effect from a proposed treatment were also considered eligible. Decision aids and educational interventions were eligible only if communicating cardiovascular risk was the principal component. Studies looking at surgical risk, or effects of unrelated medication (e.g. painkillers) on cardiovascular risk were excluded.

Outcomes of interest were accuracy of risk perception, decisional conflict, likelihood to take treatment, treatment use, risk factor levels, and rates of cardiovascular events.

7.2.3 Inclusion criteria—qualitative studies

Qualitative studies which looked at the perspectives of patients (with or without prior CVD), clinicians, or the general public on specified cardiovascular risk communication tools or strategies were eligible to be included. Reports of face-to-face interviews and focus groups were eligible, telephone interviews and quantitative analyses of question-
naires were excluded. Studies which looked at patient perspectives on vascular risk in an abstract way, without reference to a specific tool or communication strategy were not eligible for inclusion.

7.2.4 Data extraction

I extracted data from the included studies using a standard template for quantitative studies, and a textual summary for qualitative papers. Where papers reported relevant results graphically only, measurements were taken from an enlarged scan of the original paper using a computer raster graphics package.

7.2.5 Synthesising results

For RCT data, where comparisons and outcomes were judged sufficiently similar, results from individual trials were combined by meta-analysis. Heterogeneity was measured using the $\chi^2$ test using a cut-off of 0.1 for significance, and the $F$ test using a cut-off of 50%. Since a variety of strategies and clinical scenarios are assessed, the random effects model was used to give a more conservative estimate of precision, even where there was no statistical heterogeneity. Analyses were carried out using the statistical software R using the rmeta package.\(^{480}\)

Where comparisons and outcomes were reported by a single paper, I have reported the results narratively.

For the qualitative data, I carried out a narrative synthesis following the steps recommended by the Economic and Social Research Council (UK) (ESRC) research methods programme guidance.\(^{443}\) This was developed to encourage systematic and reproducible approaches to narrative synthesis and promotes transparent reporting and the assessment of the robustness of the results. The guidance provides a toolbox of different methods for reviewers. I used textual summary, tabulation, and thematic analysis to synthesise the results, as described in detail in Chapter 4.

Emerging themes were extracted and organised using the One Sheet of Paper (OSOP) method\(^{449}\), using the textual summaries and the full text of papers when needed. To increase rigour, this stage was done in duplicate and independently by both me and
CMcK. A final list of themes and the relations between them was agreed by discussion and consensus. The full text papers were then coded according to the presence or absence of themes. The small size and design of qualitative research mean it is not usually possible to draw statistical conclusions. Although the occurrence of a theme in more than one paper does not imply that it is important or common in the population studied, we used the presence of themes in multiple studies as one indicator of robustness.

7.2.6 Quality appraisal—quantitative papers

The quality of included RCTs was appraised independently by me and CMcK using the Cochrane Risk of Bias tool, and differences resolved by discussion. The Cochrane Risk of Bias tool is a method for judging the impact of common biases in RCTs on the conclusions from systematic reviews. Seven bias domains (random sequence generation, allocation concealment, blinding of participants/personnel, blinding of outcome assessment, incomplete outcome data, selective reporting of outcomes, and other) are assessed; each included RCT is judged to be at high, low, or unclear risk of bias in each domain. Studies were included regardless of quality.

The strength of evidence of the main conclusions were categorised using the Grading of Recommendations Assessment, Development and Evaluation Working Group (GRADE) criteria, which incorporated the information on study quality. GRADE provides a framework for assessing the quality of evidence from quantitative studies; evidence supporting each outcome assessed by the review is categorised using the following definitions:

- **High**: Further research is very unlikely to change our confidence in the estimate of effect
- **Moderate**: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- **Low**: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- **Very low**: Any estimate of effect is very uncertain.
7.2.7 Quality appraisal—qualitative papers

The quality of included qualitative studies was assessed using an adaptation of the Cochrane Risk of Bias tool, which is described in full in Chapter 4 on Page 112. The use of quality assessment when reviewing qualitative research has been debated owing to the lack of agreement among researchers about what criteria should be used, the multitude of possible qualitative methods, and the role of subjective judgement in analysis.\textsuperscript{561} In addition, quality checklists do not lend themselves to assessing whether qualitative studies have problems in their theoretical approach.\textsuperscript{458} Such issues are often idiosyncratic to individual studies, and we therefore discuss these in addition to the quality checklist.

For these reasons, the quality scores were used as an indicator of robustness of conclusions, and studies with low scores were not excluded.

7.3 Results

7.3.1 Characteristics of included studies

23 RCTs and four qualitative studies were included in the analysis (see figure 7.1 for PRISMA flowchart). Reasons for exclusion for selected studies (where the decision was based on a subtle deviation from the selection criteria) are presented as an appendix (see Appendix F on Page 351).

7.3.2 Methods evaluated in the studies

The studies evaluated a wide range of methods of risk communication. Vascular risk, and potential risk change with treatment were represented textually as percentages, natural frequencies, absolute risks, relative risks, numbers needed to treat, heart age, and as verbal descriptions. Graphical formats included faces charts, bar charts, and traffic lights (examples of each of these formats were presented in Chapter 2 [Figure 2.5 on Page 54]).
15,297 records identified through database searching

15,172 records excluded following title screen

25 additional records identified through other sources

15,322 records screened by title

15,172 records excluded following title screen

150 records screened by abstract

109 records excluded following abstract screen

41 full text papers obtained and screened

14 records excluded after reviewing full paper

23 RCTs included in quantitative synthesis

4 qualitative studies included in synthesis

**Figure 7.1:** PRISMA flowchart: flow of studies through the systematic review of RCTs and qualitative studies
7.3.3 Quality of studies

The results of the risk of bias assessment for the RCTs are presented in Figure 7.2 on Page 172. Most of the included studies were judged to have a low risk of bias in the domains of randomisation, allocation concealment, and presenting complete outcome data. However, most included studies were judged to be at high risk of bias in the domains of blinding of participants and personnel, and blinding of outcome assessment. Most included studies did not have a published protocol, so it was not possible to judge whether all evaluated outcomes were reported. The study by Benner & Erhardt was noted to have strong involvement of a pharmaceutical company which manufactures antihypertensives and statins; the company took part in the design, data collection, analysis, and write up of the paper.

7.3.4 RCTs comparing risk communication v usual care

Fifteen RCTs (13,036 participants) compared various risk communication strategies with usual care (see Table 7.1 on Page 173 for characteristics of these studies and description of the interventions evaluated). None of the trials with a usual care control measured the effect of risk communication on clinical outcomes directly, most measured risk factor levels or patient satisfaction outcomes.
The studies are generally of low risk of bias with the exception of the blinding domains—the intrinsic difficulty in blinding communication interventions is the most important source of bias overall.

**Figure 7.2:** Risk of bias assessment of the included RCTs.
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Participant characteristics</th>
<th>Real risk</th>
<th>Interventions</th>
<th>Type of risk communicated</th>
<th>Main outcomes</th>
<th>Follow up time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lopez-Gonzalez</td>
<td>2014</td>
<td>3151 public health workers undergoing routine employment health screen</td>
<td>yes</td>
<td>percentage risk v heart age v advice with no risk component</td>
<td>10 year CVD risk/heart age</td>
<td>blood pressure; lipid profile; exercise self-report; smoking; change in risk estimates</td>
<td>12 months</td>
</tr>
<tr>
<td>Welschen</td>
<td>2012</td>
<td>261 people with type II diabetes</td>
<td>yes</td>
<td>natural frequencies and faces charts v usual care</td>
<td>10 year CVD risk</td>
<td>appropriateness of risk perception; illness perceptions; attitude and intention to change behaviour; satisfaction with communication; anxiety about CVD</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Powers</td>
<td>2011</td>
<td>89 patients from primary care, uncontrolled hypertension</td>
<td>yes</td>
<td>bar chart v information leaflet without risk information</td>
<td>10 year CVD risk</td>
<td>risk perception and worry; risk factor knowledge; risk reduction preferences; Decisional Conflict; medication adherence; health behaviours; blood pressure</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Soureti (A)</td>
<td>2011</td>
<td>1187 people with obesity, no previous CVD</td>
<td>yes</td>
<td>heart age v web-based planning tool v combined v educational information without risk</td>
<td>heart age</td>
<td>intention to change diet; self-reported saturated fat intake</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Mann</td>
<td>2010</td>
<td>150 primary care patients with diabetes</td>
<td>yes</td>
<td>decision aid with personalised risks presented as faces chart v control printed information about dietary modification</td>
<td>10 year CHD risk, and estimate of change in risk with statin</td>
<td>appropriateness of risk perception; self-reported adherence to statins; Decisional Conflict; knowledge about heart disease and statins</td>
<td>6 months (adherence); immediately after intervention (other outcomes)</td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Participant characteristics</td>
<td>Real risk</td>
<td>Interventions</td>
<td>Type of risk communicated</td>
<td>Main outcomes</td>
<td>Follow up time</td>
</tr>
<tr>
<td>---------------</td>
<td>------</td>
<td>-----------------------------------------------------------------------------------------------</td>
<td>-----------</td>
<td>-------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Weymiller</td>
<td>2009</td>
<td>98 primary care patients with diabetes</td>
<td>yes</td>
<td>decision aid with personalised risks presented as faces chart v control printed information about dietary modification</td>
<td>10 year CHD risk, and estimate of change in risk with statin</td>
<td>knowledge, Decisional Conflict, self-reported adherence</td>
<td>6 months (adherence); immediately after intervention (other outcomes)</td>
</tr>
<tr>
<td>Benner</td>
<td>2008</td>
<td>1103 primary care patients with hypertension, estimated vascular risk &gt; 10%, and no previous CVD</td>
<td>yes</td>
<td>educational booklet with percentage absolute risk as frequencies and bar chart all compared with 'typical' risk v usual care</td>
<td>10 year CVD risk, comparison risk of 'healthy' individual</td>
<td>change in Framingham score, blood pressure, lipid levels, smoking rates</td>
<td>6 months</td>
</tr>
<tr>
<td>Krones</td>
<td>2008</td>
<td>1132 primary care patients primary or secondary prevention population</td>
<td>yes</td>
<td>computer-based risk presentation using faces chart and natural frequencies v usual care</td>
<td>10 year CVD</td>
<td>change in Framingham score, satisfaction, decisional regret</td>
<td>6 months</td>
</tr>
<tr>
<td>Grover</td>
<td>2007</td>
<td>3053 primary care, untreated dyslipidaemia 23% with CVD</td>
<td>yes</td>
<td>bar chart (primary prevention group also had heart age) v usual care</td>
<td>8 year CVD risk; estimate of change on statin, with lifestyle change, and both</td>
<td>lipid levels; blood pressure; change in CVD risk estimates</td>
<td>12 months</td>
</tr>
<tr>
<td>Maasland</td>
<td>2007</td>
<td>67 people after stroke or TIA</td>
<td>yes</td>
<td>computer educational tool with text information individualised to risk factor profiles v usual care</td>
<td>individual risk factor levels compared with ideal</td>
<td>knowledge about risk factors</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Participant characteristics</td>
<td>Real risk</td>
<td>Interventions</td>
<td>Type of risk communicated</td>
<td>Main outcomes</td>
<td>Follow up time</td>
</tr>
<tr>
<td>-----------------------</td>
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<td>-----------</td>
<td>-------------------------------------------------------------------------------</td>
<td>---------------------------</td>
<td>---------------------------------------------------------------------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>van Steenkiste&lt;sup&gt;571&lt;/sup&gt;</td>
<td>2007</td>
<td>490 primary care patients without CVD</td>
<td>yes</td>
<td>decision support tool vs usual care; risk described in words, natural frequencies and percentages, and comparison risk to others in the group</td>
<td>10 year CVD risk</td>
<td>proportion who perceived themselves at 'high' risk in absolute terms and compared with peers; 'appropriateness' of anxiety and perceived risk; self report of lifestyle changes</td>
<td>6 months</td>
</tr>
<tr>
<td>McAlister&lt;sup&gt;281&lt;/sup&gt;</td>
<td>2005</td>
<td>434 people with atrial fibrillation</td>
<td>yes</td>
<td>decision aid with audio book and visual chart communicating risks/benefits of aspirin and warfarin vs usual care</td>
<td>2 year stroke risk, risk reduction and risk of adverse effects with warfarin and aspirin</td>
<td>change in anti-thrombotic therapy; appropriateness of anti-thrombotic therapy</td>
<td>3 months</td>
</tr>
<tr>
<td>Montgomery&lt;sup&gt;283&lt;/sup&gt;</td>
<td>2003</td>
<td>217 primary care patients with newly diagnosed hypertension</td>
<td>yes</td>
<td>computerised utility assessment with risk and decision analysis vs information video and leaflet about high blood pressure vs both interventions vs neither intervention</td>
<td>CVD risk, time-frame not reported</td>
<td>Decisional Conflict; knowledge of hypertension; anxiety; antihypertensive prescription</td>
<td>3 months</td>
</tr>
<tr>
<td>Man-Son-Hing&lt;sup&gt;280&lt;/sup&gt; (A)</td>
<td>1999</td>
<td>287 people with atrial fibrillation taking aspirin</td>
<td>yes</td>
<td>decision aid with audio book and visual chart communicating risks/benefits of aspirin and warfarin vs usual care</td>
<td>2 year stroke risk, risk reduction and risk of adverse effects with warfarin and aspirin</td>
<td>reported ability to make decision; adherence to this decision; knowledge, expectations; Decisional Conflict; satisfaction with decision making process</td>
<td>6 months</td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Participant characteristics</td>
<td>Real risk</td>
<td>Interventions</td>
<td>Type of risk communicated</td>
<td>Main outcomes</td>
<td>Follow up time</td>
</tr>
<tr>
<td>-------------</td>
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</tr>
<tr>
<td>Kreuter</td>
<td>1995</td>
<td>1317 primary care patients</td>
<td>yes</td>
<td>estimated risk presented graphically and numerically</td>
<td>10 year risk of death from heart attack, and death from stroke</td>
<td>change in perceived risk</td>
<td>6 months</td>
</tr>
</tbody>
</table>
Meta-analyses were conducted of the effects of CVD risk communication on risk factors from the included trials. These are presented in Forest plots in Figures 7.3–7.12, on Pages 179–188. No significant difference was found in systolic or diastolic blood pressures (difference for risk communication vs control in systolic BP –2.49, 95% CI –5.22 to 0.24; diastolic –2.02, 95% CI –4.54 to 0.5; see Figures 7.3 and 7.4). There was no difference in LDL cholesterol, but a statistically significant but small reduction in total cholesterol with risk communication (difference in total cholesterol with risk communication vs control –0.16, 95% CI –0.31 to –0.02; LDL 0.0, 95% CI –0.05 to 0.05; see Figures 7.5 and 7.6). Risk communication significantly reduced Framingham CVD risk estimates, but by less than 0.5 percentage points (absolute difference in Framingham score for risk communication vs control [%] –0.45, 95% CI –0.77 to –0.13; see Figure 7.8 on Page 184).

Communicating risk significantly improved Decisonal Conflict scores versus usual care (difference with risk communication vs control –3.3 points, 95% CI –5.14 to –1.47; scores out of 100; typical score in control group [from the weighted median trial] 18.5/100).

One trial (by Krones et al.) found risk communication significantly reduced the Decisional Regret scale at 6 months (14.7 points with risk communication vs 18.1 points with usual care; mean difference: –3.39, 95% CI –6.26 to –0.53). The Decisional Regret scale is designed to be used some time after a decision has been made, and has been found to correlate well with Decisional Conflict scores.

### 7.3.5 Heterogeneity in analyses—possible causes

All the analyses showed strongly significant heterogeneity. This seems to have been introduced by the trial by Lopez-Gonzalez et al. which was added when the search was updated in the latter stages of conducting this review (none of the analyses indicated statistical heterogeneity prior to this update, and from visual inspection of forest plots, it appears that heterogeneity is due to the difference between the Lopez-Gonzalez trial and the one by Grover).

This trial was the only one which compared heart age with usual care. A post-hoc sensitivity analysis was conducted which excluded the data from the heart age arm (see Figure 7.12 on Page 188). Excluding this data did not make any important difference to
the pooled result or heterogeneity statistics.

7.3.6 Adherence to treatment

Adherence rates were reported in 3 RCTs, but I did not pool these data due to the large differences in adherence measures used between trials. The RCT by Powers included only people already prescribed treatment and found similar adherence (measured by participant self-report) between groups at 3 months (46% with risk communication, 49% with usual care, \( P = 0.55 \), number analysed not reported). The RCT by Weymiller found 63% in each arm reported still taking statins at 3 months; of these statin users, more missed one or more doses in the usual care group (2/33 [6%] with decision aid \( \text{OR} \) 6/29 [21%] with control), OR for adherence 3.4, 95% CI 1.5 to 7.5). Man-Son-Hing (study A) found the majority adhered to their initial treatment decision by 6 months, but with no significant difference between groups (123/129 [95%] with decision aid \( \text{OR} \) 125/134 [93%] with usual care, \( P = 0.44 \)).

Data from the Steenkiste and Kreuter trials on perceived risk are not reported here further, since they report only proportions of people who perceived themselves to be at high risk without any further definition, both these trials found that risk communication did not significantly change the proportion of people who perceived themselves at increased risk. Mann reported ‘no significant difference’ in knowledge between the risk communication and control groups (numbers not reported).

7.3.7 RCTs comparing different risk communication strategies v each other

Eight RCTs (8,993 participants) compared risk communication strategies versus each other (see Table 7.2 on Page 189 for characteristics of these studies and the interventions assessed). There were no similar comparisons and outcomes across studies to allow meta-analyses to be conducted. I have therefore presented these results narratively.
**Figure 7.3:** Forest plot: change in systolic blood pressure (mean difference in mmHg); risk communication v control
Study  |  Risk communication |  Control  
--- | --- | --- 
Powers 2011 | 44  | 74.900000  | 13.266499  | 45  | 76.70 | 12.74559  | -1.80 | [-7.21; 3.61]  
Grover 2007 | 1510 | -3.800000  | 7.900000  | 1543 | -3.60 | 7.70000  | -0.20 | [-0.75; 0.35]  
Maasland 2007 | 30  | -6.200000  | 19.939007  | 27  | -5.40 | 19.93901  | -0.80 | [-11.17; 9.57]  
Brenner 2008 | 245 | -9.900000  | 15.778000  | 233 | -7.20 | 16.12200  | -2.70 | [-5.56; 0.16]  
--- | --- | ---  
Random effects model 3698 | 2823  | -2.02 | [-4.54; 0.50]  

**Figure 7.4:** Forest plot: diastolic blood pressure (mean difference in mmHg); risk communication v control
Study | Total | Mean | SD | Total | Mean | SD | Mean difference | MD | 95% CI
--- | --- | --- | --- | --- | --- | --- | --- | --- | ---
Lopez−Gonzalez 2014 | 1869 | −0.1273016 | 0.2313356 | 975 | 0.1388240 | 0.245273 | -0.27 | [-0.28; -0.25] |
Brenner 2010 | 245 | −0.3700640 | 1.3216140 | 233 | −0.2601058 | 1.316847 | -0.11 | [-0.35; 0.13] |
Grover 2007 | 1510 | −1.5125600 | 0.8831900 | 1543 | −1.4115500 | 0.916860 | -0.10 | [-0.16; −0.04] |
Maasland 2007 | 30 | −1.1000000 | 2.6330000 | 27 | −1.6000000 | 2.633000 | 0.50 | [-0.87; 1.87] |

Random effects model | 3654 | 2778 | Mean differenc | MD | 95% CI
--- | --- | --- | --- | --- | ---
Heterogeneity: $I^2$=88.6%, $\tau^2$=0.0124, $p<0.0001$

**Figure 7.5:** Forest plot: serum total cholesterol (mean difference; all results converted to mmol/L); risk communication v control
<table>
<thead>
<tr>
<th>Study</th>
<th>Risk communication</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grover 2007</td>
<td>1510 -1.32608 0.764050</td>
<td>1543 -1.32608 0.769230</td>
</tr>
<tr>
<td>Maasland 2007</td>
<td>30 -1.20000 2.821558</td>
<td>27 -1.40000 2.821558</td>
</tr>
</tbody>
</table>

Random effects model 1540

Heterogeneity: $I^2$-squared=0%, $\tau^2$-squared=0, $p=0.7895$

Mean difference

<table>
<thead>
<tr>
<th></th>
<th>MD</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk comm</td>
<td>0.0</td>
<td>[-0.05; 0.05]</td>
</tr>
<tr>
<td>Control</td>
<td>0.2</td>
<td>[-1.27; 1.67]</td>
</tr>
</tbody>
</table>

Figure 7.6: Forest plot: serum LDL cholesterol (mean difference in mmol/L); risk communication vs control
Study Maasland 2007
Risk communication
Total 30 Mean 0 SD 2.069
Control
Total 27 Mean 0.3 SD 2.069

Mean difference
MD 0.3
95% CI [1.38; 0.78]

Favours risk communication
Favours control

**Figure 7.7:** Forest plot: body mass index (mean difference in kg/m$^2$); risk communication v control
**Figure 7.8:** Forest plot: Framingham CVD risk estimates (mean difference in % risk over 10 years, analyses for Framingham total risk, and for heart disease and stroke specific risks); risk communication v control
**Figure 7.9:** Forest plot: Decisional conflict score (mean difference in scores, all scaled as scores out of 100 [some papers reported scores out of 5]); risk communication v control
<table>
<thead>
<tr>
<th>Study</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Fixed effect model</th>
<th>Random effects model</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediately after intervention</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montgomery 2003</td>
<td>87</td>
<td>34.8</td>
<td>10.3</td>
<td>97</td>
<td>36.8</td>
<td>13.8</td>
<td>0.16 [0.45; 0.13]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Welschen 2012</td>
<td>108</td>
<td>32.4</td>
<td>11.4</td>
<td>112</td>
<td>34.7</td>
<td>10.9</td>
<td>0.21 [0.47; 0.06]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fixed effect model</td>
<td>195</td>
<td>34.4</td>
<td>11.2</td>
<td>209</td>
<td>36.8</td>
<td>13.8</td>
<td>0.19 [0.38; 0.01]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random effects model</td>
<td>195</td>
<td>34.4</td>
<td>11.2</td>
<td>209</td>
<td>36.8</td>
<td>13.8</td>
<td>0.19 [0.38; 0.01]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months follow up</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Montgomery 2003</td>
<td>77</td>
<td>0.3</td>
<td>10.9</td>
<td>83</td>
<td>2.2</td>
<td>11.1</td>
<td>0.17 [0.14; 0.48]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Welschen 2012</td>
<td>102</td>
<td>34.1</td>
<td>11.2</td>
<td>102</td>
<td>33.9</td>
<td>11.7</td>
<td>0.02 [0.26; 0.29]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fixed effect model</td>
<td>179</td>
<td>34.0</td>
<td>11.2</td>
<td>185</td>
<td>34.2</td>
<td>11.3</td>
<td>0.09 [0.12; 0.29]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random effects model</td>
<td>179</td>
<td>34.0</td>
<td>11.2</td>
<td>185</td>
<td>34.2</td>
<td>11.3</td>
<td>0.09 [0.12; 0.29]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $I^2=0\%$, $\tau^2=0$, $p=0.829$

**Figure 7.10:** Forest plot: anxiety, immediately after intervention, and at 3 months (pooled as standardised mean differences—no units); risk communication v control
<table>
<thead>
<tr>
<th>Study</th>
<th>Risk communication</th>
<th>Control</th>
<th>Standardised mean difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worry about CVD, 2 weeks</td>
<td>108 0.2 2.0</td>
<td>112 3.4 1.8</td>
<td>-1.68 [-1.99; -1.37]</td>
</tr>
<tr>
<td>Worry about CVD, 3 months follow up</td>
<td>102 0.4 1.9</td>
<td>102 3.5 1.6</td>
<td>-1.76 [-2.08; -1.43]</td>
</tr>
<tr>
<td>Worry about stroke, immediately after intervention</td>
<td>44 41.5 4.9</td>
<td>45 41.2 4.8</td>
<td>0.06 [-0.35; 0.48]</td>
</tr>
<tr>
<td>Worry about stroke, 3 months follow up</td>
<td>44 36.2 4.9</td>
<td>45 34.6 4.8</td>
<td>0.33 [-0.09; 0.75]</td>
</tr>
<tr>
<td>Worry about heart disease, immediately after intervention</td>
<td>44 43.6 5.0</td>
<td>45 40.6 4.9</td>
<td>0.60 [0.18; 1.03]</td>
</tr>
<tr>
<td>Worry about heart disease, 3 months follow up</td>
<td>44 39.1 5.0</td>
<td>45 37.6 4.8</td>
<td>0.30 [-0.11; 0.72]</td>
</tr>
</tbody>
</table>

**Figure 7.11**: Forest plot: worry about developing cardiovascular disease, immediately after intervention and at 3 months (meta-analysed as standardised mean differences—no units); risk communication v control
Figure 7.12: Sensitivity analysis: excluding heart age intervention; systolic blood pressure (mean difference in mmHg); risk communication v control
Table 7.2: RCTs comparing different risk communication strategies versus one another; characteristics of studies. *Real risk*—participants were provided with a genuine calculation of risk using their own risk factors, compared with trials which presented participants with the risk of a hypothetical person.

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Participant characteristics</th>
<th>Real risk</th>
<th>Interventions</th>
<th>Main outcomes</th>
<th>Follow up time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>heart age v percentage absolute risk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lopez-Gonzalez</td>
<td>2014</td>
<td>3151 public health workers undergoing routine employment health screen</td>
<td>yes</td>
<td>percentage risk v heart age v advice with no risk component</td>
<td>blood pressure; lipid profile; exercise self-report; smoking; change in risk estimates</td>
<td>12 months</td>
</tr>
<tr>
<td>Souretti (B)</td>
<td>2010</td>
<td>413 people who were obese or smoked, recruited online</td>
<td>yes</td>
<td>heart age v 10 year percentage</td>
<td>perceived risk; anxiety; desire to stop smoking; desire to change immediately after intervention</td>
<td></td>
</tr>
<tr>
<td><strong>heart age v individual risk factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charlson</td>
<td>2008</td>
<td>660 people post coronary artery stenting or angioplasty</td>
<td>yes</td>
<td>heart age + potential years gained for improvements in each risk factor v listed risk factors with normal ranges</td>
<td>death; stroke; myocardial infarction; Class III-IV angina or severe ischaemia</td>
<td>2 years</td>
</tr>
<tr>
<td><strong>gain v loss frame</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carling</td>
<td>2010</td>
<td>1528 people recruited from television programme</td>
<td>no</td>
<td>10 year AR gain v 10 year AR loss v 1 year AR loss v no intervention</td>
<td>hypothetical decision to take hypertension treatment</td>
<td>immediately after intervention</td>
</tr>
<tr>
<td><strong>ARR v RRR</strong></td>
<td></td>
<td></td>
<td>no</td>
<td>ARR v RRR v NNT v years of life gained</td>
<td>Hypothetical decision to use treatment; Correlation of first decision with decision after seeing all information</td>
<td>immediately after intervention</td>
</tr>
<tr>
<td><strong>NNT, mean time to event (all), mean time to event for (subgroup)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Halvorsen</td>
<td>2007</td>
<td>1754 volunteers identified as high risk in national health survey in Norway</td>
<td>no</td>
<td>average postponement of event for population v average postponement of event for a subgroup v NNT</td>
<td>Hypothetical decision to use treatment; perceived ease of understanding</td>
<td>immediately after intervention</td>
</tr>
<tr>
<td><strong>verbal v numeric presentation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

189
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Participant characteristics</th>
<th>Real risk</th>
<th>Interventions</th>
<th>Main outcomes</th>
<th>Follow up time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knapp</td>
<td>2004</td>
<td>120 people with coronary artery disease taking a statin</td>
<td>yes</td>
<td>verbal v numeric likelihood of medication side effects</td>
<td>perceived risk of side effects, perceived severity of side effects</td>
<td>immediately after intervention</td>
</tr>
<tr>
<td>Man-Son-Hing</td>
<td>2002</td>
<td>198 people aged 60 to 80 with no AF, given a hypothetical scenario about deciding between aspirin and warfarin in someone with AF</td>
<td>no</td>
<td>quantitative (numbers + faces risk chart) v qualitative description (e.g. very low/moderate); low risk message v moderate risk message</td>
<td>Decisional Conflict, hypothetical treatment choice</td>
<td>immediately after intervention</td>
</tr>
</tbody>
</table>
Absolute risk reduction \(\times\) relative risk reduction \(\times\) number needed to treat \(\times\) estimated life prolongation  The RCT by Stovring et al. (1169 volunteers from the general population) used a four-armed design which compared the effects of absolute risk reduction (ARR), relative risk reduction (RRR), number needed to treat (NNT), and estimated prolongation of life (number of estimated additional years of healthy life) without heart attack on a hypothetical decision to start treatment.\(^5\) Information was given on hypothetical MI risk, and the effects of a fictional medication which resembled a statin.

It found that RRR led to the highest rates of decisions to take treatment (ARR 61%, RRR 73%, NNT 67%, prolongation of life 56%, significance not reported). Participants were later presented with information in all four formats and a pictorial format, to examine where initial decisions was most similar to the ‘considered’ decision. It found that decision concordance was highest with ARR (ARR 94%, RRR 91%, NNT 89%, prolongation of life 90%).

Heart age \(\times\) percentage absolute risk  The RCT by Lopez-Gonzalez (3153 people recruited from routine employer’s health check) found a small reduction in blood pressure, cholesterol, and overall estimated CVD risk with heart age compared with percentage risk, but no significant difference in BMI (systolic \(-2.1\) mmHg, 95% CI \(-2.51\) to \(-1.61\); diastolic \(-1.11\), 95% CI \(-1.47\) to \(-0.75\); total cholesterol \(-0.26\) mmol/l, 95% CI \(-0.28\) to \(-0.24\); BMI \(-0.10\), 95% CI \(-0.51\) to \(+0.31\)).\(^6\)

The RCT by Soureti (413 people who smoked or were obese by self report) compared CVD risk presented as heart age compared with a percentage risk, both using an internet tool.\(^7\) It found no significant difference in perceived risk, self reported as ‘high’, ‘medium’ or ‘low’ (\(P = 0.477\) for perceived individual risk, \(P = 0.993\) for perceived risk compared with others). It also found no significant differences in credibility, resultant worry, or perceiving information as a ‘wake up call’ between formats (79% with heart age \(\times\) 74% with percentage, \(P\) reported as \(\gg 0.05\), other statistics not reported).

Heart age plus enhanced risk factor information \(\times\) basic risk factor information  The RCT by Charlson et al. (660 people post coronary artery stenting or angioplasty) compared an enhanced heart age with basic risk factor information.\(^8\) The heart age
group received information about the number of years expected improvement in their heart age obtained by modifying risk factors. The control group received a list of their risk factor values alongside the normal biologic ranges. It found no significant difference in mortality, overall vascular events, MI, angina, or stroke between groups at 2 years (for heart age v control: mortality 4.1% v 4.4%, P = 0.83, MI 4.2% v 4.4, P = 0.8774, angina 33.0% v 28.2%, P = 0.1787, stroke 1.3% v 0.6%, P = 0.4475, overall 39.1% v 34.2%, P = 0.23).

NNT v mean time to event (all) v mean time to event (for subgroup) The RCT by Halvorsen et al. (1754 volunteers from the general public) compared hypothetical medication information as a mean additional time to event for all, with mean additional time to event for a high risk subgroup, and with NNT. The mean time to event for all group were told that heart attacks would be postponed by 2 months for all patients. The mean time to event for a subgroup were told that heart attacks would be postponed by 8 months for 1 in 4 patients. Consent to drug therapy was highest with NNT (NNT 93%, mean time to event [all] 69%, mean time to event [subgroup] 82%, P < 0.001).

Qualitative v quantitative risk Two RCTs compared risk presented in words versus numbers. The RCT by Man-Son-Hing et al. (198 volunteers from outpatient medical clinics with no history of AF) compared a quantitative risk presentation versus a verbal qualitative presentation of a hypothetical 2 year stroke and major haemorrhage risk for someone with AF. The quantitative presentation was natural frequencies together with a faces chart. The RCT found no significant difference in Decisional Conflict between quantitative and qualitative risk (scores scaled to 1–5: 1.8 with quantitative v 1.9 with qualitative, P=0.89). For the subgroup receiving the moderate risk message, significantly more people chose warfarin with the quantitative presentation (choices with quantitative risk: 52% aspirin, 17% warfarin, 19% none, 13% unsure; choices with qualitative risk: 64% aspirin, 8% warfarin, 4% none, 24% unsure, P = 0.01), there was no significant difference in the subgroup receiving a low-risk message.

The RCT by Knapp et al. (120 patients post MI or coronary artery surgery who were taking a statin) compared presenting information about statin side effects in a qualitative or quantitative format. It found participants perceived side effects to be more likely
with verbal risk compared with numerical risk (patient estimate of likelihood of rare side effect [pancreatitis] 18.0% with verbal risk vs 2.1% with numerical risk, P < 0.001, frequent side effect [constipation] 34.2% with verbal vs 8.1% with numerical, P < 0.001).

**Gain vs loss framing** The RCT by Carling et al. (4606 people recruited via a television programme, 1528 analysed) compared the effects of risk frames on the hypothetical likelihood to use hypertension medication. This four-armed trial compared a 10-year positive frame (i.e. expected proportion of people who would remain healthy), a 1-year positive frame, a 10-year negative frame (the expected proportion who would develop CVD), all versus no intervention. All risks were presented as natural frequencies out of 1000. Participants were asked to make a first decision after seeing a randomly allocated risk communication format. Afterwards, participants were shown all the remaining formats and asked to make a fully informed decision.

After the first format was presented, fewer people in all three risk presentation groups decided to start medication compared with no intervention, and the differences among groups were significant (56% with 10 year positive frame, 66% with 10 year negative frame, 63% with 1 year negative frame, 80% with no intervention, P < 0.001).

Those given the 1-year negative frame were least likely to change after being presented with all formats (decisions changed: 24% with 10 year positive frame, 28% with 10 year negative frame, 19% with 1 year negative frame, 34% with no intervention, significance not reported).

**7.3.8 Summary of GRADE data for main outcomes**

A GRADE assessment of the principal analyses is reported in Figure 7.13 on Page 194.

Risk communication caused either no reduction, or a small clinically insignificant reduction in blood pressure (systolic and diastolic), lipids (total cholesterol and LDL), and Framingham scores (moderate quality evidence).

Risk communication resulted in a moderate reduction in Decisional Conflict scores (moderate quality evidence).

The effect of risk communication on patient anxiety, disease specific worry, perceived
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Studies</th>
<th>Initial score (RCT = 4)</th>
<th>Risk of Bias</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Publication bias</th>
<th>Total score</th>
<th>GRADE</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk factors</strong></td>
<td></td>
<td></td>
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<tr>
<td>Systolic BP</td>
<td>Lopez-Gonzalez, Powers, Grover, Maasland, Brenner</td>
<td>4</td>
<td>-1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>Moderate</td>
<td>a</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>Lopez-Gonzalez, Powers, Grover, Maasland, Brenner</td>
<td>4</td>
<td>-1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>Moderate</td>
<td>a</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>Lopez-Gonzalez, Grover, Maasland, Brenner</td>
<td>4</td>
<td>-1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>Moderate</td>
<td>a</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>Grover, Maasland</td>
<td>4</td>
<td>-1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>Moderate</td>
<td>a</td>
</tr>
<tr>
<td>Framingham score</td>
<td>Powers, Grover, Krones, Brenner</td>
<td>4</td>
<td>-1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>Moderate</td>
<td>a</td>
</tr>
<tr>
<td><strong>Patient reported outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decisional conflict</td>
<td>Mann, Powers, Montgomery, Man-Son-Hing</td>
<td>4</td>
<td>-1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>Moderate</td>
<td>a</td>
</tr>
<tr>
<td>Anxiety (general)</td>
<td>Montgomery, Welschen</td>
<td>4</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td></td>
<td>0</td>
<td>Very low</td>
<td>a, c, d, f</td>
</tr>
<tr>
<td>Worry (about future illness)</td>
<td>Powers, Welschen</td>
<td>4</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td></td>
<td></td>
<td>1</td>
<td>Very low</td>
<td>a, c, d</td>
</tr>
<tr>
<td><strong>Effect on patient opinions and knowledge</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perceived risk</td>
<td>Powers, Steenkiste, Kreuter</td>
<td>4</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td></td>
<td></td>
<td>1</td>
<td>Very low</td>
<td>a</td>
</tr>
<tr>
<td>Knowledge</td>
<td>Mann</td>
<td>4</td>
<td>-2</td>
<td>-1</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>Very low</td>
<td>a, b, e</td>
</tr>
</tbody>
</table>

**Comments**
- a: Risk of Bias points deducted for lack of blinding of participants, and lack of blinding of outcome assessment
- b: Directness point deducted for use of multiple and non-standardised knowledge assessment tools
- c: Directness point deducted for use of non-standardised outcome assessments for anxiety and worry
- d: Point deducted for imprecision due to small population size (<200 participants per arm)
- e: Risk of Bias points deducted for incomplete reporting of outcome data
- f: Consistency point deducted for inconsistent results from two small RCTs

Figure 7.13: GRADE assessment of studies: effects of risk communication. v no risk communication
risk, and knowledge about risk factors appears to be minimal, but this is uncertain (very-low quality evidence).

7.3.9 Qualitative studies

I included four qualitative studies, which reported individual interviews or focus group studies of patients and clinicians. Participants were interviewed after or during the demonstration of a specific risk communication tool or strategy (see Table 7.3 on Page 196).
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Setting</th>
<th>Participant characteristics</th>
<th>Methods</th>
<th>Study question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gale</td>
<td>2011</td>
<td>UK</td>
<td>17 patients and 13 GPs</td>
<td>Semi-structured</td>
<td>Perspectives on tool for communicating cardiovascular risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>interviews</td>
<td></td>
</tr>
<tr>
<td>Hill</td>
<td>2010</td>
<td>Australia</td>
<td>319 patients and 18 GPs</td>
<td>6 focus groups</td>
<td>Perspectives and preferences for 16 graphical and textual formats for communicating cardiovascular risk</td>
</tr>
<tr>
<td>Goldman</td>
<td>2006</td>
<td>US</td>
<td>50 patients recruited from primary care clinics and newspaper adverts</td>
<td>7 focus groups</td>
<td>Perspectives and preferences for 3 graphical presentations: faces chart, bar chart AR, and bar chart of heart age</td>
</tr>
<tr>
<td>Weiss</td>
<td>2003</td>
<td>UK</td>
<td>15 people newly diagnosed as hypertensive</td>
<td>Semi-structured</td>
<td>Perspectives on shared decision making, and decision analysis tool incorporating risk (qualitative sub-study of Montgomery RCT, also included)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>interviews</td>
<td></td>
</tr>
</tbody>
</table>
A summary of the risks of bias of the qualitative studies is shown in Figure 7.14 on Page 198.
### Figure 7.14: Risk of bias assessment of the included qualitative studies

<table>
<thead>
<tr>
<th>Qualitative studies</th>
<th>Is this study qualitative?</th>
<th>Is the study context clearly described?</th>
<th>Is there evidence of researcher reflexivity?</th>
<th>Is the sampling method clear and appropriate?</th>
<th>Is the data collection method clear and appropriate?</th>
<th>Is the analysis method clear and appropriate?</th>
<th>Are the claims supported (depth, detail, and richness)?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gale 2011</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hill 2010</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Goldman 2006</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Weiss 2003</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Key:
- **+** = low risk of bias
- **-** = high risk of bias
- **?** = unclear risk of bias
One of the studies was linked to the RCT by Montgomery (reported above) and examined patient perspectives on that study’s risk communication tool.583

7.3.10 Report of qualitative thematic synthesis

Absolute risks presented were perceived as not important Several participants in two of the studies (Gale, Hill) reported feeling that the size of absolute risk estimates did not concern them. The risks presented in these studies were considered by the researchers to represent high risk.

“It was too confusing and what does it really mean, 16% of a risk, well that to me is too low, I wouldn’t do anything about that. If it said 75%, that’s different.” participant from Hill

Likewise, a participant from Gale likewise felt the risk reduction from medication was not important when described in absolute terms:

“Simple information such as a difference of 2% well it’s not worth having the patient worry about it. I suggest the doctor doesn’t tell the patient until it gets to a percentage where the difference counts and I think that is about 15, 20, 30 going up that way. I think the figures will worry the patient more unnecessarily” participant from Gale

Importance to patients of preventing cardiovascular disease Only one study (Gale) examined participants perspectives on the outcomes assessed, one participant described why preventing heart disease might not be important to him.

“I think something has got to go wrong sometime… I think if I had diabetes I would be more worried. I think it [heart attack] is quite a nice way to go-just pop your clogs!” participant from Gale

However, the vast majority of participants in this study did wish to make some efforts to prevent CVDs.
Impact of population statistics vs personal statistics, as perceived by patients  Participants in the studies by Hill, Gale, and Goldman reported that they felt some distrust of population statistics, and desired information which referred to them as individuals. Specifically, information referring to risk among a group of people (bar charts and faces charts) was regarded by participants from Goldman as ‘too dry’ and ‘too statistical’.

A participant from Goldman discussed this further:

“People are interested in themselves, it’s about them, it’s not about them in the population, it’s about them on that day and how it’s actually going to affect them at the time.”

Several participants in two studies (Goldman and Gale) were concerned about where the statistical data came from.

“You’ve got to look at other things that most people won’t look at. Is this clinical information, or is this statistical information? Have they actually ran these people through a series of physical tests to come up with these numbers? Or are they just drawing these numbers from medical records?”

“Well if you’ve been given information, it can be false I think. I think people are chancing their arms sometimes you know, with all these Professors and research, I think that on occasion they are wrong and it makes you a bit dubious you know so in my case I am going with the tried and trusted.”

One participant from Hill described being more likely to act on individual risk information.

“When you look at it that way, you may take that on board a little more for yourself rather than think, oh well, it doesn’t apply to me, I don’t need to worry. But if it’s related to you…you will own it.”

Conversely, information which described an individual risk (heart age, thermometer) was shown in the studies by Goldman and Hill. These display types were not felt to have the same problems, and many participants described that they felt motivated to take action.
“I’m worried by this, because I’m a fair way up that arrow … scared, it really impacts, I feel urgency especially being in the high red zone.” participant from Hill

“No, you ain’t gonna forget that [the age]. Those numbers [actual age and heart age] are a hell of a lot easier than the first 3 you plugged in there, the HDL, whatever the heck that is.” Participant from Goldman

One participant from Goldman agreed that heart age was impactful, but was concerned about the effect that an inaccurate heart age may have on a patient:

“But you know, you’ve got to keep in mind that it may not be accurate. So you could be reading something on there. And when you walk in to see your physician, he can tell you something a little different. Something like that would make the person probably be concerned. So when he walks in there, now his blood pressure is up. I’m concerned about the numbers that this computer is going to show you which may not be accurate. It might give you a heart attack. You know.”

Time-frame preferences Only the study by Hill examined perspectives on risk time-frames. Most participants were concerned that a 10 year time-frame was too distant, and wouldn’t encourage change. One participant felt a five year window would be more useful:

“I like to see what my risk is and I’d like to know before the five years is up so I can do something about it.” participant from Hill

One participant in the same study, however, preferred a 10 year time-frame:

“An assessment over the next ten years, I reckon it would give me more chance to plan if I had to make significant changes.” participant from Hill
7.3.11 Desire for shared decision making

Participants varied in their desire to participate in decision making. This is illustrated by a participant from one study:

"The doctor is doing his own job isn’t he? We don’t know how to cure it. He knows better than us... so you ought to listen to what he says. If I had to go and see him and he says take these tablets then I have got no choice, I should take it” participant from Gale

The authors of the Weiss study describe that one participant found the risk communication helpful in reaching a decision. The quote provided could be interpreted to mean that the participant, who was undecided, felt the decision aid made a firm recommendation rather than presenting options.

“Though I wasn’t sure until we went right through it the he put it back through on what the computer ended up with ... then I accepted the fact, you know, that it [taking tablets] was giving me a bigger chance.” participant from Weiss

One participant from the Weiss study stated that he would be content to go along with the decision made by the tool. The Weiss study examined what they describe as a ‘decision analytic decision aid’, which took the user through a series of outcomes and determined their relative preferences for each; it did produce a recommendation at the end of this process. Though this tool was designed to help patients make their own decision, this particular participant did not seem to feel the decision was his own.

7.4 Discussion

In this review, I sought to evaluate the effects of communicating CVD risk, and determine whether any particular strategy should be recommended. I also aimed to synthesise qualitative studies of CVD risk communication, and examine the possible influences of patient and clinician experiences and the outcomes reported in the quantitative papers.
There was no evidence on the effect of risk communication on the clinical endpoints of CVD or mortality. However, individual risk factor levels were near identical with risk communication and usual care, and at all time points from the time of intervention to 12 months. Given the minimal effect of risk communication on any CVD risk factor, a change in CVD or mortality rates does not seem plausible. Improved clinical outcomes are not a prerequisite for the use of risk communication. Indeed, as discussed in Chapter 3, there are moral and ethical arguments in favour of sharing risk information, even if outcomes worsen.584

The RCTs which examined different risk communication strategies were difficult to draw strong conclusions from. The eight RCTs assessed heterogeneous comparisons and outcomes, and three used a hypothetical situation (i.e. they did not recruit participants actually facing the decision). Only one of these RCTs (that by Man-Son-Hing et al.) assessed the quality of decision making using a tool such as the Decisional Conflict Score. Overall, these RCTs find effects well established in other areas of health risk communication.201 Relative risk reductions had greater impact than absolute risk reductions, negative and positive framing of the same statistic led to different outcomes, and verbal descriptions of risk were perceived as greater than the ‘equivalent’ numerical presentation. For CVD specific formats, the RCTs by Lopez-Gonzalez et al. did find that heart age significantly reduced blood pressure and total cholesterol; although the size of these reductions was modest, they were measured at a 12 month follow-up. As the trial authors note, this does appear to be an impressive effect from a communication intervention administered on a single occasion and taking less than 5 minutes. This is given some support from several participants from the qualitative studies, who described that the individualised risk formats (heart age and traffic lights) had greater presentational impact. However, there are some inconsistencies in the data collected by this RCT which reduce confidence in the results.

As discussed in the results section on Page 177, there was strongly significant heterogeneity in most of the analyses, which seemed to be introduced by the trial by Lopez-Gonzalez et al. (this trial was added after the search was updated in the latter stages of conducting this review), which found small but strongly significant improvements
in most risk factors with risk communication. As a consequence, a random effects model was used for the meta-analysis, which would tend to produce a more conservative estimate of the intervention effects. The heterogeneity did not seem to be explained by the use of heart age in this trial (this was the only trial in these analyses which used this intervention), since the sensitivity analysis without this data produced the similar results. Possible explanations for the heterogeneity include setting (this was the only trial in Spain, and the only trial which was conducted in employee health checks), and differences in the intervention used between trials.

This trial had an unusually narrow distribution of outcome values. For example, the standard deviation in the Lopez-Gonzalez trial for change in systolic blood pressure at 12 months in the control group was 3.6mmHg. Such a consistency in two blood pressure measurements taken 12 months apart seems intuitively unlikely, and is discrepant with the SD of 13.2mmHg for the same outcome and time-point in the similarly sized trial by Grover; a similar pattern was observed in analyses of all outcomes which included this trial. I corresponded with the trial’s lead author who rechecked the original dataset and responded that the published values were correct, and confirmed that the values were correct standard deviations, and not standard errors (which is a common explanation for such a discrepancy). Incongruent distributions such as this have been associated with problems in trial conduct, and may indicate problems in the quality of data collection, or even falsified data. Whether this trial is a genuine outlier, or whether there are undetected problems in the way that it measured blood pressure is unclear. The small standard deviation has the effect of affording the the trial a large weight in the analysis. The results of the analyses are likely to be robust nonetheless, the size of absolute differences between the Lopez-Gonzalez trial and the other trials was small, but addition of this trial did move some outcomes from showing no significant difference to a small significant improvement.

Fears that communicating risk information may lead to worse health outcomes are not supported by these results. However, nor do they find a substantial improvement

\[The\ value\ is\ also\ discrepant\ with\ the\ SD\ of\ the\ change\ in\ systolic\ blood\ pressure\ across\ individual\ arms\ in\ 24\ RCTs\ from\ the\ Cochrane\ review\ on\ first\ line\ drug\ treatments\ for\ hypertension\ (SD\ range\ 11–23\ mmHg\ for\ systolic\ pressure)\]
in Decisional Conflict scores. Some explanations for the failure of CVD risk communication to produce improvements in outcomes may be found in the interview studies. The absolute improvement in CVD risk obtained with treatment was widely felt to be unimportant. The relative and individualised risks were perceived to have greatest impact. But it is population absolute risks which have been found to have the greatest transparency and fidelity, and have gained widespread uptake in decision aids and risk communication guidance. Most interventions were trialled in the context of decisions to start medication for individual risk factors. In the context of medications which produce small absolute risk reductions for any individual (particularly for those found to have a low or medium baseline risk), this lack of effect is perhaps not surprising.

The results of one of the interview studies suggest a paradox in risk time-frames. Some interviewees felt a shorter time-frame would be more likely to produce a change in behaviour, looking at CVD risk 10 years away was perceived as too distant to contemplate. However, reducing the period assessed to, say, 5 years would reduce the small absolute risk reductions further. US guidance recommends the use of lifetime risk assessments for those aged 20 to 59 not at high 10-year risk, which produces in a larger percentage risk. I found no trial evidence evaluating this strategy. Given the results of the qualitative study, the possibility that longer term outcomes produce less incentive for behaviour change should be considered.

The RCT data enabled precise estimates of the effects of risk communication on risk factors, and the included studies were generally of good quality. The qualitative data, though of good quality, was limited in quantity and scope which may limit its generalisability. Further qualitative studies around patient perspectives on cardiovascular risk are needed to confirm the findings here, and to find if they are repeated in different populations.

In practice, communicating CVD risk should not be seen in itself to be a useful intervention for improving clinical outcomes. However, risk communication in this context may modestly improve patient satisfaction with their decisions, and clinicians need not fear that allowing patients more involvement in decision making will lead to worse outcomes. For future research, the qualitative studies presented here demonstrate that
patients may have different perspectives on risk communication strategies to their clinicians. A deeper understanding of patient perceptions and preferences could help optimise the presentation of specific risk communication components.
8.1 Introduction

The systematic review in Chapter 6 demonstrated that patients with hypertension often have views and experiences of hypertension which widely differ from the biomedical view; particularly around the role of stress and symptoms. This echoed the findings of the research on lay epidemiology by Davison and colleagues described on Page 94, where ‘coronary candidates’ (those regarded as at risk of heart disease) did not match the epidemiological view. However, existing qualitative studies (as reviewed in Chapters 2, 3 and 6) have largely examined the concept of CVD risk in a binary way (for example, the study by Davison and colleagues investigated reasons participants perceived themselves to be at risk or not). This contrasts with probabilistic sense of risk, as used in CVD risk estimation algorithms, decision aids, and being the approach widely recommended by CVD guidelines (as reviewed in Chapter 2).
Despite the wealth of psychological research into how best to communicate risk probabilities (reviewed on Page 52), most studies have focused on ease of understanding, and the accuracy by which recipients perceive risk afterwards. In practice, most of the studies evaluated risk understanding by asking participants to answer a hypothetical question. For example Schwartz et al., after giving study participants risk information on mammography in various formats, asked them to estimate, out of 1000 women like them, how many would die from breast cancer if they were, and were not screened.

A number of small-scale quantitative surveys have been published which attempt to examine the accuracy of patients’ risk perception in CVD. These studies all collected risk factor data and calculated a risk score for each participant (typically the 10-year risk estimate of CVD). Participants were then asked to estimate their own probability of developing CVD as a percentage; participants who guessed close to the algorithm estimate were said to be accurate.

However, asking participants to report risk in this way poses some difficulties. First, as discussed on Page 62, the risk of developing CVD may be regarded as a single event probability, that is, patients will either develop the condition or not. The risk scores described in Chapter 2 (Page 37) in reality describe the average risk across a population; but such population risks have been shown to be very frequently misunderstood when applied to individuals. Second, this approach assumes that being able to repeat a statistic with fidelity demonstrates understanding. However, it would be entirely possible for a study participant to remember and recall a risk percentage (and the risk communication thus being said to be successful), yet without grasping the meaning in terms of their personal likelihood of developing CVD. Patient perspectives on the context and meaning of CVD risk, and the implications of these for health decisions and behaviours, have not been studied. To investigate these issues, this Chapter presents a qualitative study examining patient perspectives on future CVD risk.

This study seeks to investigate patient understandings and experiences around future CVD risk, and understand the consequences of these perspectives for risk understanding and treatment decisions. This study aims to identify areas where patient perspectives could inform future CVD risk communication strategies, which could potentially
improve their effectiveness.

Specifically, this study set out to seek patient perspectives on the following topics:

1. What do patients understand to be the consequences of hypertension?
2. What ideas do patients with hypertension have about likelihood of developing CVD?
3. What language and concepts do patients use in their discussion and understanding of risk?
4. What are patient perspectives on the effects of treatment for hypertension?
5. For patients who take medication, would they contemplate stopping? And what do they perceive or imagine the effects of stopping would be?
6. How do patients respond to example risk information, presented in a similar format to currently available decision aids?

8.2 Methods

This qualitative study comprised a series of semi-structured interviews conducted with patients from two GP practices in south London in contrasting areas.

8.2.1 Ethics

Ethical approval was sought and granted at a meeting of the Proportionate Review Subcommittee of the National Research Ethics Committee London, at Wandsworth Research Ethics Committee on 15 June 2011. Research governance approvals were granted by the NHS research and development (R&D) office in Lambeth, where both practices were situated (approval documents available in Appendix B on Page 335).

8.2.2 Eligibility criteria

I sought participants who had a diagnosis of hypertension regardless of whether they had been prescribed treatment. Participants with uncomplicated hypertension were
eligible; those with pregnancy-related hypertension, diabetes, or a previous history of any complications relating to hypertension (CVD or renal disease) were not eligible. I interviewed people with uncomplicated hypertension, since this group would have experience of being diagnosed with an asymptomatic cardiovascular risk factor and making treatment decisions, but no personal experience of complications.

**Development of the interview schedule** I piloted and refined a draft of the interview schedule at a meeting of the King’s College London (KCL) Stroke Research Patients and Family Group. As a result of this meeting I avoided using the word *risk* where possible, to avoid confusion with its alternative meaning, *hazard*, and instead used *probability*, *likelihood*, or *chances*. The group also reported that asking participants about the risk of future serious illness should not be distressing; particularly when it was made clear that I was not providing participants with new information about their own risk, merely seeking their existing ideas. The final interview schedule is provided in Appendix D on Page 346.

During the first two interviews I found it difficult to engage with the participants about risk; I felt my questions might have been too abstract. To overcome this, I developed an example decision aid (Figure 8.1 on Page 211) which I showed to participants to facilitate discussion of CVD risk. The example decision aid was given to the remaining participants towards at the end of the interview, in order to avoid biasing earlier discussions about their ideas of risk.

**Sampling strategy** This study used *purposive sampling*, which may be defined as active selection of participants who are most likely to answer the research question. This contrasts with random or probabilistic strategies which are typically used in quantitative research, and which aim to produce results which can be statistically generalised.

I aimed for a *maximum variation* sample: that is, one which included participants of a range of ages, ethnic groups, a variety of times since diagnosis, and approximately equal numbers of men and women. Such a strategy is appropriate for qualitative research, since the aim is not to analyse frequencies, but to uncover as much as possible the full range of ideas and themes which exist in a group.
Should I start a new medicine (amlodipine) for high blood pressure?

For any one person, we can’t be certain whether or not they will have a complication from high blood pressure (a stroke, a heart attack, or dying).

However, we can accurately estimate what will happen to a group of people on average.

Imagine 100 people who are similar to you (same sex, same blood pressure, cholesterol, and smoking status).

On average, over 10 years...

<table>
<thead>
<tr>
<th>if all 100 people took amlodipine</th>
<th>if all 100 did not take amlodipine</th>
</tr>
</thead>
<tbody>
<tr>
<td>19 people would die</td>
<td>22 people would die</td>
</tr>
<tr>
<td>8 people would have a stroke</td>
<td>13 people would have a stroke</td>
</tr>
<tr>
<td>9 people would have a heart attack</td>
<td>12 people would have a heart attack</td>
</tr>
<tr>
<td>15 people would get swollen ankles</td>
<td>3 people would get swollen ankles</td>
</tr>
</tbody>
</table>

Figure 8.1: Example decision aid shown in interviews to facilitate discussion about risk. This was introduced by saying, “I am going to show you some information about medication for high blood pressure as an example. It has some statistics on it which are not about you personally, and this information changes a lot from person to person. They were designed for a 64 year old man with high blood pressure who smokes.” Where the participant themselves might fit this description, I modified the hypothetical patient description to ensure the participant wouldn’t regard the information as personal to them. Data on benefits of treatment taken from Wright & Musini, adverse effects from Dougall & McLay.
At the beginning of recruitment, I had intended to conduct the research at a single GP practice in southeast London. However, after interviewing the first 10 participants, most had a high-income job, and most were retired. In order to adjust the balance of interviewees, I changed site, and completed the remaining interviews at a second GP practice located in an area with greater average socio-economic deprivation. I obtained confirmation from the Research Ethics Committee and from the local NHS R&D department that this change would not require any additional approvals. Since purposive strategies allow the researcher deliberate choice over recruitment, it is regarded as legitimate (and often good practice) to adapt recruitment strategies through the course of the study.592

Practically, the sampling strategy also needed to meet the requirements of the ethics committee, which stipulated that, as a researcher, I must not have any access to any identifiable patient-level information without explicit advance consent; this presented a challenge since a purposive strategy requires some knowledge about potential participants before deciding whether they should be invited.

The sample size was not determined a priori. In common with most qualitative studies, interviews were conducted until data saturation was reached; that is, when no new themes seemed to be arising in the analysis.396,594 In practice, I made notes and transcribed and conducted an initial analysis of data in parallel with conducting the interviews to allow this decision to be made. The two practices, and how these issues were overcome at each are described below.

**Description of the general practices** The first practice had approximately 19,000 registered patients, and was located in Gipsy Hill in southeast London. The practice was staffed by eleven GPs and four practice nurses. One of the nurses had specialised in the care of cardiovascular disease, and the care of patients with hypertension was shared between their regular GP and this one specialist nurse.

At this practice, participants were recruited as follows. A list of all patients who had a diagnosis of hypertension, but no record of previous stroke, MI, angina, pregnancy, or diabetes was generated by one of the surgery doctors via a search of the electronic
record, and an pseudo-anonymised version (containing age-group, sex, broad ethnic
group, and number of years since diagnosis) was sent to me. From this list of 1,300 can-
didates I selected 70 candidates, aiming for a maximum variance in socio-demographics
and time since diagnosis. One of the doctors from this practice sent out invitation let-
ters by post to all 70, and over the study period 32 returned response slips indicating
willingness to participate in principle. From those willing to participate, I completed
interviews with twelve, before deciding to complete the remainder of the interviews at
another practice.

The second practice had 13,000 registered patients, and was located in Kennington
in south east London. This practice comprised eight GPs and six nurses, three of whom
were nurse practitioners. This practice was selected since it was located in an area with
greater socio-economic deprivation; similar to the first practice, it had a multi-ethnic
population and cared for a large number of people with hypertension.

At this practice, in an attempt to increase recruitment of harder to reach groups (those
from ethnic minority groups, those of working age), all clinicians at the surgery were
asked to identify potential participants from their surgery list, tell them about the study,
and ask if they would be prepared to participate. I attended the practice several times
for recruitment, and met with clinical staff before their booked surgeries to discuss
groups I was targeting. I met with those who consented directly after their clinic ap-
pointment, and offered to conduct the interview straight away if they were willing, or
at another time if more convenient. From the second practice, twelve patients were in-
vited by their doctor to take part, and all twelve agreed to participate.

All participants were offered the choice of being visited at home for the interview, or
being interviewed at their surgery, though in practice all chose to attend the surgery.

**Conflict between role as a GP and interviewer** The dual role of a clinician as a re-
searcher may affect participant responses, and make maintaining impartiality as a re-
searcher difficult. In the case of this study, I was concerned that participants who
were aware I am a GP would be less likely to talk openly about medication non-adherence,
and about views they may perceive I would disapprove of as a doctor.
In order to minimise this as much as possible, I dressed casually for the interviews, and introduced myself as a student. For convenience, the interviews were conducted in the participants own GP practices in a non-clinical room, and I arranged chairs so they did not resemble a typical doctor-patient set up.

However, the ethics committee asked that I note on the information leaflet which was sent out initially (usually several weeks before the interview) that I was also a doctor who didn’t work in the practice. Additionally, a partner in the first practice had discussed with two of the participants that they would be interviewed by another GP. The consent form did make clear, however, that no information would be communicated to their own doctor, and I reiterated this in the interviews.

It is possible, nonetheless, that participants were reticent to talk openly about non-adherence to prescription medication or alternative treatments in this context.

8.2.3 Data capture and coding

Interviews were audio recorded, and transcribed verbatim. Data were managed and coded using the Dedoose software package. To analyse the interview transcripts, I used the method of thematic analysis as described by Ziebland & McPherson. This can be seen as a modified version of grounded theory, where analytical categories are developed from the data, rather than defined beforehand. Specifically, the interview transcripts were coded line-by-line using Dedoose. I did not use a fixed code list, but rather developed codes iteratively, with new codes added as needed to describe the themes found in the interview text.

Dedoose allows hierarchies of codes to be used. For example, where a participant described that they made sure to take all tablets as prescribed since a friend had a stroke, this could be coded with a top-level code of ‘adherence to medication’, with sub-codes of ‘factors promoting adherence’, and ‘knowing others who developed complications’. These codes and sub-codes allow the generation of custom reports, where all pertinent text snippets across the interviews can be retrieved. Each report contains the full range of experiences relating to a top-level theme from the interviewees.

Finally, these reports were used to produce a final analysis, in which connections and
groupings between themes can be made. Ziebland describes this as the One Sheet of Paper (OSOP) method,\textsuperscript{449} in which the issues from report texts are identified in depth, and written down on a single (often large) sheet of paper together with a code identifying the participant. The researcher can place themes in closer proximity to others which appear to be related. By doing this iteratively, a map of the themes develops, and lines can be drawn in to represent the connections. The output of this stage is a map of concepts and their relationships, from which the supporting evidence (the relevant text snippets) may be retrieved.

The small sample size, variation in the exact content of the interviews, and the sampling strategy mean that this study is not able to draw statistical conclusions about how frequently themes might occur in the general population. To avoid drawing unfounded conclusions, and in common with other similar studies, exact proportions of participants describing each theme are not described; instead terms such as ‘few’, ‘many’, and ‘some’ are used.\textsuperscript{449}

\section*{8.3 Results}

\subsection*{8.3.1 Characteristics of participants}

A total of 24 interviews were conducted, and a description of the study population is given in Table 8.1 on Page 216.

Participants were aged from 51 to 90, with 46\% male. 54\% were born in the UK, the remainder were born in Africa (21\%), the Caribbean (13\%), France, Ireland, and the USA (each 1 participant [4\%]). Self reported ethnicity was 54\% white British, 13\% white other, 21\% black African, 13\% black Caribbean. Participants were diagnosed with hypertension between 2 months and 33 years prior to the interview. Twenty-two participants were prescribed regular medication (with varying levels of adherence). One participant had taken medication previously but decided to stop, and one participant was in the process of considering medication with her GP.
Table 8.1: Characteristics of participants

<table>
<thead>
<tr>
<th>Interviewee code</th>
<th>Practice code</th>
<th>Age</th>
<th>Sex</th>
<th>Occupation</th>
<th>Country of birth</th>
<th>Ethnicity</th>
<th>Time since diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>HC</td>
<td>73</td>
<td>M</td>
<td>Retired, chauffeur</td>
<td>UK</td>
<td>white British</td>
<td>5 years</td>
</tr>
<tr>
<td>B</td>
<td>HC</td>
<td>67</td>
<td>F</td>
<td>Retired, worked in public relations</td>
<td>USA</td>
<td>white US</td>
<td>3 months</td>
</tr>
<tr>
<td>C</td>
<td>PG</td>
<td>56</td>
<td>M</td>
<td>Assistant head teacher at state secondary school</td>
<td>UK</td>
<td>white British</td>
<td>19 years</td>
</tr>
<tr>
<td>D</td>
<td>PG</td>
<td>63</td>
<td>F</td>
<td>General practitioner</td>
<td>UK</td>
<td>white British</td>
<td>12 years</td>
</tr>
<tr>
<td>E</td>
<td>HC</td>
<td>65</td>
<td>M</td>
<td>Retired, train driver for London Underground</td>
<td>Barbados</td>
<td>black Caribbean</td>
<td>15 years</td>
</tr>
<tr>
<td>F</td>
<td>PG</td>
<td>78</td>
<td>M</td>
<td>Housewife, school dinner lady</td>
<td>UK</td>
<td>white British</td>
<td>5 years</td>
</tr>
<tr>
<td>G</td>
<td>PG</td>
<td>66</td>
<td>M</td>
<td>Retired, police officer</td>
<td>UK</td>
<td>white British</td>
<td>3 years</td>
</tr>
<tr>
<td>H</td>
<td>PG</td>
<td>90</td>
<td>M</td>
<td>Retired, chemist working on pharmaceuticals</td>
<td>UK</td>
<td>white British</td>
<td>33 years</td>
</tr>
<tr>
<td>I</td>
<td>HC</td>
<td>71</td>
<td>M</td>
<td>Retired management consultant</td>
<td>UK</td>
<td>white British</td>
<td>3 years</td>
</tr>
<tr>
<td>J</td>
<td>PG</td>
<td>84</td>
<td>M</td>
<td>Retired petrol chemist</td>
<td>UK</td>
<td>white British</td>
<td>6 years</td>
</tr>
<tr>
<td>K</td>
<td>PG</td>
<td>64</td>
<td>F</td>
<td>Housewife</td>
<td>France</td>
<td>white French</td>
<td>15 years</td>
</tr>
<tr>
<td>L</td>
<td>PG</td>
<td>72</td>
<td>M</td>
<td>Retired labourer and odd-job man</td>
<td>Ghana</td>
<td>black African</td>
<td>30 years</td>
</tr>
<tr>
<td>M</td>
<td>HC</td>
<td>51</td>
<td>F</td>
<td>Cleaner</td>
<td>Nigeria</td>
<td>black African</td>
<td>6 years</td>
</tr>
<tr>
<td>N</td>
<td>PG</td>
<td>79</td>
<td>F</td>
<td>Artist</td>
<td>UK</td>
<td>white British</td>
<td>5 years</td>
</tr>
<tr>
<td>O</td>
<td>PG</td>
<td>52</td>
<td>F</td>
<td>Legal assistant</td>
<td>Jamaica</td>
<td>black Caribbean</td>
<td>2 months</td>
</tr>
<tr>
<td>P</td>
<td>PG</td>
<td>75</td>
<td>F</td>
<td>Retired, psychotherapist</td>
<td>UK</td>
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<td>10 years</td>
</tr>
<tr>
<td>Q</td>
<td>PG</td>
<td>79</td>
<td>F</td>
<td>Retired, primary school teacher</td>
<td>UK</td>
<td>white British</td>
<td>30 years</td>
</tr>
<tr>
<td>R</td>
<td>HC</td>
<td>68</td>
<td>F</td>
<td>Retired, hospital canteen worker</td>
<td>UK</td>
<td>black Caribbean</td>
<td>15 years</td>
</tr>
<tr>
<td>S</td>
<td>HC</td>
<td>79</td>
<td>F</td>
<td>Retired, delivered letters in UK government</td>
<td>UK</td>
<td>white British</td>
<td>7 years</td>
</tr>
<tr>
<td>T</td>
<td>HC</td>
<td>71</td>
<td>M</td>
<td>College lecturer in building</td>
<td>Nigeria</td>
<td>black African</td>
<td>33 years</td>
</tr>
<tr>
<td>U</td>
<td>HC</td>
<td>71</td>
<td>F</td>
<td>Retired, office manager in food factory</td>
<td>Zimbabwe</td>
<td>white African</td>
<td>20 years</td>
</tr>
<tr>
<td>Interviewee code</td>
<td>Practice code</td>
<td>Age</td>
<td>Sex</td>
<td>Occupation</td>
<td>Country of birth</td>
<td>Ethnicity</td>
<td>Time since diagnosis</td>
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<td>----------------------</td>
</tr>
<tr>
<td>V</td>
<td>HC</td>
<td>64</td>
<td>F</td>
<td>Textiles trader</td>
<td>Nigeria</td>
<td>black African</td>
<td>2 years</td>
</tr>
<tr>
<td>W</td>
<td>HC</td>
<td>84</td>
<td>M</td>
<td>Retired, chemistry teacher</td>
<td>UK</td>
<td>white British</td>
<td>20 years</td>
</tr>
<tr>
<td>X</td>
<td>HC</td>
<td>75</td>
<td>F</td>
<td>Retired civil servant</td>
<td>Ireland</td>
<td>white Irish</td>
<td>20 years</td>
</tr>
</tbody>
</table>
8.3.2 Consequences of high blood pressure

A wide variety of consequences of having high blood pressure were described by participants; these could be broadly grouped as CVD consequences, and somatic consequences. Most of the participants described the possibility of developing an illness due to high blood pressure, particularly if not controlled, including stroke, heart attack, and kidney disease.

Several participants described complications as being sudden, unpredictable, and severe; many reported sudden death as an important consequence of untreated hypertension.

Several others described sudden increases in blood pressure as harmful, as illustrated by the following two quotes:

Well I mean I think it can be sort of damaging for the heart as, you know, if it really goes high. And I mean you could get a stroke, you know, number of things really.

*Quote 8.1: Interview Q*

At one point, it was extremely high, I borrowed my neighbours cuff, whatever you call it...sphyg...and er, the systolic was over 200 and I got a little frightened...

*Quote 8.2: Interview D*

Several participants described physical sensations they attributed to raises in blood pressure: these included headache and breathlessness. One participant, who attributed physical symptoms to an acute increase in blood pressure, described how the absence of physical symptoms was an important marker of good control.
I am very careful about it, I have no problem with the blood pressure. If I feel that my head will explode. I relate it with the blood pressure, the only thing I do is I sit down and relax. I breathe deeply, and then with the relaxation it’s finished, it’s happened one in three months no more.

Quote 8.3: Interview K

8.3.3 Explanations for hypertension

All participants volunteered explanations as to why their blood pressure was raised. These explanations varied widely. Most of the participants explained their hypertension by way of conventional biomedical risk factors; the majority mentioned one or more of advancing age, obesity, a family history, poor diet, and lack of exercise as contributing.

Two of the participants described a model of interacting risk factors; one described her family history of hypertension was modified by the fact she was a healthy weight:

No because it had always been very normal. I was sort of surprised in a way, I couldn’t attribute anything that I was doing any differently but I guess those things just happen. I mean certainly it does run in the family, I mean my mother had high blood pressure and my brother does but my brother is immense, he is so obese that [pause] but I always thought that was part of his problem.

Quote 8.4: Interview B

The second participant described how healthy living could offset the effects of advancing age:

So I don’t think it’s an age thing, but if you’re a person who looks after yourself you’re in a different category. A child who’s not looked after properly, who’s probably obese is probably going to have high blood pressure.

Quote 8.5: Interview O

Several of the participants who were born outside of the UK attributed their hyper-
tension to their new environment. This is illustrated by the following quotes, the first participant originally from Jamaica, the second from Nigeria:

I remember in the Caribbean, I only used to eat fish fruit and veg. I never used to eat lots of stuff that people ate like carbohydrates, rice… I never like those kind of things. And I never ate red meat. Coming here, my diet changed, you know eating lots of things I wouldn’t eat, and drinking a lot of things I wouldn’t drink.

**Quote 8.6:** Interview O

Yes those in the village they have no problem in relation to oversize. And those in the city they are cooking, it looks very attractive McDonalds, or fries, or it’s going to change, and I pity them. Because as you know if you are fat, it’s not healthy.

**Quote 8.7:** Interview T

More than half of participants identified that stress contributed to their hypertension. Stress was regarded as highly important, and for several the primary cause of hypertension. One participant, typical of several others, perceived that stressful life events were a trigger:

When I was about 50, then when my daughter was 18 to 19 going to university is when the trouble arrived. I started to have some blood pressure, some high blood pressure. With the worry of the children they tried some hashish or something like that because it was trendy to do that, it worries me, and the son didn’t take his studies seriously.

**Quote 8.8:** Interview K

Two participants felt their personality type, being someone who ‘bottles up’ emotion, as being a cause of hypertension; one of these participants felt was as a result of his upbringing:
And the stress at work and everything. The problem is I don’t actually feel stress like a normal person. I don’t think. I don’t think “ooo I’m stressed”. I think I just…don’t know what I would do…I don’t shout and scream at people. I think I’m quite…because as a young man I was trained severely to deal with stress, you know how pilots speak on aircraft, I was trained to keep it in myself. Which is probably unhealthy.

_Quote 8.9:_ Interview C

Other participants reported various sources of stress as contributing to their raised blood pressure, including stress from work, financial difficulties, and family.

### 8.3.4 Reluctance to consider future risk of illness

A large portion of the interview comprised questions about perceptions of risk. Participants were asked both if they had thought about this previously, and also asked whether they considered themselves likely or unlikely to develop a complication of hypertension in future. However, around half of participants did not provide any sort of estimate of whether they would be at risk of hypertension complications themselves, even after prompts.

Many participants expressed a desire to avoid contemplating future risk of disease. Key reasons expressed by participants included: finding the consideration of future serious illness unpleasant or stressful; perceiving that looking at future risk did not make sense due to old age; and having other active health problems which were perceived as more serious, making CVD risk less relevant.

The concept that contemplating future risk of heart disease of stroke was unpleasant is illustrated by the following quote:

> I don’t know whether I would want to know if I’m at risk of stroke, because it would be quite upsetting if I’m at high risk.

_Quote 8.10:_ Interview C

Similarly, one participant (who was aged 90) attributed his reluctance to consider
future risk to a happy life.

I tell you, it’s an amazing life. I don’t worry about ill health.

*Quote 8.11:* Interview H

One participant would only say that he prayed for a good outcome:

I don’t know. I just pray to God to give me a peaceful death. I pray to God. Not stroke. I don’t like stroke. Because when you see people who have suffered a stroke I’d prefer to die...

*Quote 8.12:* Interview T

During this part of the interviews, several participants expressed that a key benefit of maintaining good health was that they could avoid thinking about future risk. This is illustrated by one participant (who had a number of other ongoing health problems including chronic pelvic pain and arthritis), who had been reassured about the health of her heart following some investigations:

I mean I’ve had a couple of angiograms and my arteries seem to be fine, so I haven’t really gone into it. As I say, to me, it’s the least of my medical problems, I haven’t really…I don’t feel like frightening myself with stuff.

*Quote 8.13:* Interview D

Another participant described a similar benefit of a healthy lifestyle:

I have always relied on good health and good living to obviate any need to question these things.

*Quote 8.14:* Interview J

Another participant hinted that he felt saw himself as being at low risk, but also that being on medication meant he did not need to contemplate it further.
Will I get a stroke? No I don’t think I will. I haven’t considered it.
Because I’m on the medication to stop it.

*Quote 8.15: Interview C*

### 8.3.5 Response to example risk charts

All participants except one appeared to understand the risk chart’s intended meaning, and from their discussions and questions, appeared to understand the statistics presented. The exception was participant V who did not engage in discussion around the decision aid, saying only, ‘It’s good to take tablets’. At the time I had the impression she had found it difficult to understand both the text and statistical contents of the tool.

Participants were mixed in their opinion about risk estimates, with around half expressing a strong desire to have such information, and around half stated that they would not find it useful.

For one participant, contemplating future risk of CVD seemed like criticism, whereas people who were in good current health deserved praise:

> I wouldn’t be bothered with this, it just complicates things you know, it doesn’t keep things simple, I think the important thing for me is to make each of those, each one of us has been made responsible for our own body and I think the medical profession could do a great deal to help with that, making people be proud of their bodies perhaps, they’re always very critical of our bodies, “you’re too fat, you’re too thin, you’re too this”, instead of saying you know, I’ve not had one doctor say to me, “you know, you’ve done a marvellous job, you’re seventy-five years old, you’re as healthy and as well as you are, you’re keeping your life”

*Quote 8.16: Interview P*

Several participants expressed surprise at the content of the risk tool, explaining that they expected medication to have a bigger effect. This is illustrated by one participant, who expected that medication would abolish the risk of stroke altogether:
I like the statistical evidence. Is this factual?

*Well it’s factual, but it represents a typical person… How effective the medicine is varies quite dramatically from person to person…*

I was given the impression that it was ‘take that and you’ll be fine’ ‘take that and you won’t have a stroke…’ but not according to this [pointing at example tool]…

**Quote 8.17:** Interview C

One participant, surprised by what she saw as a small benefit of treatment, wondered if it would lead people to stop their treatment:

In the people dying, people having a stroke and people having a heart attack, I mean I realise it’s double which is a lot but I thought it would be more like three or four times…So I tell you what it would do, is make me think oh it doesn’t seem to make all that much difference whether I take the tablet or not which, um, might you know have a…If I had side-effects from it and I saw that, I’d think well maybe it isn’t worth it or maybe it’s not worth it all the time, maybe I can skip it when I’m on vacation or something like that, that’s what it would do to me.

**Quote 8.18:** Interview B

**Moral imperative to treat hypertension**

Two participants felt that it would be better if everyone took treatment, and voiced a concern that others would choose not to have treatment due to low absolute benefits. The first of these participants, who had some experience with statistics, was concerned about whether statistics could mislead others:
he’d say “well, if there’s 2% out of a hundred”…there was a discussion this morning on the Today programme about some health issue in which…it’s all about this business of whether packages should be plain or not…and people will say “well frankly it’s only a difference of 1%, does it matter”, Well I think you get into a dangerous game and I think if you can say…even if it’s 2%, it matters, but out there I think there would be a lot of people saying “well…”.

Quote 8.19: participant I

The second participant was concerned that the risk chart, and giving the opportunity for decision-making would interfere with a moral imperative to take medication for hypertension, which he regarded as a dangerous illness.

I disagree with this, I don’t know what the numbers would be but I disagree with it because I mean I think common sense with blood pressure or no blood pressure, when we’re ill, we go to the doctor to get medication to get us better. So if you’re not taking medication depends on what we have, I don’t care what it is, it won’t have been worse, it won’t be worse, it can cause trouble. I mean you must stay at home if you had pneumonia for instance, pneumonia is a dangerous thing, you go to your doctor, you get treatment and you get better.

Quote 8.20: participant E

One participant who grew up in the USA described similar thoughts, which she attributed to exposure to advertising.
I can remember there used to be ads in the US that, because people used to have very bad side-effects from blood pressure medicine and there used to actually be ads saying, you know, “If you won’t take it for yourself, take it for your loved ones”, or something like that. I mean there were big campaigns…you know, on billboards and signs and stuff like that.

*Quote 8.21: participant B*

All participants were asked hypothetically whether the absolute benefits the example risk presentation (if they applied to them) would change their decision to take medication (since almost all took medication, this usually meant deciding to stop). None of the participants, including the two who were worried about others stopping, answered that they would stop treatment themselves.

One participant explained that, for her, even a small absolute benefit of treatment would be worth taking:

> Well yeah…cos if four people die here, and six people die here…you’d want to take the tablets. It’s about living longer isn’t it.

*Quote 8.22: Interview S*

### 8.3.6 Interpreting population risks—“I think I might be *that one*”

Several of the participants reported a pre-existing idea of whether they would, or wouldn’t develop CVD, and reported that data from risk estimates was unlikely to change that view. This certainty is illustrated by one participant, who expressed disbelief after seeing the example chart, feeling already convinced of outcome of not using blood pressure treatment:
If like me, I don’t take treatment, someone will die, not like straight away, they die, it’s not having stroke, the person will just die because…

*Do you think that would definitely happen?*

Yeah. For people that do have blood pressure, if they don’t use medicine, I’m telling you, they die, they have stroke.

*Quote 8.23: Interview M*

However, many of these participants seemed to identify with the affected part of the fraction. For example, the decision aid shown to the participant described that, if not taking amlodipine, 22 out of 100 people would expect to die. These participants thought that they would likely be one of the 22 (rather than the intended meaning, of having an equal probability of being any one of the 100). This is illustrated by one participant, using nearly identical wording to several others:

One person in a hundred is still one too many, and I’d be one of those.

*Quote 8.24: Interview U*

For several of these participants, this idea seemed to be precautionary, that is, it was preferable to them to assume they would be affected by a complication in order that they could take any necessary action to prevent it; being subtly different from truly perceiving they would certainly be affected. This is illustrated by one participant who explained the reason for this as partly precautionary (she preferred to assume to worst case, and be prepared for it), and partly since information about groups would not feel applicable to her as an individual:
Well, I think that I might be *that* one [laughs] or one of those, if I stopped taking it, that would die from it or would have a stroke, so, you know, I would rather take the tablets than take that chance. …I don’t think I would [find the statistical information useful], you know, because I’m an individual, you know what I mean? If I was in a group therapy with other people my age and we was all talking about it, it would probably be more interesting and you would get feedback from them which would make you think ‘Well maybe, he’s not a doctor but he makes common sense, you know, of what he’s saying, so I’ll go with that’, you know what I mean?

*Quote 8.25: Interview F*

However, this idea did not seem to be precautionary for all, and several participants appeared to perceive a certainty about developing, or not develop illness. Several of the participants expressed the idea that certain people are ‘stronger’, that is, more resistant to illness than others. A weak person would be susceptible to illness in general, not specifically CVD. One participant described how ‘strong’ people would be more likely to survive stroke:

> If you don’t die, because sometimes some people are strong in their body, you have stroke.

*Quote 8.26: Interview M*

Another participant (who was not taking treatment) used the same ‘strong’ and ‘weak’ terminology, perceiving that weaker people were likely to die from hypertension. He perceived himself as being likely to avoid illness, and contrasted this with his wife:
No, because straight away, statistics show, that you’ve interviewed 100 people and this is what you’ve come up with. I think there are certain people, I keep referring to me, there’s certain people who are stronger and some are weaker. You know, my wife’s very weak, she would take any tablet you gave her for anything; she wouldn’t take two a day but she’d take one a day of those tablets, you know what I mean, and if they said she had chronic whatever she would read about it and say ‘Yes, yes, I’ve got this, this sounds [like] me.

*Quote 8.27: Interview A*

One participant although not using the terminology ‘strong’ and ‘weak’, described a similar concept regarding her sister, that living an unhealthy lifestyle had led to a susceptibility to illnesses in general:

She didn’t really look after her body much. She didn’t do any exercise, it was all sitting down. And she’s had a stroke, she had a stroke before the age of 80. She’s now…she’s 82…she’s very sedentary, she’s surprisingly upbeat for having had a stroke…she’s too overweight, and so on. I just feel she’s constantly having little infections.

*Quote 8.28: Interview P*

### 8.3.7 Using peers as a reference group

Several participants talked about their risk of CVD by comparing themselves to peers or family (illustrated by Quote 8.28 above). The participant who had training in statistics reported his own risk in a similar way.
I’d say probably in the top five to ten percent of people of my age, myself, well I’ve always played sport, played rugby until I sort of got too old and too crooked and knocked and played squash ever since and golf with the occasional other bit and piece thrown in but basically always played squash, played League Squash to a reasonable standard and we gradually all got older together so we now potter around a doubles court three times a week as an excuse for a few pints!

*Quote 8.29: Interview I*

One participant explained the fact she had not developed complications from hypertension by comparing her own response to the diagnosis with that of her father-in-law’s; her own reaction included obtaining and taking medication, addressing being overweight through bariatric surgery, and keeping as active as possible.

My father in law was diagnosed as having quite high blood pressure, and he turned himself into an invalid practically, he did nothing, and it made matters worse as he died suddenly of a heart attack…So that’s a completely different reaction to mine I think.

*Quote 8.30: Interview C*

### 8.3.8 Risk factors important to individuals

Although the risk chart contained wording to state that the people represented were similar to the hypothetical patient in terms of known risk factors (age, sex, ethnic group, smoking history, and cholesterol levels), many participants expressed a view that these statistics would still not be representative of what an individual might expect.

For some of these participants, risk factors outside of what is conventionally measured were highly important, and their absence led them to see the charts as unreliable, and that they would not apply to them personally.

Several participants felt that even though a particular risk factor was described as measured, it was not accorded enough importance. This is illustrated by two partici-
pants with opposing views about their family history, who felt that risk estimates would not have given this due weight.

I always want to live longer. But it’s not in my lineage. We never suffered…just go. My senior brother just died 2 years ago. And he never had any illness until just once. My father was the same. My father lived to one-twenty years old, and I understand he never suffered any illness. But that time he just go. The same thing happened to my senior brother last time. What I have in mind about will happen to me. I’ve made up my mind that that is what will happen to me. Of course.

Quote 8.31: Interview T

Yeah, I would worry about it if I stopped the tablets. I’m worried about it, because he [her husband] was on blood pressure tablets, weren’t you, and he stopped taking them, the doctor said he could stop taking them, and I worry about that. I think, you know, can you stop taking them?

And so if, now that you’re on the tablets, and you’ve mentioned that the doctor said that your blood pressure’s been good, would you consider that a stroke is a likely or an unlikely thing to happen now, being on the tablets?

I think it probably likely.

Still probably likely?

Yeah, I think so, because I think it’s in my family, so, and I think that’s got a lot to do with it.

And do you think the tablets, how good do you feel the tablets are at preventing?

I don’t really know. I just think that by taking them, you know, it’s probably going to, it may not stop it, but it might do.

Quote 8.32: Interview F

One participant felt that the risk tool would not have taken into account his healthy lifestyle:
Yeah, but if it could be more personalized. Because I don’t smoke, I hardly drink, I mean I do drink, I’m not a monk, but it kind of goes in phases.

Quote 8.33: Interview C

Several participants went further, and since individuals are unique, questioned whether a group could ever be regarded as similar:

it does say ‘imagine a hundred people who are similar to you’ but you see, who is? no person is similar to…you know…

Quote 8.34: Interview I

It’s too vague isn’t it really, I mean, if you had a hundred people who were literally the same as me, say, it would be quite interesting…but...

Quote 8.35: Interview X

8.3.9 The doctor knowing a patient as an individual

More than half of those interviewed valued being able to trust in their doctor to make the best decisions. Many of these participants talked about trust without prompting when asked about decision making in general. For several of these participants, a trusted doctor would know the patient as an individual and give individualised advice, which was seen as preferable to the information on the risk tool, which was seen as more generalised. This is illustrated by the following quote:

Because it means you trust your treating practitioner. You trust your medical provider. You know, the person who will ultimately know you better than anyone else. And once you build that trust and relationship which is so important in these matters, you can move on from there.

Quote 8.36: Interview O
However, although trust in doctor was highly valued, several participants had concerns about their doctors either currently or in the past. One participant voiced a concern that her doctor did not see her as an individual:

I don’t think they see me as a human being, I’m a statistic, I’m a patient, I don’t feel that I as [first name] matter, and that’s understandable, why should they, they see hundreds of patients. I have a slight suspicion, I won’t say it’s huge, I don’t go around saying, “oh, these doctors, they don’t know what they’re talking about”, or anything like that, I’m not at that level but I’m at the level where I wonder if she’s really thinking about how this is going to affect me.

Quote 8.37: Interview P

Several participants described avoiding a particular doctor after an experience where they lost trust. For the participant who had stopped medication, losing trust in his doctor was a key factor in his decision to stop hypertension treatment. In this case, the participant perceived his doctor had tried to mislead him about whether long-term antibiotics (for an unrelated condition) might have caused an adverse effect.

After the 10 years we finally broke it down, I thought it was nerves at first because of the job I was doing, you know, picking up these different people, but we narrowed it down to I was allergic to penicillin, but it took 10 years to discover that. I mean, I was given penicillin to get rid of this, and that’s why my whole body reacted in the way it did and I was quite ill, you know. So that was a bad period, but you assume, when you come to the doctor, that they know what they’re doing, because during your life you have teachers telling you what to do, the army tells you what to do, but when you come to see a doctor they’re giving you information for your own sake, you know what I mean, so you accept it more readily, and that’s what I did, and now, thank God, I’m not on penicillin any more and I’m back to normal.

Quote 8.38: Interview A
One participant described that an episode where she felt her doctor had appeared flippant or insensitive about her heart rhythm problem led to a breakdown in trust.

And the other thing was the same doctor, the one I would see second as it were, about three years before, said ‘did we ever tell you that you might need a pacemaker And this was…I saw him about once in three years. And I couldn’t understand why they wouldn’t tell me that. I mean if you suspected that one of your patients might need a pacemaker…not immediately. I said ‘how will I know’…‘Oh you’ll have a funny turn’ he said. [Sighs] Now I know why I didn’t see him as often as the other one I trusted.

Quote 8.39: Interview N

One participant, who had worked as a GP herself, described an experience where she felt her surgeon advised her wrongly:

I felt I was bounced into it, and I wasn’t heavy enough really for their criteria, but I’ve got a fatty liver, and I had hypertension, so those two things they thought were a good enough reason to do a gastric band, but I subsequently think they were probably wrong, so. I don’t know.

Quote 8.40: Interview D

Factors which led participants to trust their doctors included knowing a doctor for many years, having a doctor who listened to a patient’s concerns and understood their values. For a few of these participants, a trusted doctor could provide a valuable service, allowing the participant to carry on with their life and not have to contemplate future illness. For these participants, having their doctor contemplate disease risks on their behalf was desirable.

8.3.10 Testing treatments for side-effects

When asked about the risk of possible side-effects, around half of participants described a process where they would try a new treatment and assess for side-effects.
yeah, I mean that’s why things get reviewed don’t they? You know, if you try something and it’s not and it’s say “oh well we’ll give you something, we’ll try this one”.

**Quote 8.41:** Interview Q

Most participants said that, in general, the possibility of adverse effects would not deter them from a treatment. One participant who had used this approach, in a quote typical of several, described that he valued information about possible adverse effects. Information about whether they were common or not was less interesting, since he would try the medication to find out whether he was affected or not.

*Is it important for you to know about whether the side-effects happen often or not often?*

It don’t, I wouldn’t say often, I think all they need to do “It is a possible side-effect”.

*I understand.*

That’s good enough I think. They don’t have to put on there “often” or “not so often”, the fact that somebody reported, reported somewhere along the line or the fact that they have tested it, I don’t know where they get the information from, but the fact that it come back as a result of taking this, you may get this, that’s good enough. I don’t think they’re got to put down how often or how regular. It might only happen once but it is a side-effect, it should go on.

**Quote 8.42:** Interview E

For one participant, the patient’s role in decision making was to try the medication the doctor recommended, and report back if they experienced a side-effect:
I think it’s the doctor who should choose. Because normally he should know what should be the best. But the doctor should tell the patient if there’s a side effect. So if the patient has a side effect they will straight away come back and change the medicine. But it’s not for the patient to have a choice about the medicine, not at all, because we don’t know. We take that medicine because it has a lovely name…or…it’s ridiculous.

Quote 8.43: Interview K

Several participants described that they had experienced a symptom they suspected to be a medication adverse effect. In practice, these participants often found it difficult to know whether they were really experiencing a medication adverse effect or whether the symptom had another cause. This uncertainty was typified by a quote by one participant:

Well I kind of get tired at 4 o’clock in the afternoon. And I fall asleep at home in the evenings, but I think I might be like that anyway. I’ve got no control. I haven’t got another me without taking pills.

Quote 8.44: Interview C

8.3.11 Mistrust of statistics

In response to the example risk communication tool, two participants (both with some statistical expertise) voiced hesitancy around accepting statistical information, being concerned that statistics were often designed to mislead; as illustrated by the following quote:

Oh yeah, I mean averages, you can do anything with statistics I know, [lowers voice] I used to do things [laughs].

Quote 8.45: Interview B
8.3.12 A lay model of future risk

These findings can be summarised as a lay model of CVD risk understanding, as shown in Figure 8.2. Explanations for CVD risk were remarkably consistent among the participants. Many described epidemiological risk factors of family history, and lifestyle risk factors (including smoking, alcohol, being overweight, sedentary lifestyle and poor diet). Additional factors which were perceived as important were stressful circumstances, relating to family, work, or finances, and a personality which tended to internalise or ‘bottle up’ stress.

The attitudes to future risk can be grouped into three types, each representing around one third of interviewees. First, were the group who did express ideas about their own risk. This group universally spoke in terms of comparisons with peers or family members. The second group felt that the risk of an individual was impossible to know, often due to seeing every individual as unique. The population-based risk scores presented were typically seen as irrelevant. Some in this group who described the idea of strong, or weak individuals described being more likely to belong to the affected or unaffected portion of the risk fraction. Finally, the third group did not provide any indication of their own risk. For some in this group, considering the future risk of CVD was an unpleasant task in itself. Many in this group adopted a precautionary principle; assuming they would be at very high or certain risk of CVD unless they took action. Preventative activities, such as medication and a healthy lifestyle, therefore relieved these participants of the worry of future illness.

8.4 Discussion

This study sought to examine patient experiences and ideas about cardiovascular risk from a qualitative perspective. Participants had complex ideas of their own risk, which were based on the interplay of various risks. Many of these factors overlapped with epidemiological risks, in particular lifestyle factors (including family history, advancing age, being overweight, alcohol excess, poor diet, and lack of exercise). Other factors were also reported as important, which did not overlap with epidemiological risk fac-
Figure 8.2: A model of lay understanding of CVD risk
tors; stressful circumstances, and a personality which internalises stress were reported very widely. The participants who migrated to the UK perceived that the change in lifestyle after migration was an important risk. A few participants discussed a concept of strong and weak individuals; those who are inherently prone to developing illness, and those who can resist it.

All participants were aware of complications of hypertension, including stroke, heart attack, and kidney disease. Several participants reported sudden death as a complication; for many participants, complications were a result of a sudden increase in blood pressure.

A key underlying theme was the concept of patients as individuals. Notably, no-one who was interviewed described their own risk in terms of probability. Around half of the participants expressed doubt that a risk communication tool could apply to them personally. Many of these participants felt that the use of the phrase ‘people who are similar to you’ was of dubious reliability, since they felt the reference group would not be sufficiently similar to them. For some participants, ensuring that statistical estimates took adequate account of factors they held important would lead them to be useful. However, for many, no population statistic would be applicable to them as individuals, since no two people are exactly alike. Similarly, several participants did not interpret the risk presentation as probabilistic, but instead pointed at the numerator of the fraction saying, ‘I’d be one of those ones’.

For different reasons, adverse effects probabilities were not regarded as important. The majority of those interviewed reported being happy to try new medications no matter what the likelihood of adverse effect. They preferred to try a new drug, then either stop the treatment or see their doctor if a side-effect became apparent. This echoes the reports in the qualitative systematic review by Pound et al. in 2005, which described the practice of testing new treatments in chronic disease management.

Many of the participants expected that medication would be highly protective; several expressed surprise at the small size of benefit displayed on the risk chart example; one of whom expressed disbelief. Several participants expected medication would provide absolute protection against complications from hypertension. This mirrors the
results of quantitative analyses of patient expectations of treatment for a number of conditions; a systematic review found the majority of 27,323 participants of 35 studies overestimated the benefit, and underestimated harm from a wide range of medical treatments.898

8.4.1 Parallels between lay perspectives, and academic research on risk

Parallels may be drawn between many of the themes raised in this study, and debate about the problems with risk communication raised in the academic literature. The concerns expressed by participants echo the reference class problem described in the Literature Review chapter on Page 62. Given that individuals have an unlimited number of characteristics and can potentially belong to many populations, to which population does the risk presentation belong? Several existing decision aids do report a clear denominator,599–601 but some do not make this distinction. The Heart-to-Heart decision aid by Sheridan et al. gives risk information in the following format:

your risk of having a cardiovascular event in the next 10 years is 11%602

The key difference in this study is that the example risk description did have a clearly stated reference population.1 Here, all but one participants appeared to understand the reference category, but most perceived it to be irrelevant. Many participants of this study voiced ideas that their personal characteristics could not be adequately incorporated into a statistical estimate.

8.4.2 Comparison with peers—an acceptable risk language

Of the participants of this study who did express an idea of their own risk, all used comparisons to peers and family members. This used spontaneously by most of the participants, and including a number of those who wished to avoid consideration of risk in a probabilistic sense. Interestingly, this method also overcomes the reference class problem: participants explicitly compared their risk with people they regarded as not similar to themselves.

1Stated as ‘Imagine 100 people who are similar to you (same sex, same blood pressure, cholesterol, and smoking status).’
This has many similarities with the *Dundee Heart disease rank*, in which individuals are assigned a position in a ‘coronary queue’ of 100 people. The queue position was determined by reference to 10,359 men and women aged 40–59 in the Scottish Heart Health Study. This reference group, like the peers and family members described here, were not differentiated by risk. Risk ranking systems were not used by any of the decision aids described in Chapter 2, and have not been tested in an RCT, but may be an acceptable and understandable way to communicate risk, except in those who prefer to avoid discussion of risk altogether.

8.4.3 **Strengths and weaknesses of the sampling strategy**

The sampling strategy was successful in recruiting people of a wide range of geographic, ethnic, and socio-economic backgrounds, and with a wide range of durations since diagnosis and recruiting both men and women. People of a good range of ages were recruited; participants ranged from 51 to 90, corresponding roughly with the age-specific disease burden found in population studies. However, I was unable to recruit anyone younger than aged 50, (the expected prevalence of hypertension for those aged 40-49 is around 20%, although most this group will be either unaware, or aware but untreated). This group may have different attitudes towards risk and information than the older age groups.

There are several possible reasons why this group were hard to reach. First, this group may be more likely to work full time, and although I offered the opportunity for evening or Saturday interviews, they may have not seen this as a priority. Second, the expected prevalences include those who are unaware of their hypertension, and also those who are aware but untreated and therefore less likely to attend their GP. The sample may be additionally skewed in that only two of the participants were not using medication. Reasons for this may include coding practices at the surgeries (i.e. the code for hypertension might have been added to a patient record on commencement of medication only). Additionally, few participants reported having been involved in the decision to take medication, and indeed one expressed surprise that this was possible. With this in mind, hypertensives who both are aware of their condition and also choose to
attend their GP for follow up might be expected to have high rates of treatment. These issues could be overcome by recruiting outside of general practice; possibly as part of employer-based health screening.

Although all the participants who were prescribed medication reported taking it regularly, when discussed in more detail suboptimal adherence was widespread and typical of that reported in the literature elsewhere, for reasons including forgetting, and deliberate omission to avoid side effects.

Finally, this chapter reports a small scale study in one area of South London. Repeating interviews elsewhere would provide more robust evidence as to whether the themes reported here generalise. Conducting similar interviews with people risk of other health conditions would uncover whether the themes reported here exist more widely, which could have important implications for decision aids in disease prevention more generally.

8.4.4 Risk factors important to individuals

A key finding of this study is that many participants had strong ideas about what factors influenced their own risk of disease. Various participants perceived that factors including family history, diet, exercise, and stress were particularly relevant to their own risk. This mirrors the findings of previous qualitative research. Walter et al. conducted a systematic review of qualitative studies looking at the influence of family history of a range of chronic diseases on perceived risk. They found that having a family member affected by illness did cause a sense of vulnerability. However, participants ideas of how family history affected their own risk also took into account other factors. These factors included those used in medical risk assessment (e.g. the number of affected relatives, and their age when they developed the illness), but also other factors, including the emotional quality of the relationship, or geographical closeness. The review authors proposed the explanation that participants held personal mental models of health and disease causation which they used to personalise risk information.
8.4.5 Comparison with other studies

Few published qualitative studies have examined the perspectives of healthy individuals on their future risk of CVD. A systematic review by Garside et al. (search date 2008) identified 9 qualitative studies which discussed perspectives on CVD risk, but all focused on knowledge of risk factors rather than risk in the probabilistic sense. The closest research is that by Davison and colleagues discussed in Chapter 2, who published a series of papers describing their qualitative study in South Wales, which focused on the causation of CVD. Of particular relevance to this study, the authors described difficulty in translating population-level data to individuals. Specifically, participants in this study had strong ideas of the type of person who was a ‘candidate’ for heart disease, typically a person with multiple and markedly high lifestyle risk factors (which the authors attribute to the successful penetration of health promotion campaign messages). Each encounter with an individual who doesn’t meet this extreme risk picture (which as the authors note, accounts for most heart disease incidence) is regarded as an anomaly or random incident. Paradoxically, Davison argues, health promotion messages focusing on lifestyle risk factors causes more heart disease to be regarded as random. Wiles found similar results in people recovering from MI.

The finding that many found contemplating their own cardiovascular risk an unpleasant task, and avoided doing so is in contrast with the findings from the review in Chapter 7, which found no significant difference in anxiety or disease-related worry with risk communication. One possible explanation for this discrepancy, given the attitudes to risk estimates found here, is that the risk communication tools examined in Chapter 7 may not have been perceived as applicable, and thus may not have led to any emotive response.

8.4.6 Conclusions

Risk communication requires not just the successful transmission of a statistical probability, but also the communication of the context and meaning of the number. This study finds, in CVD at least, patient concepts of risk may lead to different interpreta-
tions of risk information to those intended by clinicians and limit their usefulness. In practical terms, clinicians should make allowances for those who do not wish to contemplate risk; indeed some of these patients might find a trusted clinician willing to make the decision on their behalf to be a valuable service. For those who do wish to have risk information, tools which incorporate risk factors which are important to patients are likely to be perceived as more applicable. Ranking an individual's risk against their peers might be more acceptable, understandable, and relevant than conventional probabilistic approaches.
9.1 Introduction

This thesis seeks to make recommendations about how shared decision making could be improved in cardiovascular disease prevention, and, as discussed in the Theoretical Framework chapter (Chapter 3), how research on patient perspectives can be better incorporated into shared decision making interventions. This chapter brings together the results from the individual studies presented previously to address this aim, a process often described as triangulation.\textsuperscript{607–609} This chapter will argue that many of the patient perspectives identified by the thesis studies have scientific validity; dismissing them as myths or misunderstandings is therefore incorrect, and may be counter-productive. Finally, an example decision aid which is sensitive to key patient concerns and understandings about health is presented.
9.2 Triangulation of results

This chapter follows the approach suggested by Ó’Catháin et al., who describe the triangulation process as follows. First, the source studies are conducted and analysed individually using conventional methods. Then, the findings from the studies are listed on a single page. Individual studies are then assessed as to whether they agree with each finding (termed convergence), provide complementary information, or disagree (termed discrepancy).\textsuperscript{507} One method for achieving this is known as a convergence matrix;\textsuperscript{608} which, put simply, tabulates key themes across studies, noting where studies agree, disagree, or provide complementary information. A summary of the main findings from the thesis together with the contribution of each Chapter to the finding is provided in Table 9.1 (on Page 249).

9.3 Overview of thesis results

Chapter 5 described an analysis of data from the South London Stroke Register (\textit{sLsR}), finding that more around 70\% of those with stroke had one or more risk factor diagnosed previously; around 30\% had one or more risk factor which was diagnosed but untreated. Black ethnicity and female sex were associated with increased likelihood of antihypertensive drug prescription; the prescription of other \textit{CVD} prevention medications did not vary by ethnicity or sex. There were particularly low rates of use of anticoagulants in \textit{AF}, and particularly so among older participants. There were no associations between the prescription of any class of preventative medication and socio-economic status.

Chapter 6 systematically reviewed qualitative studies around patient perspectives on hypertension and medication-taking. The review included 52 studies from 16 countries. This review found that participants widely described symptoms which they attributed to raises in blood pressure. Although participants described that being overweight, drinking alcohol, salt consumption, a sedentary lifestyle, and family history were important factors for developing hypertension, studies reported that participants widely perceived stress to be the most important cause. A consequence reported in many stud-
ies was that participants stopped medication at times when stress or symptoms were not present. Participants additionally reported widespread concerns about serious medication side effects; participants feared addiction, or long term ‘build up’ in the body.

Chapter 7 described a systematic review and synthesis of RCTs and qualitative studies examining the effects of CVD risk communication. This review found 15 RCTs comparing CVD risk communication versus usual care, 8 RCTs comparing different risk communication strategies versus each other, and four qualitative studies examining patient perspectives on specific CVD risk communication strategies. Meta-analysis of RCTs found that communicating CVD risk had negligible effect on CVD risk factors (blood pressure, lipid levels, BMI, or combination risk scores) at times from 3–12 months. Communicating risk did modestly improve Decisional Conflict scores. Eight RCTs compared risk communication strategies versus each other; similar to studies done of risk communication, indicating that RRRs and verbal descriptions of risk may lead to inflated perceptions of risk compared with ARRs as a percentage; one RCT found that heart-age led to a modest but statistically significant improvement in blood pressure and cholesterol levels. The RCTs comparing different strategies had important quality limitations, however, including investigating hypothetical scenarios rather than genuine health decisions, lack of measurement of the quality of decisions, and possible problems in data quality in one RCT. From the qualitative studies, participants described a lack of trust in population-level statistics, and that they were too ‘academic’—i.e. not directly applicable to them in real life. Formats which presented data framed as the risk of an individual (e.g. an individual’s heart age), were perceived as more relevant than population frames (e.g. a percentage risk estimate).

Chapter 8 described a thematic synthesis of qualitative interviews of 24 patients from two contrasting GP practices in south London. Participants from this study were approximately evenly split between those who wished to avoid discussions of CVD risk, and those who welcomed it. For those who wished to avoid contemplating risk, explanations included seeing future CVD risk as a low priority in the context of advancing age, or other current health problems which were perceived as more pressing. For several participants, contemplating CVD risk was perceived as unpleasant and unnecessary;
these participants preferred to delegate health decisions to a trusted doctor. Among those welcoming risk discussion, there were widespread concerns that population risks could not apply to them personally. Many explained that risk estimates did not adequately take into account key personal characteristics, including good health of family members, and changes made to lifestyle; these participants saw themselves as unique individuals. A few disputed the use of the phrase ‘people who are similar to you’ as used on the example decision aid, explaining that others could not be sufficiently similar to them to make a such a risk estimate useful. Several participants interpreted risk probabilities differently from their intended meaning, since they identified strongly with either the affected or unaffected portion of the risk fraction. Participants widely compared their risk with peers: this appeared to be an acceptable method for discussing risk even among those who did not wish to engage in discussions about risk in a probabilistic sense.
Table 9.1: Summary of key findings from the individual studies. Notes: A. a large proportion of participants did not use medication for known risk factors; B. Chapter 6 did find financial difficulties were an important barrier to treatment, but only in studies from the US and Brazil; C. the exception was AF, where older age was associated with much lower use of treatment; D. heart age was preferred in the qualitative part since it provided individual rather than population information; however (limited) evidence from RCTs did not show any difference in outcomes compared with communicating population risks.

<table>
<thead>
<tr>
<th>Findings</th>
<th>Chapter 5</th>
<th>Chapter 6</th>
<th>Chapter 7</th>
<th>Chapter 8</th>
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<tr>
<td>Perceived importance of stress to hypertension</td>
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<td>agree</td>
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<td>Perceived symptoms from hypertension</td>
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<td>Hypertension abates when stress absent</td>
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<td>Absence of symptoms indicates blood pressure reduction</td>
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<td>Hypertension leading to sudden death during period of BP elevation</td>
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<td>Lay models of risk factor interaction</td>
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<td>Desire to avoid medication</td>
<td>complementary(^A) agree</td>
<td>agree</td>
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<tr>
<td>Concern about long-term accumulative side effects</td>
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<td></td>
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<tr>
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<td></td>
<td>disagree(^B)</td>
<td></td>
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<tr>
<td>Effect of age (lack of)</td>
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<td>Risk perceived in comparison with peers</td>
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<td>Lack of effect of current risk communication strategies</td>
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<td>Absolute risk too small to be worth acting</td>
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<td>Mistrust of information perceived as biased, or with agenda</td>
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<td>Perceived moral responsibility to take treatment</td>
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<td>Current health problems more important than future prevention</td>
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249
<table>
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<th>Chapter 6</th>
<th>Chapter 7</th>
<th>Chapter 8</th>
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<tr>
<td>Testing medication for side effects</td>
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9.4 Difference between patient perspectives and current interventions

A key theme across the studies (particularly from Chapter 6, 7, and 8) was a mismatch between patient experiences and understandings, and the approach taken by current decision aids and educational interventions. Currently available decision aids (reviewed on Page 69) and educational interventions (on Page 46) have much in common.

In their development process, nearly all had very limited or no patient involvement in their development. The few that did include patient perspectives typically included one or two patients on the authorship group. In two of these cases, the patient representatives had substantial expertise, being senior members of CVD charities or part of guideline committees. These patient authors, in their background knowledge and perspectives on CVD, would likely not be typical of target users of the interventions.

In their content, the information presented in the interventions was heavily biomedical; most described information about the causation of CVD and treatment effects, often scientifically. Risks were frequently presented, but in a variety of ways. Some used the best practices described in the psychological literature (presentation of absolute risks as natural frequencies or percentages with a graphical display; as described on Page 51), but many did not.

Finally, when tested in RCTs, these interventions showed modest or no benefits in any outcome. Although the RCTs were limited by their small sample sizes, no consistent differences were shown in Decisional Conflict scores or in adherence to treatment. The systematic review in Chapter 6, and the qualitative study in Chapter 8 suggest that the approaches taken by existing interventions could be improved. In both of these chapters, the majority of participants were already well aware of both conventional risk factors for CVD, and the implications of untreated risk. This echoes the study of Davison and colleagues of ‘lay epidemiology’ in South Wales, which found that participants readily accepted health promotion messages from the media and public health campaigns.
9.4.1 Stress and symptoms

In the qualitative studies examined in Chapter 6, and also in the study in Chapter 8, many participants perceived their hypertension was caused by stress. Many of the participants had reasonably detailed knowledge of conventional risk factors for hypertension (including overweight, alcohol excess, dietary salt, and sedentary lifestyle), but in terms of importance, stress was held most highly.

Out of the decision aids reviewed in Chapters 2 and 3, only one (that by Lalonde and colleagues) made any mention of stress. This DA described stress as one of the key risk factors for hypertension, and described relaxation, counselling, and ‘biofeedback’ as possible options for CVD prevention.

Although widely discussed, there remains considerable uncertainty about the relationship between stress and hypertension. In their 2009 systematic review, Sparrenberger and colleagues systematically reviewed observational studies which assessed the association between stress (either acute or chronic) and hypertension. They included 14 international cohort and case-control studies with a total of 52,049 participants. The authors conducted a narrative synthesis, and tentatively concluded that acute stress did not appear to be associated with hypertension, but that chronic exposure to stressors, and having chronic symptoms of stress were both likely associated. Analysis was difficult due to the heterogeneity of measures of stress used. Additionally, many of the studies did not adequately control for potential confounding factors.

The effect of interventions to reduce stress on CVD has been examined in a 2009 Cochrane systematic review of 25 RCTS, and subsequently in a 2014 review by Nagele and colleagues of 17 RCTS. Both reviews conducted meta-analyses and found small reductions in blood pressure with intervention (Cochrane: 5/3 mmHg, 95% CI 8/5 to 3/2 mmHg; Nagele: [ranges presented only] change in systolic BP -10 to +1 mmHg, change in diastolic BP -12 to +10 mmHg). However, both reviews found important quality problems in the trials included, including inadequate randomization sequence generation, allocation concealment, and blinding in the majority of trials. The Cochrane review concluded that the small apparent improvement in blood pressure with relaxation would be...
readily explained by the effects of bias.\textsuperscript{547}

A 2015 meta-analysis which included 25 cohort studies including a total of 603,838 participants examined the association between weekly hours worked and CVD.\textsuperscript{611} After adjustment for age, sex, and socio-economic status, there were substantial increases in the incidence of both stroke and coronary heart disease in those who worked >55 hours per week (CHD: RR 1.13, 95% CI 1.02 to 1.26; stroke: RR 1.33, 95% CI 1.11 to 1.61). The increase in CHD appeared to be explained by increased conventional risk factors among the longer-working participants, however the difference in stroke existed even in those studies which adjusted for conventional risk factors. Thus looking at stress in isolation, scientifically the picture is conflicting and uncertain. Nonetheless in context of the overwhelmingly strong evidence supporting the ‘conventional’ risk factors for CVD (reviewed in Pages 22–26), the primacy with which participants in the qualitative studies regarded stress seems unwarranted.

Likewise, the review in Chapter 6 and the qualitative study in Chapter 8 found widespread evidence that patients reported symptoms that they perceived to be caused by an elevation in blood pressure. A consequence described in the review was that when symptoms abated, many participants perceived that their blood pressure had normalised (and hence treatment might no longer be necessary). This perception was linked to the finding in Chapters 6 and 8 that sudden rises in blood pressure level were a key concern of many participants; this was widely perceived to be the mechanism by which stroke and MI occurred.

Patient described experiences of symptoms are widely contradicted in health information, as in the following examples:

\begin{quote}
High blood pressure (hypertension) usually has no obvious symptoms and many people have it without knowing.
\end{quote}

NHS choices website\textsuperscript{612}
There’s a common misconception that people with high blood pressure, also called HBP or hypertension, will experience symptoms such as nervousness, sweating, difficulty sleeping or facial flushing. The truth is that HBP is largely a symptomless condition. If you ignore your blood pressure because you think symptoms will alert you to the problem, you are taking a dangerous chance with your life.

American Heart Association: the Myth of Symptoms

The evidence from studies examining symptoms in hypertension is, however, less clear than this patient information suggests. Kjellgren et al. examined a series of 1013 patients in Sweden, and found between 52–57% reported symptoms (most frequently headache and dizziness), and that symptoms reduced in prevalence among those taking medication. A 1972 study of 6672 participants with hypertension from the United States Health Examination Survey of Adults evaluated the connection between blood pressure level, and headache, epistaxis, fainting, dizziness, and tinnitus. It found that lower BP (<140/90mmHg) was significantly associated with increased reports of fainting. There was no significant association between reports of the other symptoms (headache, epistaxis, dizziness, or tinnitus) and blood pressure level. However, the study did find small but statistically significant increases in the proportion reporting headache, tinnitus and dizziness in participants with hypertensive retinopathy (typically indicating very severe hypertension). Chatellier et al. reported in their 1982 study of 1771 people with hypertension who didn’t receive treatment that reports of symptoms were common (headache 41%, palpitations 29%, nocturia 20%, dizziness 21%, and tinnitus 14%). They likewise found that the presence of symptoms was not significantly associated with the degree of raised blood pressure. However, they did find that both lack of physical exercise, and the presence of anxiety were strongly associated with increased levels of symptoms. Similar findings have been reported by several additional studies. In summary, counter to the claims in patient information, symptoms are very frequently reported in people with hypertension. However, there is no good evidence that the absence of symptoms is associated with good control of blood pressure,
nor that hypertension itself causes the symptoms.

9.4.2 Need for ‘culturally sensitive’ interventions

The reduced rates of hypertension control among black populations in the UK\textsuperscript{618} and US\textsuperscript{619} motivated a large proportion of the qualitative work reviewed in Chapter 6, which aimed to find if cultural practices or understandings of illness play a role. Several included studies’ conclusions recommended that clinicians should take a more culturally sensitive approach to hypertension management.\textsuperscript{21-24,377,515} These were typically in studies which focused on a specific ethnic minority group. However, the studies in this thesis suggest that this may be a simplistic approach. First, the analysis of the South London Stroke Register found that black African and black Caribbean participants were significantly more likely to receive treatment for their hypertension than the white population (though notably, adherence data was not available and could in principle differ between ethnic groups).

From the systematic review of qualitative papers in Chapter 6, the key finding was the remarkable similarity in lay experiences and understandings worldwide, particularly around the meanings attributed to stress, and perceptions of symptoms. There was additionally evidence from the SLSR analysis presented in Chapter 5 that black ethnic participants with diagnosed hypertension were more likely to be prescribed medication than white participants (counter to the conclusions of individual qualitative studies suggesting black ethnic groups would be more likely to avoid treatment). This Chapter found no significant difference in the likelihood of using preventative medication to treat other CVD risk factors associated with ethnicity.

One qualitative study in London did evaluate both white and black Caribbean ethnic groups, finding differences, with black Caribbean patients reporting concerns about medication building up over time in the body, patterns of low medication taking.\textsuperscript{372,468} The Netherlands study by Beune et al. found a preference for alternative or herbal treatments for hypertension which existed equally in the majority white Dutch population and in migrant populations. Each group, however, had a different range of traditional treatments to draw on; the white Dutch participants favouring homeopathy, and the
Surinamese traditional herbs.\textsuperscript{181}

The review in Chapter 6 raises an interesting question of \textit{why} diverse populations hold such similar understandings of hypertension. One possibility (raised by the authors of two of the qualitative studies) is that the use of the term ‘hypertension’ itself might contribute, suggesting ‘tension’ or stress.\textsuperscript{459,502}

Indeed, experiences of stress were reported similarly by participants of an included study from South Korea.\textsuperscript{520} The Korean term for hypertension is ‘hyul ap’, and is literally translated as ‘high blood pressure’, but the same term is used colloquially to describe a reaction to a stressful event.\textsuperscript{1} A systematic investigation of language used around hypertension internationally is beyond the scope of this thesis; and whether use of language is the cause (rather than the consequence) of lay understandings is uncertain.

The findings of the studies in the thesis suggest that rather than targeting specific cultures or ethnic groups, educational materials should incorporate information on prevalent lay experiences, understandings, and concerns about treatment.

\textbf{9.4.3 Risk factors perceived as important - ‘people like you’}

Participants in qualitative studies in the review in Chapter 7 and the study in Chapter 8 expressed the feeling that statistical risk estimates did not apply to them personally. For many of participants of Chapters 8, risk estimates did not sufficiently take account of the particular risk factors which they perceived to be most important.

Emmons \textit{et al.} reported similar findings in their focus group study, which examined patient perspectives on the Harvard Cancer Risk Index (a tool which presents a personalised estimate of cancer risk to patients based on their weight, smoking, alcohol consumption, family history, and history of inflammatory bowel disease).\textsuperscript{620} They found many of the participants held certain factors as important which were not incorporated by the tool (including poverty, air pollution, and exposure to toxic waste). The absence of these factors caused these participants to view the resultant risk score with some scepticism.

The choice and weighting of variables in the underlying \textit{CVD} risk algorithms, by con-\textsuperscript{1}Personal correspondence from the Korean GP who translated this qualitative paper
trast, is guided by statistical and pragmatic concerns. For example, QRISK2 deliberately selected risk factor variables which are routinely collected in electronic health records. This allowed the use of a vast dataset (health records from 11 million patients) to derive model parameters; and also allows clinicians to calculate risk estimates in the consultation using data which often already exists on the patient record, and without the need for onerous collection of additional data.

The trade-off of this approach, however, is that the model is highly dependent on the variables which happen to have been collected. In primary care records, blood pressure, cholesterol levels, and smoking status are readily available with good data completeness. Diet and physical activity, although both recognised as important risk factors, are not routinely collected (and are much more complex to collect data on and quantify). The participants’ concerns, reported in Chapter 8, that risk estimates were not applicable since they did not take into account their lifestyle changes are therefore valid.

This is reminiscent of the reference class problem (described on Page 62), where individualised probabilities are highly dependent on how one decides to characterise the individual. This problem can be illustrated with reference to QRISK2 as an example. One could conceive a hypothetical risk model, which gives equal population performance to QRISK2, but which identifies a different population as being at high-risk. Figure 9.1 on Page 258 illustrates one such model.

The two models illustrated in this Figure demonstrate that prediction errors are highly dependent on the model used. Both models are well calibrated from a population point of view (20% of the population with a risk score of 20% will go on to develop CVD). The variables used in QRISK2, and therefore the individuals selected as being at high risk, may be seen from the patients point of view as arbitrary. QRISK2 explained 33% of the variation in CVD outcome in men and 40% for women. In the context of other current risk models, this is good performance. However, since most of the variation is currently unexplained, its utility in providing individual risk estimates is limited.

In future, better understanding of novel risk factors and improved modelling techniques provide avenues for improvements in accuracy. Despite these new developments, it remains possible that a proportion of CVD occurs at random, and is therefore
Figure 9.1: The reference class problem—a scaled rectangle diagram showing a hypothetical risk model (in blue), with identical population performance characteristics to QRISK2 (in pink), but which labels a different subset of the population. Although the models are calibrated accurately on a population basis (20% [with good accuracy] of those who test positive will develop CVD over 10 years), whether any individual tests positive is highly dependent on the assumptions of the model.

inherently unpredictable. In this case, honesty about the limitations and reasons for variable selection are key to allay patient concerns.

9.4.4 ‘I think I would be that one’

A number of participants in the qualitative study (Chapter 8) appeared to interpret risk probabilities differently to their intended meaning. Instead of understanding a probability which described the uncertainty about whether any individual would develop CVD, they identified with a single icon. For these participants, CVD was something which was inevitably going to happen or not.

This notion is long-recognised in the psychological literature on risk, being described by Gigerenzer as ‘single event probabilities’\(^1\)\(^{200}\) CVD may be described as a single event probability, since any individual has either a 100% risk or 0% risk of developing it (which is testable empirically after the fact).

This theme likewise been identified in qualitative research examining prevention of
other diseases. Kim and colleagues conducted focus groups with 34 people aged from 52 to 90 without dementia, examining their understandings about future risk. They found a very similar pattern in the way participants felt susceptible to dementia as found in CVD in Chapter 8, describing three main patterns. The first group described fear of dementia rather than a likelihood: similar to the participants in Chapter 8 who did not wish to contemplate their future risk. The second group were described by the authors as ‘rational’ and weighed up their lifestyle risks and personal characteristics when judging risk. The third group felt dementia was inevitably going to happen or not, and was unpredictable in advance.

9.4.5 ‘Build up’ of medication in the body

None of the blood pressure-lowering agents in wide use have been reported to be associated with long-term accumulation in the body, dependence, or addiction. However, as discussed earlier (Page 33), important adverse effects are often missed in clinical trials, meaning that post-marketing surveillance and adverse events reporting by clinicians are important routes for gaining knowledge about drug harms. The consequence is that important adverse events data may not be available until many years after data on the primary efficacy outcome. Recent prominent examples of drugs with important adverse effects not known at the time of licensing include rosiglitazone for diabetes, and sibutramine for obesity. Both were found in long-term trials to increase the risk of CVD and CVD-related death and were withdrawn by regulators more than ten years after their initial approval and release.

Nonetheless, the principal agents recommended in current hypertension guidelines have been in wide use for several decades (dates of first UK licensing: nifedipine CCB 1977; captopril [ACE inhibitor] 1981, indapamide [thiazide-like diuretic] 1977), which reduces the likelihood of unknown adverse effects.1

1according to Summaries of Product Characteristics retrieved from http://www.medicines.org.uk/emc/ on 31st August 2015
9.5 How to address patient concerns in communication

For many of the patient concerns reviewed above, it would be simplistic to dismiss them as myths or misunderstandings. In fact, many of the key concerns of patients are in areas of scientific uncertainty, or areas (such as stress and symptoms) where it is the importance attributed to a factor which is discrepant with the scientific research rather than the factor itself.

Chapter 2 described how the motivation to allow patients to make their own decisions around health might not necessarily align with the public health agenda to increase uptake of CVD prevention. In practice, some of the decision aids contained information aimed at persuading patients to engage in a particular action. A widespread finding in the studies in Chapter 6 was the concern about medication ‘building up’ over time in the body, or the development of dependence or addiction. This concern is not unique to hypertension, and has been reported in patients who were prescribed medication for a number of long-term conditions. In hypertension, this concern was in some cases linked with an idea about a sedative mechanism of effect of treatment (which might logically follow from the understanding of hypertension as an illness caused by severe stress).

This raises the question of whether promoting adherence might paradoxically reduce the likelihood of medication-taking. Insisting on continuous medication-taking and warning of the dangers of stopping seems unlikely to reassure patients who are concerned about addiction. Counter-intuitively, rather than insisting on adherence, clinicians could reassure patients that they would not expect any adverse effects on stopping medication. The knowledge that they could safely decide to stop medication in future might even encourage more to choose to start it.

Patients in the qualitative studies highly valued trust in their doctors, but were sceptical about any health advice which was seen as trying to persuade or coerce them to take a course of action. Thus information which appears to ignore or deny legitimate patient concerns is likely to be counter-productive. An alternative approach would be to acknowledge these common patient concerns, and describe honestly scientific uncer-
tainty where it exists.

Given that hypertension drugs are long-established, reasonably strong reassurance could be provided about the lack of evidence of accumulation or addiction, but there should also transparency that quantifying adverse effects is an imperfect science. Associations with stress could be acknowledged and the current scientific uncertainty described, but the context that other risk factors appear to have stronger effects given. Common awareness of symptoms should be presented, but also that it is not clear that blood pressure itself causes them, and that the absence of symptoms does not reliably show that blood pressure has normalised.

An example decision aid, showing how information on CVD risk might be presented in light of the findings of the thesis is shown on Pages 264–265. This figure is provided to illustrate the key concepts from the thesis, and is not likely to exhaustively describe all the information a patient might require. A leaflet format is used as an example, but the information might equally be communicated orally or using an interactive computer tool.

### 9.6 Implications for risk communication

The present research has identified some problems for current risk communication strategies in the context of CVD prevention. First, as demonstrated in Chapter 7 the strategies described in RCTs do not appear to have any substantial effect on CVD risk factors; and have only modest effect in improving decision quality.

Participants in the qualitative studies reviewed in Chapter 6, and the qualitative study in Chapter 8 revealed a number of common concerns. Many patients felt that risk estimates would not apply to them personally, that they did not take account of particular risk factors which they perceived to be important, and that they doubted the accuracy of academic studies (with ‘academic’ having connotations of being overly theoretical, and being distant from everyday life).

Many participants also perceived the risk of CVD, and probability of benefit from treatment were too small to be meaningful. Guideline producers have noted this phenomenon, and in an attempt to increase uptake of prevention have suggested presenting
lifetime risk estimates (over which the probability of CVD is increased) to those at lower risk.\textsuperscript{11}

As dryly noted by Jackson, the lifetime risk of death is 100%.\textsuperscript{626} Given that CVDs cause around half of all deaths, a lifetime CVD estimate therefore provides more information about the mode of death rather than the risk of death, and will inevitably produce a large probability which does not help identify people with raised risk.

There were suggestions from the qualitative studies that this approach might be counter-productive from the patient perspective. Presenting risk over 10 years for some participants reduced the relevance of the information, since they perceived the risk of CVD to be too distant in the future to be worthy of immediate action. Therefore presenting shorter time-frames (over which time CVD risk, and treatment absolute benefits would be even smaller) is likely to be most relevant to patients, but paradoxically result in smaller motivation to take action.

One potential solution to some of these problems may come from how many of the participants in Chapter 8 described their own risk. Rather than a describing an individual or population risk as a probability, participants discussed their risk in relation to their peers and close family.

This is reminiscent of the Dundee Rank, a method described by Tunstall-Pedoe for assigning an individual a rank out of 100, representing their likelihood of developing coronary heart disease compared to others of the same sex and age-group. They described how this rank could be presented to patients, describing how far away they were from the front of the ‘coronary queue’.

In the context of the patient concerns elicited in Chapters 7 and 8, a Dundee Rank has some appealing characteristics. Patients are presented with a risk as a comparison to others who are undifferentiated by risk factors. In other words, this denominator is other people explicitly \textit{not} like them except for age. This risk presentation also avoids the need to set a time-frame: a population rank is not time-dependent.

An illustration of how this information could be presented is given on the final page of the example decision aid on Page 265. Since the user is represented by a single icon among the population, it is possible that this format might prove easier to understand.
for those in the interviews in Chapter 8 who identified with one of the icons in the risk charts (rather than the intended meaning of the standard icon arrays, that the person had an equal chance of being any of the icons).
High blood pressure

How does high blood pressure cause problems?

High blood pressure very gradually causes damage to the large blood vessels (arteries) which take blood from the heart to the rest of the body.

If blood pressure remains high for a long time (usually for years), the damage caused to blood vessels can eventually result in a stroke or heart attack.

Sudden increases in blood pressure (for example during periods of stress, working hard, or exercising) are usually safe, and are not likely to cause a stroke or a heart attack.

Does high blood pressure cause symptoms?

A large number of people with high blood pressure do notice symptoms from time to time. The most common symptoms are headache, sweating, a sensation of a rapid heart beat, and breathlessness.

If you do get symptoms, they are probably not caused by your blood pressure going up suddenly. Perhaps surprisingly, most people's blood pressure stays high even at times when they have no symptoms.

Measuring your blood pressure and noting the numbers is the only reliable way to tell if it's gone up.

What is the connection with stress?

Being under stress does make blood pressure go up. However, being overweight, not being physically active, getting older, and drinking alcohol are usually more important.

In most people, blood pressure has several causes. Addressing stress alone usually doesn't improve blood pressure.

Do I have to take medication for life?

If you decide to take medication, you are free to choose how long to take it for. Tablets do not 'build up' in the body over time, and are not addictive. They can be safely stopped at any time.

The key downside to stopping is that your blood pressure will usually become high again.

Figure 9.2: Example decision aid illustrating thesis conclusions (Part 1 of 2)
Risk of developing heart attack or stroke

Consider a group of 20 men, picked at random, of about your age. We estimate that you would be the 3rd most likely to develop a heart attack or stroke.

If you chose to take medication for blood pressure, your risk of heart attack and stroke would reduce. We estimate you would move to 8th place.

The vast majority of people will have no side effects, but some do (less than 10% in total). It is impossible to predict who will be affected, the only way to know for sure is to try the treatment.

For those who do have a side effect, the most frequent are:
- Swelling of the feet and ankles
- Headache
- Tiredness

A range of other side effects have been reported, but are less common. If you have side effects which bother you, you can safely stop the treatment. Medication does not build up in the body over time, and is not addictive.

Figure 9.3: Example decision aid illustrating thesis conclusions (Part 2 of 2)
Such a rank may be calculated by a simple transformation of a conventional percentage risk calculated for an individual (e.g. via QRISK2 or a Framingham score), given knowledge of the population distribution of these CVD risk estimates.\(^{628}\)

The original Dundee Rank has been criticised since it included a wide age range (from 40–59 years).\(^{629}\) Given the results of the qualitative study this may pose a problem for communication also, since patients may not regard people within a 20-year age band as sufficiently similar. However, given the availability of large scale research databases based on primary care records (the CPRD contains data on 4.4 million patients),\(^{630}\) population distributions for narrower age groups should be easily calculable. One consideration is that risk ranks are age and sex dependent, so the rank value is not comparable between people from different groups. In other words, being 10th in line for developing CVD has a very different meaning for a line comprising 40 year old women compared with 60 year old men. For this reason, the statistic would not be particularly helpful for clinicians in identifying a high-risk population. No RCTs or qualitative studies were found evaluating the effects of presenting risk as a ranking, and therefore the proposed tools would require refinement and evaluation.

### 9.7 Implications for future research

For future studies of CVD risk communication the results from the thesis suggest areas of good practice. First, measures to mitigate problems in quality found in the RCTs in Chapter 7 could be taken, including: improving blinding,\(^{631}\) and assessing both standardised scores of decisional quality (e.g. the Decisional Conflict score) and clinical outcomes. The results from the qualitative studies of Chapter 7 and Chapter 8 emphasise the complex manner in which risk is interpreted by patients. Studies which simply assess whether a participant can recite a percentage accurately are unlikely to elucidate how patients interpret the information, and the consequent effects on decision-making and health behaviours. Incorporating qualitative data collection as part of risk communication RCTs, and recruiting participants who are genuinely facing treatment decisions (rather than being asked to imagine a response to a hypothetical situation) would help to address this problem.\(^{632}\)
For the development of SDM interventions more widely, the research presented in this thesis suggests that the IPDAS guidelines on patient involvement in DA development could be strengthened. As discussed on Page 73, the IPDASi tool for assessing the quality of DAs simply requires that patients are involved in the creation, review, and field-testing of an intervention: criteria which can be met with minimal patient involvement. By contrast, use of qualitative research, as done in Chapters 6, 8, and 7 can provide a more detailed understanding of information needs, and help ensure that interventions are interpreted as intended.

As demonstrated by the large volume of studies retrieved in Chapter 6, it may not be necessary to conduct new qualitative studies in a disease area. For example, a number of qualitative systematic reviews syntheses have been conducted examining patient understandings of health problems; including in haemodialysis\textsuperscript{633}, viral hepatitis\textsuperscript{634}, type I diabetes\textsuperscript{635}, psychosis\textsuperscript{636}, and self-monitoring of blood pressure.\textsuperscript{637} Use of systematic reviews in this way is an important strategy to reduce research waste, by preventing unnecessary duplication of labour and ensuring that the findings of existing studies are acted upon.\textsuperscript{638,639}

Finally, the decision aid presented on Pages 264–265 illustrates features which may overcome key problems in previous CVD decision aids, including acknowledgement of key patient concerns, presentation of risk using a method designed to be understandable and acceptable, and with an attempt to avoid messages which might have unintended consequences. However, these strategies have not been evaluated as part of an intervention. Evaluating a decision aid with these components in an RCT would demonstrate whether or not they improve the decision making process, and whether they affect behaviours and outcomes.

9.8 Strengths and weaknesses of the research

The strengths and weaknesses of the individual studies are presented in their respective Chapters; here I discuss their implications for the findings of the thesis as a whole. The key strength of the research in the thesis was the use of qualitative methodologies to understand patient perspectives around decision making for CVD prevention. In par-
ticular, synthesising results from multiple qualitative studies resulted in a higher confidence that the findings were genuine, and also provided evidence of geographic spread and consistency. This represents a major improvement in comparison with the methods used in existing DAs, which had important deficiencies in their patient involvement. Qualitative research, and particularly systematic use of the large number of qualitative studies which have already been conducted, could provide a more rigorous method for patient involvement in health education and SDM in other areas.

It may be argued that a weakness of qualitative research is the lack of external validity: that findings from small studies with non-random sampling strategies do not provide evidence of the frequency of the findings in the general population. Among the studies in the thesis, there is strongest evidence for generalisability from the systematic review in Chapter 6, where the key themes were found consistently in a large number of qualitative studies done internationally.

However, there is somewhat less certainty that the findings from the single qualitative study in Chapter 8 are widespread. The use of a purposive sampling strategy (as done in this Chapter) is regarded as an important method of ensuring the validity of qualitative findings. This together with the fact that principal themes found were repeated in multiple interviews provides some reassurance that the findings are valid in the setting and population studied (people with hypertension but no prior CVD in primary care in south London).

Additionally, the fact that several of the key themes identified in Chapter 8 were also identified in other studies from the systematic reviews in Chapters 6 and 7 (mistrust of population statistics, and perceiving benefits of treatment to be too small to be worth pursuing), and also in studies examining cancer and dementia prevention (unwillingness to contemplate future risk, perceiving risk to be certain, perceiving risk to be inaccurate since did not incorporate factors patients felt important), lends some credibility to these findings.

It should be noted that current DAs were created without reference to any qualitative research on patient perspectives. The qualitative study in Chapter 8 successfully used an example decision aid as a springboard for discussions about risk, which in many cases
were otherwise difficult to instantiate. Therefore conducting further qualitative inter-
views around some of the DA adaptations depicted on Pages 264 and 265 would be a
feasible method for ensuring validity and making further refinements before testing in a
trial.

9.9 Conclusions

Existing educational and SDM interventions for CVD prevention have not adequately
taken into account patient understandings of illness and risk (which often have scientific
validity). For education, patient understandings of hypertension causation, the rela-
tionship with stress and the connection with symptoms should be acknowledged and
addressed. Formats currently used to present risk in DAs do not appear to have an im-
portant effect on either the quality of decision-making, or clinical outcomes. Presenting
risk with more honesty about the uncertainties present in its calculation, and using for-
mats which align with how patients understand risk are promising routes to improving
the effectiveness of communication, and should be tested in trials.


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The research presented in this thesis has been additionally been presented and published in the following venues:

**Chapter 6**
- The Society for Academic Primary Care, London Annual Scientific Meeting, January 2012
- European Stroke Conference, Lisbon, May 2012
- BMJ, July 2012\(^6_{41}\)

**Chapter 5**
- Stroke, July 2013\(^6_{42}\)

**Chapter 8**
- The Society for Academic Primary Care, London Annual Scientific Meeting, January 2014

The journal versions are appended in the next pages.
Lay perspectives on hypertension and drug adherence: systematic review of qualitative research

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Abstract

Objective To synthesise the findings from individual qualitative studies on patients’ understanding and experiences of hypertension and drug taking; to investigate whether views differ internationally by culture or ethnic group and whether the research could inform interventions to improve adherence.

Design Systematic review and narrative synthesis of qualitative research using the 2006 UK Economic and Social Research Council research methods programme guidance.

Data sources Medline, Embase, the British Nursing Index, Social Policy and Practice, and PsycInfo from inception to October 2011.

Study selection Qualitative interviews or focus groups among people with uncomplicated hypertension (studies principally in people with diabetes, established cardiovascular disease, or pregnancy related hypertension were excluded).

Results 59 papers reporting on 53 qualitative studies were included in the synthesis. These studies came from 16 countries (United States, United Kingdom, Brazil, Sweden, Canada, New Zealand, Denmark, Finland, Ghana, Iran, Israel, Netherlands, South Korea, Spain, Tanzania, and Thailand). A large proportion of participants thought hypertension was principally caused by stress and produced symptoms, particularly headache, dizziness, and sweating. Participants widely intentionally reduced or stopped treatment without consulting their doctor. Participants commonly perceived that their blood pressure improved when symptoms abated or when they were not stressed, and that treatment was not needed at these times. Participants disliked treatment and its side effects and feared addiction. These findings were consistent across countries and ethnic groups. Participants also reported various external factors that prevented adherence, including being unable to find time to take the drugs or to see the doctor; having insufficient money to pay for treatment; the cost of appointments and healthy food; a lack of health insurance; and forgetfulness.

Conclusions Non-adherence to hypertension treatment often resulted from patients’ understanding of the causes and effects of hypertension; particularly relying on the presence of stress or symptoms to determine if blood pressure was raised. These beliefs were remarkably similar across ethnic and geographical groups; calls for culturally specific education for individual ethnic groups may therefore not be justified. To improve adherence, clinicians and educational interventions must better understand and engage with patients’ ideas about causality, experiences of symptoms, and concerns about drug side effects.

Introduction

Hypertension is a major health problem in both developed and developing countries and is estimated to cause more than 13% of deaths annually. Despite national and international guidelines and initiatives for hypertension, population based studies have found that around two thirds of people with hypertension are either untreated or inadequately controlled, including a substantial number who remain undiagnosed.

Among those with a diagnosis of hypertension, the World Health Organization has stated that low adherence to treatment is a key factor impeding good control and has called for research into adherence promoting interventions. Estimates of the rate of poor adherence or non-adherence to treatment range from 30-50%. The causes of poor adherence are complex and include complicated drug regimens, the costs of drugs, older age, poor social support, cognitive problems, and depression.

In 2005 a study reviewed the qualitative research on drug taking in a wide range of medical conditions and found that patients often actively decided not to take drugs (intentional non-adherence) rather than unintentionally omitting them. To date, several patient educational interventions aimed at promoting drug adherence in hypertension have been tested in randomised controlled trials, but most simply informed patients about the importance of adherence and were ineffective.
A better understanding of patients’ perspectives, through qualitative research, is therefore critical to provide an explanation of the low rates of treatment, adherence, and control and why educational interventions have so far failed, and to inform the development of evidence based interventions to improve management. Indeed, authors of studies of lay epidemiology suggest that clinicians’ failure to recognise how people understand disease causation and risk is one of the key obstacles to the success of public health programmes.10,12

We carried out a systematic review and narrative synthesis of qualitative studies on hypertension. Specifically, we examined lay understandings about the causes of hypertension and perspectives on drug taking. We also investigated how patients’ perspectives varied among different cultures and ethnic groups.

Methods

We searched electronic databases (Medline, Embase, the British Nursing Index, Social Policy and Practice, and PsycInfo) from inception until October 2011 and hand searched reference lists of relevant papers. The search strategy combined established methodological terms for qualitative research,13 with specific terms for hypertension (see supplementary appendix 1).

Study selection

We included reports of face to face qualitative interviews and focus groups published in peer reviewed journals looking at patient perspectives on hypertension and drug taking; telephone interviews and quantitative questionnaire analyses were excluded. We included studies of people with uncomplicated hypertension and excluded those principally (over 50%) of people with existing cardiovascular disease or diabetes or who were pregnant. Studies were included regardless of quality. One reviewer (IJM) carried out the search and did an initial screen of titles. Clearly irrelevant titles were excluded at this stage. The remaining abstracts were independently considered for inclusion by two reviewers (IJM and CMcK). Disagreements were resolved by discussion. There was no language limitation for inclusion, and translations were obtained for non-English language papers.

Data synthesis and analysis

We carried out a narrative synthesis following the steps recommended by the UK Economic and Social Research Council (ESRC) research methods programme guidance.14 This was developed to encourage systematic and reproducible approaches to narrative synthesis and promotes transparent reporting and the assessment of the robustness of the results. The guidance provides a toolbox of different methods for reviewers. We used textual summary, tabulation, and thematic analysis to synthesise the results.

Developing a theoretical model

The narrative synthesis guidance recommends developing a hypothesis before data are collected.14 We hypothesised that patients’ understanding and experiences of hypertension might contribute to low rates of drug adherence and blood pressure control.

Developing a preliminary synthesis and exploring relations in the data

IJM used a standard template to extract a textual summary of the populations, research question, and results of the included studies; a sample of these was checked by CMcK. Relations in the data were explored through thematic analysis. IJM and CMcK independently extracted and organised emerging themes using the “one sheet of paper” method,15 using the textual summaries and the full text of papers when needed. A final list of themes and the relations between them was agreed by discussion and consensus. The full text papers were then coded according to the presence or absence of themes. We tabulated these codes by country to examine similarities and variation across cultures.

Qualitative research does not permit statistical inferences: the occurrence of a theme in more than one paper does not imply that it is important or common in the population studied. It may, however, provide a greater degree of certainty that the theme is valid, even if in a few people, and therefore we have reported the number of studies where a particular theme was found.

Assessing the robustness of the synthesis

We assessed the quality of the included papers using the checklist by Dixon-Woods and colleagues (box). We used specific criteria for each area to give a score out of 11; one reviewer (IJM) assessed the quality of each paper. The use of quality assessment when reviewing qualitative research has been debated owing to the lack of agreement among researchers about what criteria should be used, the multitude of possible qualitative methods, and the role of subjective judgment in analysis.16 Therefore we did not exclude papers with low quality scores but used the scores to provide one indicator of the robustness of the synthesis.

We then carried out two sensitivity analyses by reanalysing the data after removing groups of studies thought to be possible sources of bias. Firstly, we examined whether study quality affected the conclusions by assessing the effect of removing lower quality studies (scoring <9 out of 11) from the synthesis. Secondly, to find if the large number of studies in ethnic minority groups had led to unrepresentative conclusions, we carried out a sensitivity analysis only looking at studies that were not in ethnic minority groups.

Results

Overall, 59 papers reporting 53 qualitative studies met the inclusion criteria (figure 1 and table 1). The studies were from the United States (n=20), the United Kingdom (n=8), Brazil (n=7), Sweden (n=3), Canada (n=2), the Netherlands (n=2), New Zealand (n=2), Denmark (n=1), Finland (n=1), Ghana (n=1), Iran (n=1), Israel (n=1), South Korea (n=1), Spain (n=1), Tanzania (n=1), and Thailand (n=1). Forty studies used one to one qualitative interviews, 11 used focus groups, and two used a mixture of these methods. Twenty four of the 53 studies included people only from ethnic minority groups. Areas covered by study interviews included patients’ understanding of the causes, effects, exacerbating factors, and consequences of hypertension; attitudes towards drugs; and the perceived influences of stress, diet, and racism.

Narrative synthesis

Causes of hypertension and the role of stress

The main causes of hypertension reported by participants were stress, food, being overweight, family history, and alcohol (table 2). Participants widely and strongly connected stress and worries with hypertension: as a cause, an exacerbating factor, and a consequence. A participant from a Dutch study seemed to regard worry and blood pressure as synonymous17.
It is the burden of my family. BP [blood pressure] is a sort of . . . eh. Actually it doesn’t make a difference how you call it: BP or worrying too much; it seems to be the same thing.

Stress from work, unemployment, finances, and family matters were often mentioned as impediments to blood pressure control, both directly and indirectly. Most participants reported that stress led directly to increased blood pressure; but leading a stressful life also caused difficulties in finding time to take drugs, eat well, and attend clinic appointments.

Participants from 10 studies (Brazil, Iran, Sweden, United States, and United Kingdom) described reducing or avoiding stress as a consequence of their diagnosis, such as by relaxing, trying to avoid arguments, and changing jobs.18, 32 46 52 54 56-58 64 66

In three studies (Ghana and United States) a difficult life with previous long term stresses was thought to be responsible for hypertension.24-26 69

African-Americans participants in three US studies and Black Caribbean participants in a UK study thought that the stress of experiencing racism was responsible for their high blood pressure.24-26 42 52

A significant stressful event in the past was thought to be responsible for later hypertension by a few participants in four studies (Ghana, Tanzania, United Kingdom, and United States).24 42 69 70 as illustrated by a participant in the UK study:42

I was going through a lot of issues at work and I was going through a lot of issues around race and victimisation I was under extreme stress. So, I went to my doctor and that’s when I was diagnosed with high blood pressure.

In seven studies (Canada, Netherlands, Thailand, United States, and United Kingdom) hypertension was seen by some participants as a temporary or curable condition that would not require long term treatment.22 23 25 52 56 60 62

In five studies (Tanzania, United Kingdom, and United States), some participants perceived hypertension to be a distinct condition from high blood pressure,24 40 52 56 70 highlighted by a participant in a US study 40:

My blood just boils, and you don’t know what’s making it happen. You can’t help it. I can’t control it. I’m the kind of person who just can’t keep my mouth shut for nothing. That pertension can hit you at any time. It’s higher and stronger than with pressure. If you have pressure your blood is up, but not as high as with pertension.

Most participants understood that hypertension caused serious complications, such as stroke (18 studies: Brazil, Sweden, South Korea, Thailand, United Kingdom, United States), death (13 studies: Brazil, Canada, Denmark, Netherlands, Sweden, United Kingdom, and United States), and heart disease (14 studies: Brazil, Sweden, United Kingdom, and United States). Less widely reported complications included kidney disease (three studies: Brazil, United Kingdom, and United States), paralysis (three studies: Canada and United States), suicide (one study, United States), and thinning of the blood (one study, United States). Awareness of possible complications was often a source of fear, as illustrated by a participant in the study from Tanzania:45

I am afraid because I have seen a friend of mine die suddenly. She was overweight and we were living with her in the same house. She woke up in the morning with no problems, ready to leave for work; we talked until the last minute. Suddenly, she fell and died on the spot.

Participants in five studies (South Korea, Sweden, United Kingdom, and United States) described that taking drugs reduced anxiety or worries.20 41 51 52 70 This was often thought to be a direct physiological action of drugs20 51 52 but in some cases resulted from feeling protected from the complications of hypertension.44-50 However, participants in two studies (Sweden and United States)15-16 negatively perceived drugs to function as sedatives, as illustrated by a participant in the Swedish study45:

Well, that depends basically—no one kind of medication—some doctors give us like the—oh, sedatives out there to make you relax and go to sleep that you can become addicted to. But other than that, I don’t think it’s much of a dandy, but you have to watch it once you get that sedative type.

**Symptoms and their meaning**

Participants commonly (13 countries, 27 studies) reported symptoms that they connected with hypertension, particularly headache and dizziness (table 3). Participants in 16 of the studies reported that hypertension caused them no symptoms.

In 11 studies (Brazil, Denmark, Netherlands, New Zealand, Spain, Thailand, United Kingdom, and United States) a large number of participants used the presence or absence of symptoms to indicate whether their blood pressure was raised,21 22 27 28 32 35 37-39 64 72 as illustrated by a participant in the study from Denmark:65

When I got on medication I felt a change for the better in 14 days . . . the headache lifted and I felt 95 percent
well... and that’s where it’s at. It hasn’t changed since then. It’s not headache, it’s a heaviness which makes you constantly aware of the fact that there is something wrong. It’s like a chunk of lead swimming around inside the head and I can feel in the teeth and in my gums and when I’m sitting quietly in a chair I can feel the pumping pressure

Attitudes to drug taking

Participants in nine studies (Brazil, Netherlands, Thailand, United Kingdom, and United States) reported taking drugs regularly according to the prescription.21 22 23 24 25 26 27 28 32 37 56 58 60 64-73 A belief that drugs were essential is illustrated by a participant in one of the Brazilian studies:64:

It is effective if I take it every day, I can’t miss a single day

A participant in one of the US studies described how she planned to ensure she never ran out of tablets:73:

I have to make sure I do it like two weeks in advance to make sure I get there... I let the medication get to a certain number of pills and then I’ll call them... get my medication and there won’t be a break in between me taking it

Intentional non-adherence: link between hypertension, stress, and symptoms

Deliberately choosing to avoid or reduce treatment (intentional non-adherence) was a theme recurring in many of the studies. People from the Netherlands, the United Kingdom, and the United States (11 studies) reported that symptoms made them more likely to take drugs and lack of symptoms less likely to do so.21 22 27 28 29 30 36 38 People from Brazil, Denmark, the Netherlands, Thailand, the United Kingdom, and the United States (10 studies) reported they took drugs exclusively only when symptoms were present.21 22 23 24 25 26 27 28 32 37 56 58 60 64-65 A participant from the Thai study described how he came to restart treatment after a period of feeling well:66:

At that period, I did not visit the doctor because I did not have any symptoms. Then I had symptoms again. I had severe headaches, so I went to a hospital... after I took medication, my headaches were gone. I recognised that my high blood pressure had not disappeared

A participant in the Canadian study stopped taking drugs as he preferred instead to control blood pressure by reducing stress:79:

I dropped them. I didn’t last long with them. I said to myself, I’ll try to fix my pressure myself... I worked with doctors. They told me that I would end up having to take them but I didn’t want to... I’m not a big pill-taker

Studies from the Netherlands, Sweden, and the United Kingdom, reported that participants perceived that treatment was not needed at times of reduced stress, with one participant reporting that he didn’t take drugs in his home country, where he felt more relaxed.18 22 71 A quote from the Swedish study illustrates this:71:

I use my blood pressure pill after how I feel. So when I’m relaxed and not under any stress like in summer when it’s nice weather and vacation, I’ve never taken any blood pressure pills

Intentional non-adherence: dislike of side effects, fear of addiction

People widely reported intentionally missing doses (Canada,62 Netherlands,23 Thailand,40 United Kingdom,56 57 and United States31) or stopping treatment for a time without informing their doctor (Canada,23 Denmark,49 Spain,71 Netherlands,23 Thailand,40 United Kingdom,18 20 23 24 30 33 45 64). Participants from Spain, the United Kingdom, and the United States experimented with stopping treatment to see how they felt without it.23 37 45 Participants from Brazil, Canada, Spain, the United Kingdom, and the United States reported that they self adjusted their drug dose, often because of a desire to avoid side effects or a perception that their blood pressure was controlled.20 32 33 57 59 64 65 A few participants in two studies (United Kingdom and United States) omitted treatment when using alcohol or recreational drugs owing to fear of a harmful interaction.56 57 60

Participants from Canada, Thailand, the United Kingdom, and the United States (in 10 studies) reported a fear of long term problems from taking drugs. These were described as a “build up” of drugs in the body or developing a tolerance or addiction to the drugs. A participant from a UK study described his reluctance to take drugs:72:

I prefer to let nature take its course as far as my body is concerned. I’m not one to introduce anything to it if I’m feeling alright. If I’m feeling ill I will take any medication that will make me better or even cure me, but if I feel better I don’t see why I should take it, because I don’t want to be addicted to nothing other than food and water

Other adverse effects were often reported, such as ankle swelling, lethargy, and urinary frequency. Impotence was mentioned widely by men as a troublesome side effect of treatment (Netherlands, Thailand, United Kingdom, and United States).20 22 31 36 37 56 59 60 64 73

Intentional non-adherence: alternative medicines

Participants from six countries (12 studies) reported supplementing or replacing drugs with a wide range of traditional and alternative medicines (table 4):. Traditional treatments were widely perceived to be safer and more natural than drugs.

Non-intentional non-adherence

Participants described various external factors that limited their ability to adhere to treatment (non-intentional non-adherence). Participants commonly forgot to take drugs from time to time in studies from Canada, South Korea, Spain, the United Kingdom, and the United States (10 studies in total).31 34 37 39 40 44 62 65 71 Participants in eight studies (New Zealand, South Korea, and United States) reported that other commitments meant that they were too busy to take drugs or to attend medical appointments.31 34 39 44 49 60 65 79 Participants from two Brazilian studies and seven of the US studies reported that hypertension care was too expensive: the costs of drugs, healthy food, and visiting doctors were all reported as barriers.32 34 39 40 44 59 63 64 70 Participants in three of the US studies reported that not having health insurance hindered them from accessing medical care.32 39 63
Robustness of findings
The studies were generally of high quality (mean quality score 9.8 out of 11). Sensitivity analyses were done for the key themes (connecting hypertension with stress, having symptoms, using symptoms to judge blood pressure levels, taking drugs only when symptoms were present). These showed that the principal results were robust when limiting the analysis to the highest quality studies (excluding those scoring e9 out of 11 for quality), studies not carried out in an ethnic minority group, and studies done outside the United States (table 5).

Discussion
In this systematic review on people’s perspectives on hypertension and drug taking, many participants in the individual studies perceived stress to be the primary cause and exacerbating factor of hypertension. They widely described symptoms they perceived to be caused by hypertension, particularly headache, palpitations, and dizziness. Contrary to the conclusions of individual studies, these symptoms were consistent among different ethnic and geographical groups. Notably, these symptoms are also commonly reported as being caused by anxiety in the biomedical literature.87 Participants intentionally adjusted their drug dose, took drugs sporadically, and stopped altogether, often without consulting their doctor. Reasons given for reducing treatment included a perception that blood pressure had improved because of a reduction in symptoms, that drugs were unnecessary when under less stress, a dislike of taking drugs, a fear of addiction or tolerance, and side effects.

Comparison with other research on health understanding
A systematic review in 2005 included 37 qualitative studies looking at drug taking in any medical condition (including four hypertension studies also reported in this review).88 That review also found that drugs were seen as undesirable and that many participants feared dependence and tolerance. Participants often tested new drugs for a time to check for adverse effects and whether symptoms were reduced. Our review provides confirmatory evidence from a larger number of studies that these themes are important in hypertension and adds further themes important in hypertension specifically, particularly around stress and symptoms.

Quantitative research provides some evidence that the themes presented here are widespread. A UK study found that 43% of people used complementary medicine to treat hypertension.89 Two US studies found that most participants had symptoms they believed to be caused by hypertension (71-94% in the first study, 70% in the second study).90 91

Comparison with biomedical model
Stress and symptoms
The nature of the connection between hypertension and stress has been researched extensively. Acute stress has been shown to temporarily increase blood pressure levels.92 Evidence from observational studies has also shown that chronic stress can be associated with a sustained rise in high blood pressure.93 In the medical literature, however, stress is considered in the context of other important risk factors for hypertension, both modifiable and non-modifiable: age, ethnicity, family history, obesity, a sedentary lifestyle, and alcohol and salt intake.94 While participants in our review widely reported avoiding stressful situations, a meta-analysis of randomised controlled trials of relaxation interventions for people with hypertension found that they did not substantially improve blood pressure levels, nor did the trials find good evidence of an effect on cardiovascular disease or mortality.95 From the medical perspective, stress plays a small part in hypertension, whereas a recurring theme in the studies presented here was that stress was by far the most important cause.

Likewise, the biomedical literature suggests that symptoms are more likely to be connected with anxiety and stress than blood pressure itself. Although people with hypertension in observational studies have been found to report symptoms, these studies also found that symptoms did not coincide with periods of raised blood pressure when measured clinically.96 97 It was also found that these symptoms were significantly more likely in anxious people. A larger study in the general population found the same association with nervousness, but also found no link with periods of high blood pressure.98

Benefits and adverse effects
Side effects were a widely reported reason for self adjusting or stopping drugs. Participants in these studies described a range of adverse effects of treatment, many of which are listed in the medical literature, including leg swelling, urinary frequency, fatigue, and impotence.98-100 Other longer term fears about the drugs, such as the perception of addiction “building up” over time, or acting as sedatives, are not present in the medical literature. A fear of addiction is not exclusive to hypertension: qualitative studies have found that participants with other chronic medical problems reported identical views.99 Conversely, participants in several studies in this review reported seeing treatment as essential, stating they would not contemplate missing even a single day. The responses from some participants suggest they thought that treatment abolished any risk of cardiovascular disease.100 The benefit assumed by these participants is much greater than the small absolute reductions in risk found in clinical trials.101

Overlap with biomedical model
Rather than being entirely separate, participants’ understandings of hypertension overlapped with many aspects of the biomedical model. Aside from the universally strong emphasis placed on stress, the causes and consequences of hypertension reported by participants are identical to those in any medical textbook. The largest included study examined this contradiction in more depth.102 In this study individual participants often held mutually contradictory explanations, and the inconsistencies did not trouble them.

Similarities among cultural, ethnic, and geographical groups
Previous studies have examined the health beliefs of specific ethnic groups; in particular, many have been done in African-American people, to explore cultural factors influencing low rates of hypertension control.103 The authors of many of the studies in this review concluded that specific culturally appropriate education is needed, implying that their findings were unique in the particular population studied. However, the principal themes identified here were remarkably similar across geographical and ethnic groups. Participants in most of the studies perceived hypertension as a symptomatic illness associated principally with stress; this was confirmed in the sensitivity analyses looking at studies that were not restricted to minority ethnic groups, and in the non-US studies.
Differences between cultural, ethnic, and geographical groups

Racism was often reported by participants from minority ethnic groups. In several studies from the United States of African Americans and one of Filipino-Americans and one study of people of black Caribbean ethnicity in the United Kingdom, the stress caused by racism was reported to exacerbate hypertension. Migrant populations also perceived that they were more likely to have low paying jobs and experience greater economic hardship. African-American participants from two US studies reported a lack of trust of their white doctors, perceiving prejudice against them.

A UK study that compared the reports from black Caribbean and white British participants found that a large number of black Caribbean participants reported self-adjusting and stopping drugs, whereas all but one white British participant reported taking drugs regularly. Although a traditional diet was mentioned as an exacerbating factor for hypertension in many studies, this did not seem to be unique to any particular group. A Dutch study found that people of Surinamese, Ghanaian, and white European ethnicity equally thought that their traditional diet worsened their blood pressure.52

Implications for clinicians and hypertension education

The evidence presented here adds weight to the criticism of educational interventions that assume poor adherence is due to patients’ failings, either in knowledge or remembering to take drugs.92 The participants in the studies presented here did not simply have a knowledge deficit but held alternative explanations for their hypertension; many deliberately chose to avoid drugs.

This may explain why educational interventions that simply inform about the conventional medical view have proved ineffective.93 To better deal with these problems, clinicians and educational interventions must acknowledge and incorporate patients’ concerns and perspectives. Specifically, patients should be given an honest and accurate representation of the likelihood of benefit and adverse effects with treatment. The evidence of safety of long term use of drugs should be discussed, including that treatment is not thought to “build up” in the body or to cause a physical dependence. Fears about addiction could be further tackled by informing patients that they are unlikely to experience adverse effects if they decide to stop, no matter how long they have taken the treatment. This is in stark contrast to existing educational interventions, which emphasise the importance of continuous tablet taking.93

Rather than denying the possibility of symptoms, patients’ experiences should be acknowledged. Patients could be informed that people with hypertension often report symptoms but that they have not been found to be a reliable indication of fluctuations in blood pressure levels. Patients could be informed that their risk of cardiovascular disease is increased regardless of whether they have symptoms, and that treatment can effectively prevent cardiovascular disease. Stress should be placed in the context of other modifiable and non-modifiable risk factors for hypertension and cardiovascular disease; it should be noted that relieving stress alone is not likely to normalise blood pressure and that treatment is recommended at times of high and low stress.

Non-intentional factors, such as forgetting and being busy, were mentioned by many participants as reasons for not taking drugs, and there is low quality evidence from randomised controlled trials that reminder interventions may have an effect.94 However, the qualitative research suggests that reminders alone that neglect patients’ health understanding are not likely to provide a highly effective solution.

Finally, we did not find strong evidence that educational interventions for hypertension need to be tailored to a particular cultural or ethnic group; the consistency of the results presented here suggests that it is more important to take account of common understandings and experiences across the world.

Strengths and weaknesses of the review

This study used a systematic strategy for identifying, reporting, and synthesising qualitative research. Several features suggest that the results are robust. Firstly, we identified a large number of studies, which were largely judged to be of high quality. Secondly, many of the themes we identified were reported repeatedly in a large number of papers. These themes did not vary substantially across different countries. Thirdly, the results of sensitivity analyses, when we removed the groups of papers thought possible to cause bias, did not change the conclusions of the main analysis.

We chose to use the Economic and Social Research Council guidance on narrative synthesis as it both encourages transparent reporting and places a strong emphasis on assessing the robustness of results; the lack of both has been a criticism of other methods of synthesising qualitative research.95 Although no formal test of different synthesis methods versus each other exists,96 the strong evidence of themes found here and the large degree of overlap between narrative synthesis and other qualitative synthesis methodologies suggest that other methods would have produced similar results.

We made a pragmatic decision to include studies from peer reviewed journals only, to retrieve the highest quality research. It seems likely that a body of qualitative research also exists in book chapters, university theses, and conference presentations, that was not included in this review. Although we used no language restriction for inclusion of studies and included some non-English language papers, we would have missed those not listed on English language databases.

Certain groups in the research were represented disproportionately: nearly half of the studies looked at an ethnic minority population and nearly half were done in the United States. Although this presented a potential source of bias, the themes in these papers did not differ substantially from those from other countries and from studies without restriction to an ethnic group.

Implications for research

This review examined the importance of patients’ health understanding for one aspect of cardiovascular disease prevention. Syntheses of the qualitative research on other cardiovascular risk factors would complement the findings and could help inform the development of new interventions. Carrying out a systematic review when planning new qualitative research may help to avoid the unintentional examination of questions that have already been extensively researched. Finally, when developing future educational interventions, it may be more rewarding for researchers to consider shared explanations for hypertension rather than attempting to target a specific ethnic or cultural group.

Implications for practice

Lay perspectives about hypertension are often different from the medical viewpoint: worldwide, people widely perceive that
hypertension is principally a stress-related condition with symptoms and fear addiction or dependence on drugs. These commonly caused people to reduce or stop treatment. If they are to be successful at improving adherence, future educational interventions must incorporate and engage with these widespread perspectives and experiences rather than simply reiterating the biomedical view. A greater understanding between doctors and their patients must play a part in future strategies for reducing cardiovascular disease.

We thank Bom Lee for translating a paper into English and the authors of the original studies who provided copies of their papers.

Contributors: LM carried out the search, appraised the papers for inclusion, extracted and analysed the data, and drafted the paper. CMcK appraised the papers for inclusion, analysed the data, and critically revised the drafts and the final report. CDAW advised about the study design and methods and critically revised the drafts and the final report. CMcK is guarantor.

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Data sharing: No additional data available.

What is already known on this topic
Between 30% and 50% of people with hypertension do not take drugs regularly
Qualitative research in other chronic conditions showed that patients often actively decide to avoid drugs rather than unintentionally missing them
Qualitative studies have focused on the health beliefs of specific ethnic groups in hypertension, suggesting that cultural factors contribute to low rates of control

What this study adds
People with hypertension interviewed in qualitative studies often relied on the presence of stress or symptoms to determine whether their blood pressure was raised
This perceived connection led many to reduce or stop drugs in response to fewer symptoms or less stress
There seem to be few major differences in understanding of hypertension between people from different ethnic groups and countries—calls for culturally specific education by the authors of qualitative studies may not be justified
# Tables

<table>
<thead>
<tr>
<th>Study (country)</th>
<th>Study type</th>
<th>Population</th>
<th>Recruitment site</th>
<th>Specific ethnic group interviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Banen (Northern Ireland)</td>
<td>Focus groups</td>
<td>25 men and women aged 37-70; each prescribed 1-5 hypertension drugs</td>
<td>Six general practices</td>
<td>NS</td>
</tr>
<tr>
<td>Benson (UK)</td>
<td>Interviews</td>
<td>28 men and women (62% women), wide age range reported as frequency table; 50% prescribed 1 hypertension drug, 11% prescribed ≥3 or more</td>
<td>Urban general practice</td>
<td>NS</td>
</tr>
<tr>
<td>Beune (Netherlands)</td>
<td>Interviews</td>
<td>15 men and women (75% women) aged 35-65; all prescribed ≥1 hypertension drugs in past year, range not reported</td>
<td>Inner city general practices</td>
<td>African-Surinamese</td>
</tr>
<tr>
<td>Beune (Netherlands)</td>
<td>Interviews</td>
<td>46 men and women aged 35-65; all prescribed ≥1 hypertension drugs, range not reported</td>
<td>Inner city general practices</td>
<td>Ghanaian, African-Surinamese, and white European ethnicity</td>
</tr>
<tr>
<td>Blumhagen (USA)</td>
<td>Interviews</td>
<td>117 men and women (98% men), all formerly in armed forces, aged 22-79; drug use not described</td>
<td>Primary care centre for military veterans</td>
<td>Majority white</td>
</tr>
<tr>
<td>Boutain (USA)</td>
<td>Interviews</td>
<td>37 men and women aged 43-88; 89% prescribed ≥1 hypertension drugs</td>
<td>Community social events and word of mouth</td>
<td>African-American</td>
</tr>
<tr>
<td>Boutain (USA)</td>
<td>Interviews</td>
<td>30 men and women, median age 55; 83% prescribed ≥1 hypertension drugs</td>
<td>Rural parish church in south Louisiana</td>
<td>African-American</td>
</tr>
<tr>
<td>Boutin-Foster (USA)</td>
<td>Interviews</td>
<td>60 men and women (92% women) aged 29-84 with poorly controlled hypertension; prescribed drug not reported</td>
<td>General practice</td>
<td>African-American</td>
</tr>
<tr>
<td>Connell (UK)</td>
<td>Interviews</td>
<td>19 men and women aged 40-75; prescribed drug not reported</td>
<td>Inner city general practice</td>
<td>Black Caribbean from Jamaica, Guyana, and Trinidad</td>
</tr>
<tr>
<td>Costa (Brazil)</td>
<td>Interviews</td>
<td>21 people; ages and prescribed drug not reported</td>
<td>Hypertension register from primary care clinic</td>
<td>NS</td>
</tr>
<tr>
<td>Costa e Silva (Brazil)</td>
<td>Focus groups</td>
<td>25 women; ages and prescribed drug not reported</td>
<td>Hypertension register from primary care clinic</td>
<td>NS</td>
</tr>
<tr>
<td>Dela Cruz (USA)</td>
<td>Focus groups</td>
<td>27 men and women, ages not reported; all prescribed ≥1 hypertension drugs</td>
<td>Four health maintenance organisation primary care clinics</td>
<td>Filipino-American</td>
</tr>
<tr>
<td>Fimmo (Brazil)</td>
<td>Interviews</td>
<td>30 men and women aged ≥60; prescribed drug not reported</td>
<td>Interviewees were subsample of those taking part in hypertension clinical trial</td>
<td>NS</td>
</tr>
<tr>
<td>Fongwa (USA)</td>
<td>Focus groups</td>
<td>20 women aged 35-68; all prescribed ≥1 hypertension drugs</td>
<td>Inner-city free primary care clinic</td>
<td>African-American</td>
</tr>
<tr>
<td>Ford (USA)</td>
<td>Focus groups</td>
<td>25 women aged 40-74; prescribed drug not reported</td>
<td>12 rural African Methodist Episcopal churches</td>
<td>African-American</td>
</tr>
<tr>
<td>Garrie (Canada)</td>
<td>Interviews</td>
<td>29 men and women aged 28-79; prescribed drug not reported</td>
<td>Chronic disease register at local health centre and word of mouth</td>
<td>Ojibwe</td>
</tr>
<tr>
<td>Gascon (Spain)</td>
<td>Focus groups</td>
<td>44 men and women, ages not reported; all prescribed ≥1 hypertension drugs</td>
<td>Patients of primary care centres, telephone screened to find non-adherent patients</td>
<td>NS</td>
</tr>
<tr>
<td>Greenfield (Israel)</td>
<td>Interviews</td>
<td>22 men and women aged 39-75; prescribed drug not reported</td>
<td>Primary care clinic</td>
<td>Moroccan Jewish</td>
</tr>
<tr>
<td>Greer (USA)</td>
<td>Focus groups</td>
<td>37 men and women aged 25-68, 27 of whom were prescribed ≥1 hypertension drugs</td>
<td>Outpatient clinic with 21% patients uninsured, 25% covered by Medicaid</td>
<td>African-American</td>
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<tr>
<td>Heurtin-Roberts (USA)</td>
<td>Interviews</td>
<td>60 women aged 45-70; all prescribed ≥1 hypertension drugs</td>
<td>Outpatient general medical and hypertension clinics of large public hospital</td>
<td>African-American</td>
</tr>
<tr>
<td>Higginbottom (UK)</td>
<td>Focus groups and interviews</td>
<td>36 men and women aged 37-82; prescribed drug not reported</td>
<td>13 general practices with high ethnic minority populations in Midlands and north of England</td>
<td>Black Caribbean and Latino American</td>
</tr>
<tr>
<td>Horowitz (USA)</td>
<td>Focus groups</td>
<td>88 men and women, 34% aged ≥65; prescribed drug not reported, 36% reported to be uncontrolled</td>
<td>Outpatient clinics in four hospitals in east and central Harlem</td>
<td>African-American and Latino American</td>
</tr>
<tr>
<td>Johnson (USA)</td>
<td>Interviews</td>
<td>21 men and women aged 65-92 identified by their physicians as non-adherent to hypertension drugs</td>
<td>Emergency department (free blood pressure check service), and from physician’s patient lists</td>
<td>African-American</td>
</tr>
<tr>
<td>Study (country)</td>
<td>Study type</td>
<td>Population</td>
<td>Recruitment site</td>
<td>Specific ethnic group interviewed</td>
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<tr>
<td>Kjellgren** (Sweden)</td>
<td>Interviews</td>
<td>33 men and women aged 35-83; all with experience of taking ≥1 hypertension drugs at time of interview or in past</td>
<td>Half from rural general practice; half from hypertension specialist clinic in city hospital</td>
<td>NS</td>
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<tr>
<td>Lahdenpera** (Finland)</td>
<td>Interviews</td>
<td>21 men and women aged 32-63 engaged in trial of educational intervention, 2 of whom were prescribed ≥1 hypertension drugs</td>
<td>Qualitative interviews of participants in clinical trial of long term hypertension educational intervention</td>
<td>NS</td>
</tr>
<tr>
<td>Lee** (South Korea)</td>
<td>Interviews</td>
<td>26 men and women; all reported to be non-compliant, aged from 31 to &gt;65</td>
<td>Public health centre taking part in national hypertension initiative; private medical practices, and medical practices looking after employees of various companies</td>
<td>NS</td>
</tr>
<tr>
<td>Lewis** (USA)</td>
<td>Focus groups</td>
<td>40 men and women aged 21-82, all prescribed ≥1 hypertension drugs</td>
<td>Through word of mouth via respected professionals and community leaders</td>
<td>African-American</td>
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<tr>
<td>Lewis** (USA)</td>
<td>Interviews</td>
<td>21 men aged 57-86, each prescribed 1-3 hypertension drugs</td>
<td>Urban multidisciplinary care centre for elderly people serving principally low income, frail elderly people</td>
<td>African-American</td>
</tr>
<tr>
<td>Lisper** (Sweden)</td>
<td>Interviews</td>
<td>21 men and women, ages not reported; all prescribed ≥1 hypertension drugs</td>
<td>One urban primary health centre</td>
<td>African-American</td>
</tr>
<tr>
<td>Lukoschek** (USA)</td>
<td>Focus groups</td>
<td>42 men and women aged 33-63; separate groups for participants identified as non-adherent and adherent to drugs</td>
<td>Primary care clinic at large municipal hospital serving mostly uninsured or Medicaid insured patients with low education levels</td>
<td>African-American</td>
</tr>
<tr>
<td>Machado** (Brazil)</td>
<td>Interviews</td>
<td>11 men and women, ages not reported; all prescribed ≥1 hypertension drugs</td>
<td>Primary care</td>
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<td>Mohammadi** (Iran)</td>
<td>Interviews</td>
<td>Number of people and ages unclear; all prescribed ≥1 hypertension drugs</td>
<td>Recruitment site unclear</td>
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<tr>
<td>Morecroft** (UK)</td>
<td>Interviews</td>
<td>28 men and women aged 20-78, all prescribed ≥1 hypertension drugs</td>
<td>Five general practices in East Midlands</td>
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<tr>
<td>Morgan** (UK)</td>
<td>Interviews</td>
<td>60 men and women aged 35-55; 58 prescribed ≥1 hypertension drugs</td>
<td>15 inner city general practices</td>
<td>Black Caribbean, and white British</td>
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<tr>
<td>Ogedegbe** (USA)</td>
<td>Interviews</td>
<td>93 men and women, mean age 58, prescribed mean of 2 hypertension drugs; 60% reported as uncontrolled</td>
<td>Primary care practice in New York university hospital</td>
<td>African-American</td>
</tr>
<tr>
<td>Ogedegbe** (USA)</td>
<td>Interviews (some via telephone)</td>
<td>108 men and women, mean age 56 (SD 13) years, prescribed mean of 2 hypertension drugs</td>
<td>Two primary care practices in New York, first with diverse population, second predominantly serving people with low income</td>
<td>African-American</td>
</tr>
<tr>
<td>Panpakdee** (Thailand)</td>
<td>Interviews</td>
<td>16 men and women aged 34-75; 96% prescribed ≥1 hypertension drugs</td>
<td>University hospital outpatient clinic</td>
<td>NS</td>
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<tr>
<td>Peres** (Brazil)</td>
<td>Interviews (semistructured, content analysis)</td>
<td>32 men and women aged 37-81; prescribed hypertension drug not reported</td>
<td>2 inner city primary care clinics</td>
<td>NS</td>
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<tr>
<td>Proulx** (Canada)</td>
<td>Interviews</td>
<td>27 men and women recruited from adherence study, each prescribed 1 hypertension drug</td>
<td>Subsample of participants of larger clinical trial who identified themselves as non-adherent</td>
<td>NS</td>
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<tr>
<td>Rose** (USA)</td>
<td>Interviews</td>
<td>19 men aged 33-49 recruited from hypertension clinical trial</td>
<td>Subsample of participants of larger clinical trial</td>
<td>African-American</td>
</tr>
<tr>
<td>Sadala** (Brazil)</td>
<td>Interviews</td>
<td>21 men and women; ages and prescribed drugs not reported</td>
<td>Those attending an adult health programme</td>
<td>African-American</td>
</tr>
<tr>
<td>Sångren** (Denmark)</td>
<td>Interviews</td>
<td>17 men and women aged 34-50; prescribed 1-3 hypertension drugs</td>
<td>Four general practices</td>
<td>NS</td>
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<tr>
<td>Schoenberg** (USA)</td>
<td>Interviews</td>
<td>41 men and women aged &gt;65; prescribed drug not reported</td>
<td>Several local churches and local public health department clinic</td>
<td>African-American</td>
</tr>
<tr>
<td>Silva** (Brazil)</td>
<td>Interviews</td>
<td>8 men and women; ages and prescribed drugs not reported</td>
<td>Those attending an adult health programme</td>
<td>NS</td>
</tr>
<tr>
<td>Sims** (UK)</td>
<td>Interviews</td>
<td>49 men and women aged 38-84; 45 of whom were prescribed ≥1 hypertension drugs</td>
<td>General practice in south of England with nurse led hypertension clinic</td>
<td>NS</td>
</tr>
<tr>
<td>Spencer** (Ghana)</td>
<td>Interviews</td>
<td>100 men and women; ages reported as categories from 18 to &gt;75; prescribed drug not reported</td>
<td>Monthly hypertension clinic at Ghana Health Mission</td>
<td>NS</td>
</tr>
</tbody>
</table>
Table 1 (continued)

<table>
<thead>
<tr>
<th>Study (country)</th>
<th>Study type</th>
<th>Population</th>
<th>Recruitment site</th>
<th>Specific ethnic group interviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strahl(^7) (Tanzania)</td>
<td>Focus groups and interviews</td>
<td>33 men and women in focus groups, 11 of whom were interviewed individually; prescribed drug not reported</td>
<td>Small hypertension and diabetes clinic in suburb of city</td>
<td>NS</td>
</tr>
<tr>
<td>Svensson(^7) (Sweden)</td>
<td>Interviews</td>
<td>33 men and women aged 35-83, with experience of taking ≥1 hypertension drugs at time of interview or in past; 55% prescribed ≥1 hypertension drug</td>
<td>General practice and specialist hypertension clinic</td>
<td>NS</td>
</tr>
<tr>
<td>van Wissen(^7) (New Zealand)</td>
<td>Interviews</td>
<td>19 men and women (79% women) aged 41-67; all prescribed ≥1 hypertension drugs</td>
<td>Register of previous research participants from Wellington School of Medicine</td>
<td>2 Māori, rest white European</td>
</tr>
<tr>
<td>Viswanathan(^7) (USA)</td>
<td>Interviews</td>
<td>20 women, ages presented as categories from 25 to &gt;75; all prescribed ≥1 hypertension drugs</td>
<td>Community health centre, Chicago</td>
<td>African-American</td>
</tr>
<tr>
<td>Wai(^7) (New Zealand)</td>
<td>Interviews</td>
<td>20 men and women, 10 reported to have poor adherence aged 41-81, all prescribed ≥1 hypertension drugs; patients with low adherence and good adherence selected for interview</td>
<td>Auckland general practice</td>
<td>Samoan</td>
</tr>
<tr>
<td>Weaver(^7) (UK)</td>
<td>Interviews</td>
<td>11 men and women aged 41-82 with diagnosis of hypertension in past 6 months; prescribed drugs not reported</td>
<td>2 general practices</td>
<td>NS</td>
</tr>
<tr>
<td>Wexler(^7) (USA)</td>
<td>Focus groups</td>
<td>26 men and women (77% women) aged 32-71; prescribed drug not reported</td>
<td>Patients of Ohio State University primary care research clinic</td>
<td>African-American</td>
</tr>
</tbody>
</table>

NS=none specified.
<table>
<thead>
<tr>
<th>Perceived causes of hypertension</th>
<th>Countries, studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>Brazil⁴⁷, Canada⁴⁷, Denmark⁴⁷, Ghana⁴⁷, Israel⁴⁷, Netherlands⁴⁶, South Korea⁴⁷, Tanzania⁴⁷, Thailand⁴⁷ (2 studies); USA⁴⁸, UK⁴⁹</td>
</tr>
<tr>
<td>Food</td>
<td>Brazil⁴⁷, Canada⁴⁷, Israel⁴⁷, Netherlands⁴⁶, USA⁴⁶, South Korea⁴⁷, Tanzania⁴⁷, UK⁴⁹, USA⁴⁹</td>
</tr>
<tr>
<td>Being overweight</td>
<td>Brazil⁴⁷, Netherlands⁴⁶, South Korea⁴⁷, Tanzania⁴⁷, UK⁴⁹, USA⁴⁹</td>
</tr>
<tr>
<td>Family history</td>
<td>Canada⁴⁷; Netherlands⁴⁷, USA⁴⁸, Brazil⁴⁷, South Korea⁴⁷, UK⁴⁹</td>
</tr>
<tr>
<td>Lack of exercise</td>
<td>Brazil⁴⁷; Netherlands⁴⁶, South Korea⁴⁷, USA⁴⁷, UK⁴⁹</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Brazil⁴⁷; Canada⁴⁷, Netherlands⁴⁶, UK⁴⁹, USA⁴⁹</td>
</tr>
<tr>
<td>Heat</td>
<td>Brazil⁴⁷; Israel⁴⁷, Thailand⁴⁷, USA⁴⁹</td>
</tr>
<tr>
<td>Smoking</td>
<td>Canada⁴⁷; UK⁴⁹, USA⁴⁹</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Canada⁴⁷; Tanzania⁴⁹</td>
</tr>
<tr>
<td>Witchcraft/spirits</td>
<td>Canada⁴⁷, Israel⁴⁹</td>
</tr>
<tr>
<td>Exposure to cold</td>
<td>Canada⁴⁷</td>
</tr>
<tr>
<td>Too much water</td>
<td>USA⁴⁹</td>
</tr>
<tr>
<td>Over-exertion</td>
<td>Canada⁴⁷</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>Canada⁴⁷</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Canada⁴⁷</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>Canada⁴⁷</td>
</tr>
<tr>
<td>Exposure to farm chemicals</td>
<td>Canada⁴⁷</td>
</tr>
<tr>
<td>Eye strain</td>
<td>Canada⁴⁷</td>
</tr>
<tr>
<td>Nightmares</td>
<td>Canada⁴⁷</td>
</tr>
<tr>
<td>Thick blood</td>
<td>USA⁴⁹</td>
</tr>
<tr>
<td>Blood rising</td>
<td>USA⁴⁹,⁵⁰</td>
</tr>
<tr>
<td>Bad climate</td>
<td>Netherlands⁴⁷</td>
</tr>
<tr>
<td>Kidneys</td>
<td>USA⁴⁹</td>
</tr>
<tr>
<td>Resistance to blood flow</td>
<td>USA⁴⁹</td>
</tr>
<tr>
<td>Heart pumping harder</td>
<td>USA⁴⁹</td>
</tr>
<tr>
<td>Too much blood</td>
<td>Israel⁴⁹</td>
</tr>
<tr>
<td>Symptom</td>
<td>Countries (No of studies)</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Headache</td>
<td>Brazil (4), Canada (1), Denmark (1), Ghana (1), Netherlands (2), South Korea (1), Sweden (2), UK (2), USA (8)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Brazil (3), Canada (1), Denmark (1), Ghana (1), Netherlands (1), New Zealand (1), South Korea (1), Sweden (1), Tanzania (1), Thailand (1), UK (3), USA (8)</td>
</tr>
<tr>
<td>Palpitations/racing heart</td>
<td>Brazil (3), Canada (1), Netherlands (1), Sweden (1), Tanzania (1), USA (3)</td>
</tr>
<tr>
<td>Sweating</td>
<td>Brazil (1), Canada (1), Netherlands (1), Tanzania (1), UK (1), USA (1)</td>
</tr>
<tr>
<td>Tiredness</td>
<td>Brazil (3), Canada (1), Denmark (1), Ghana (1), Sweden (2), UK (1), USA (2)</td>
</tr>
<tr>
<td>Neck pain</td>
<td>Brazil (3), South Korea (1), Spain (1), USA (2)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>Brazil (2), Spain (1), Thailand (1), USA (1)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Brazil (2), Canada (1), UK (1), USA (1)</td>
</tr>
<tr>
<td>Visual changes</td>
<td>Brazil (1), Canada (1), UK (1), USA (4)</td>
</tr>
<tr>
<td>Feeling nervous/irritable</td>
<td>Brazil (2), USA (2)</td>
</tr>
</tbody>
</table>
### Table 4 | Non-drug treatments reported

<table>
<thead>
<tr>
<th>Country, study</th>
<th>Alternative treatments reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Avocado leaf tea, boldo tea, garlic, lemon balm, passion fruit juice, rosemary, sugar water, tea leaf chayote, water</td>
</tr>
<tr>
<td>Netherlands&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Acupuncture, bush suporo, blanched celery, coconut bark, cucumber, garlic, garlic tea, homeopathy, neem, papaya leaf, perekese, red cotton, tamarind, prayer</td>
</tr>
<tr>
<td>Spain&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Lemons, nettle tea</td>
</tr>
<tr>
<td>Thailand&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Jorn, hed lin cheu, khin chai, meditation, pha talai</td>
</tr>
<tr>
<td>UK&lt;sup&gt;8, 13-16, 57&lt;/sup&gt;</td>
<td>Aloe vera, banana leaf, “bitters,” “blood toner,” breadfruit leaf, cerasee, ginseng, green papaya, medina, royal jelly, soroce tea</td>
</tr>
<tr>
<td>USA&lt;sup&gt;11, 20-21&lt;/sup&gt;</td>
<td>Acupuncture, coconut oil, garlic, ginger, guava, guava leaves, herbal teas, home brewed mango leaves, lemons, lime, lemon grass, massage, noni juice, pito-pito, poliences, prayer</td>
</tr>
</tbody>
</table>
### Table 5 | Examples of sensitivity analyses

<table>
<thead>
<tr>
<th>Theme (group excluded)</th>
<th>Countries, studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stress as cause of hypertension:</strong></td>
<td></td>
</tr>
<tr>
<td>Excluding studies in specific ethnic groups</td>
<td>Brazil(^{11,15,31}); Canada(^{34}); Denmark(^{6}); Ghana(^{6}); Tanzania(^{6}); Thailand(^{6}); USA(^{4})</td>
</tr>
<tr>
<td>Excluding lower quality studies*</td>
<td>Brazil(^{11,34}); Canada(^{34}); Denmark(^{6}); Israel(^{6}); Netherlands(^{1,2}); (1 study); Thailand(^{6}); UK(^{1,2}); USA(^{2,37,39,40,47,76})</td>
</tr>
<tr>
<td><strong>Hypertension causes symptoms:</strong></td>
<td></td>
</tr>
<tr>
<td>Excluding studies in specific ethnic groups</td>
<td>Brazil(^{15,31}); Denmark(^{6}); Ghana(^{6}); New Zealand(^{6}); South Korea(^{6}); Spain(^{6}); Sweden(^{6}); Tanzania(^{6}); Thailand(^{6}); UK(^{20})</td>
</tr>
<tr>
<td>Excluding lower quality studies*</td>
<td>Brazil(^{11,15,31}); Canada(^{34}); Denmark(^{6}); Netherlands(^{2,2}); (1 study); New Zealand(^{6}); South Korea(^{6}); Spain(^{6}); Sweden(^{6}); Thailand(^{6}); UK(^{20,29,30}); (3 studies); USA(^{2,3,16,30,32,47,54,76})</td>
</tr>
</tbody>
</table>

*Quality score <9/11.*
Flow of studies through review
Trends in Risk Factor Prevalence and Management Before First Stroke

Data From the South London Stroke Register 1995–2011

Iain J. Marshall, MRCGP; Yanzhong Wang, PhD; Christopher McKEVITT, PhD; Anthony G. Rudd, FRCP; Charles D.A. Wolfe, FFPH

Background and Purpose—Vascular risk factors are suboptimally managed internationally. This study investigated time trends in risk factors diagnosed before stroke and their treatment, and factors associated with appropriate medication use.

Methods—A total of 4416 patients with a first stroke were registered in the population-based South London Stroke Register from 1995 to 2011. Previously diagnosed risk factors and usual medications were collected from patients’ primary care and hospital records. Trends and associations were assessed using multivariate logistic regression.

Results—Seventy-two percent of patients were diagnosed previously with 1 or more risk factors; 30% had diagnosed risk factors that were untreated. Hypercholesterolemia increased significantly during the study period; myocardial infarction and transient ischemic attack prevalences decreased. Antiplatelet prescription increased in atrial fibrillation (AF), myocardial infarction, and transient ischemic attack (AF, 37%–51%, P=0.001; myocardial infarction, 48%–69%, P<0.001; transient ischemic attack, 49%–61%, P=0.015). Anticoagulant prescription for AF showed a nonsignificant increase (12%–23%; P=0.059). Fewer older patients with AF were prescribed anticoagulants (age, >85 versus <65 years; adjusted relative risk, 0.19; 95% confidence interval, 0.08–0.41). Black ethnicity (adjusted relative risk, 1.17; 95% confidence interval, 1.10–1.23) and female sex (adjusted relative risk, 1.09; 95% confidence interval, 1.03–1.15) were associated with increased antihypertensive drug prescription; other medications did not vary by ethnicity or sex.

Conclusions—Antiplatelet and cholesterol-lowering treatment prescribing have improved significantly over time; however, only a minority with AF received anticoagulants, and this did not improve significantly. Overall, 30% of strokes occurred in patients with previously diagnosed but untreated risk factors. (Stroke. 2013;44:00-00.)

Key Words: primary prevention ■ stroke ■ stroke epidemiology

Stroke remains a major preventable cause of morbidity and mortality internationally.1 In addition to lifestyle modification, cost-effective drug treatments for hypertension, hypercholesterolemia, and atrial fibrillation (AF) reduce stroke risk, heart disease, and mortality.2,4 Despite international guidance aimed at improving primary prevention, risk factor control rates remain low.5–7 Suboptimal control is associated with inadequate risk factor detection and treatment, ethnic differences in risk factor susceptibility and response to treatment, socioeconomic deprivation, and poor treatment adherence.5,7–9

Several studies have found ethnic differences in stroke risk factors. A US case–control study found that hypertension and diabetes mellitus were significantly more prevalent among black than white patients with stroke, whereas AF was significantly more prevalent in white patients.10 Similar results were reported by the South London Stroke Register (SLSR) from 1995 to 1998.11 A US cross-sectional study found that apparent ethnic differences in stroke risk factors were explained by differences in income.12

We sought to examine trends from 1995 to 2011 in before-stroke risk factors and use of appropriate treatment, using data from the SLSR. We aimed to investigate variation in risk factors by age, sex, ethnicity, socioeconomic group, and stroke subtype, and factors associated with appropriate treatment.

Methods

The methods of the SLSR have been described previously13 and are summarized below. The SLSR is a population-based register recording all first strokes in a defined region of Lambeth and Southwark, with a population of 310,028 according to the 2001 UK Census, with 63% white, 28% black (9% black Caribbean, 15% black African, and 4% black other), and 9% other ethnic group. By 2011, the source population had increased to 357,308, with 56% white, 25% black (7% black Caribbean, 14% black African, 4% black other), and 18% other.
The largest increase was in those aged 49 to 59 (49%) years; the proportion aged >65 years fell by 10%.

Overlapping notification sources were used to increase data completeness. Data were collected by study nurses and field workers. Stroke diagnosis was confirmed by a study clinician according to World Health Organization criteria. Ethnicity was self-reported using 1991 UK Census criteria. To increase numbers per group, white British and white other were considered as white ethnicity; black Caribbean, black African, and black other were grouped as black ethnicity. Risk factors recorded before stroke (hypercholesterolemia [from 2001], hypertension, AF, myocardial infarction [MI], transient ischemic attack [TIA], and diabetes mellitus) and usual prescribed medication (antiplatelets, anticoagulants, antihypertensive drugs, and cholesterol-lowering drugs) were collected from patients’ general practitioners and hospital records.

Stroke subtype was determined from computed tomography or MRI results where available and classified as ischemic, intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), or undefined.

Deprivation was estimated using the Carstairs Index, which combines male unemployment, overcrowding, car ownership, and proportion in social classes IV and V in a small area. The index was derived from the 2001 census data for each lower layer super output area, covering an average population of 1500. Scores were obtained from patients’ home postcodes at the time of stroke.

Data were analyzed in 4-year groups to increase numbers per group. Demographic trends were assessed using the \( \chi^2 \) test for trends. Risk factor and medication trends were assessed in logistic regression models adjusting for age, sex, ethnicity, stroke subtype, and deprivation with the year of stroke as an explanatory variable. Associations with risk factors and prescribed medication were assessed in logistic regression models incorporating sex, age, ethnicity, stroke subtype, deprivation, and year of stroke.

P values <0.05 were regarded as statistically significant. Risk ratios were estimated using methods of Zhang and Yu. Intervariable interactions were assessed for each analysis. Analyses omitted patients with missing data. Analyses were conducted using R.

### Table 1. Trends in Demographics, Before-Stroke Risk Factors, and Treatments

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>638 (48.9%)</td>
<td>535 (49.8%)</td>
<td>537 (54%)</td>
<td>429 (49.9%)</td>
<td>0.399</td>
</tr>
<tr>
<td>Female</td>
<td>667 (51.1%)</td>
<td>539 (50.2%)</td>
<td>457 (46%)</td>
<td>448 (51.1%)</td>
<td>0.399</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1028 (78.8%)</td>
<td>753 (70.1%)</td>
<td>671 (67.5%)</td>
<td>576 (65.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black</td>
<td>216 (16.6%)</td>
<td>209 (19.5%)</td>
<td>221 (22.2%)</td>
<td>225 (25.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other</td>
<td>52 (4%)</td>
<td>62 (5.8%)</td>
<td>73 (7.3%)</td>
<td>57 (6.5%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Unknown</td>
<td>9 (0.7%)</td>
<td>50 (4.7%)</td>
<td>29 (2.9%)</td>
<td>19 (2.2%)</td>
<td>0.058</td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td>343 (26.3%)</td>
<td>362 (33.8%)</td>
<td>334 (33.6%)</td>
<td>303 (34.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>65–74</td>
<td>365 (28%)</td>
<td>276 (25.7%)</td>
<td>250 (25.2%)</td>
<td>189 (21.6%)</td>
<td>0.001</td>
</tr>
<tr>
<td>75–84</td>
<td>398 (30.5%)</td>
<td>274 (25.6%)</td>
<td>283 (28.5%)</td>
<td>242 (27.6%)</td>
<td>0.247</td>
</tr>
<tr>
<td>≥85</td>
<td>198 (15.2%)</td>
<td>160 (14.9%)</td>
<td>127 (12.8%)</td>
<td>143 (16.3%)</td>
<td>0.954</td>
</tr>
<tr>
<td><strong>Subtypes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>916 (70.2%)</td>
<td>786 (73.2%)</td>
<td>776 (78.1%)</td>
<td>699 (79.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICH</td>
<td>177 (13.6%)</td>
<td>163 (15.2%)</td>
<td>124 (12.5%)</td>
<td>88 (10%)</td>
<td>0.009</td>
</tr>
<tr>
<td>SAH</td>
<td>71 (5.4%)</td>
<td>71 (6.6%)</td>
<td>51 (5.1%)</td>
<td>20 (2.3%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Undefined</td>
<td>141 (10.8%)</td>
<td>54 (4.7%)</td>
<td>43 (4.3%)</td>
<td>70 (8%)</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>845 (69.2%)</td>
<td>555 (56.8%)</td>
<td>630 (65.1%)</td>
<td>545 (63.4%)</td>
<td>0.091</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>...</td>
<td>97 (10.5%)</td>
<td>226 (23.7%)</td>
<td>272 (31.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>209 (17%)</td>
<td>178 (18%)</td>
<td>194 (20.3%)</td>
<td>180 (20.7%)</td>
<td>0.166</td>
</tr>
<tr>
<td>AF</td>
<td>252 (20.6%)</td>
<td>138 (13.9%)</td>
<td>148 (15.3%)</td>
<td>122 (14.9%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Previous MI</td>
<td>90 (7.7%)</td>
<td>37 (4%)</td>
<td>48 (5%)</td>
<td>23 (2.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous TIA</td>
<td>196 (15.3%)</td>
<td>105 (10.6%)</td>
<td>111 (11.5%)</td>
<td>76 (8.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Treatments</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 Untreated risk factor</td>
<td>524 (40.2%)</td>
<td>184 (17.1%)</td>
<td>289 (29.3%)</td>
<td>311 (35.5%)</td>
<td>0.513</td>
</tr>
<tr>
<td>Treated hypertension</td>
<td>433/627 (52.4%)</td>
<td>373/507 (73.6%)</td>
<td>460/618 (74.4%)</td>
<td>297/540 (55%)</td>
<td>0.502</td>
</tr>
<tr>
<td>Treated hypercholesterolemia</td>
<td>...</td>
<td>54/61 (66.7%)</td>
<td>175/223 (78.5%)</td>
<td>210/270 (77.8%)</td>
<td>0.001</td>
</tr>
<tr>
<td>AF (antiplatelet)</td>
<td>88/232 (37.1%)</td>
<td>52/101 (51.5%)</td>
<td>84/147 (57.1%)</td>
<td>64/125 (51.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AF (anticoagulant)</td>
<td>30/245 (12.2%)</td>
<td>21/124 (16.9%)</td>
<td>30/147 (20.4%)</td>
<td>29/125 (23.2%)</td>
<td>0.059</td>
</tr>
<tr>
<td>MI (antiplatelet)</td>
<td>75/155 (48.4%)</td>
<td>55/77 (71.4%)</td>
<td>74/96 (77.1%)</td>
<td>45/75 (60%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TIA (antiplatelet)</td>
<td>86/174 (49.4%)</td>
<td>56/82 (68.3%)</td>
<td>71/111 (64%)</td>
<td>46/75 (61.3%)</td>
<td>0.015</td>
</tr>
<tr>
<td>TIA (anticoagulant)</td>
<td>6/192 (3.1%)</td>
<td>5/83 (6%)</td>
<td>4/111 (3.6%)</td>
<td>5/75 (6.7%)</td>
<td>0.349</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; ICH, intracerebral hemorrhage; MI, myocardial infarction; SAH, subarachnoid hemorrhage; and TIA, transient ischemic attack.
Results
Between January 1995 and 2011, a total of 4416 patients were registered (Table 1). Patient median age was 72.4 years (interquartile range, 61.2–81.1); ethnicities were white (70.5%), black (21.3%; 13.0% black Caribbean, 7.6% black African, and 0.6% black other), and other (5.7%). Stroke subtypes were ischemic (73.8%), ICH (12.7%), SAH (5%), and undefined (8.4%). White and black patients had significantly lower Carstairs scores than other ethnicities, but the difference was small (mean score [higher=more deprived]: white 9.421, black 9.662, other 10.21; \(P=0.006\)). Data completeness was high for all variables (ethnicity, 97%; stroke subtype, 96%; risk factors, 95%–97%; prescribed medication, 96%–97%). There were no significant intervariable interactions in any analysis.

Risk Factor Trends
Risk factor trends are reported in Figure 1 and Table 1. Seventy-two percentage of patients had 1 or more risk factors diagnosed before stroke. Overall risk factor prevalences were the following: hypertension, 64%; hypercholesterolemia, 24%; AF, 16%; diabetes mellitus, 19%; previous MI, 11%; and previous TIA, 12%. Hypercholesterolemia significantly increased over time (10.5%–31.7%; \(P<0.001\)); before-stroke MI and TIA significantly reduced (MI, 7.7%–2.7%; \(P<0.001\) and TIA, 16.3%–8.9%; \(P<0.001\)). Hypertension, AF, and diabetes mellitus did not change significantly over time.

Risk Factor Associations
The multivariate analyses are reported in Table 2. Hypertension, diabetes mellitus, AF, previous MI, and TIA increased significantly with age. Hypercholesterolemia was the highest in those aged 65 to 74 years. Hypertension and MI were significantly more prevalent in men; other risk factors were not significantly different between men and women.

Black patients had significantly greater prevalences of hypertension and diabetes mellitus than white patients (adjusted relative risk [aRR]: hypertension, 1.22; 95% confidence interval [CI], 1.17–1.27 and diabetes mellitus, 2.15; 95% CI, 1.91–2.39) and significantly lower AF, MI, and TIA (AF, 0.47, 95% CI, 0.35–0.60; MI, 0.58, 95% CI, 0.43–0.77; TIA, 0.76, 95% CI, 0.59–0.96). There was no association between deprivation and any risk factor. Risk factor prevalence was similar in ischemic stroke and ICH, but significantly lower in SAH (aRR for SAN vs ischemic stroke, 0.63; 95% CI, 0.52–0.75). Hypercholesterolemia, diabetes mellitus, previous MI, and AF were significantly less prevalent in ICH and SAH than ischemic stroke.

Prescribing Trends
Trends in prescribed medication are reported in Table 1 and Figure 2. Twenty-six percentage of patients had a single untreated risk factor, 13% had 2 or more risk factors. The proportions of those with risk factors prescribed appropriate treatment were hypertension, 62%; hypercholesterolemia, 75%; MI (antiplatelets), 62%; AF, 64% (anticoagulants, 17%; antiplatelets, 48%; [1% both]); TIA (antiplatelets), 58%. Prescribed treatment for hypercholesterolemia increased over time (70%–77%; \(P=0.004\)). Antiplatelet prescription for AF significantly increased (37%–51%; \(P<0.001\)); anticoagulant prescription increased, but was not significantly (12%–23%; \(P=0.059\)). Antiplatelet prescription in MI and TIA significantly increased over time (MI, 48%–60%; \(P<0.001\) and TIA, 49%–61%; \(P=0.015\)). Antihypertensive prescription did not significantly change over time.

Associations with Appropriate Treatment
The multivariate analyses are reported in Table 3. Anticoagulant prescription in AF for older patients was low and was the least in those aged ≥85 years (aRRs vs <65 years: 65–74 years, 0.41; 75–84 years, 0.77; ≥85 years, 0.19). Significantly more women with hypertension were treated than men; there were no significant differences for other risk factor treatments between sexes.

Significantly more black patients with hypertension were treated than white patients (aRR, 1.17; 95% CI, 1.10–1.15). There was no significant association between other risk factor treatments and ethnicity, or between deprivation and any risk factor treatment. ICH and SAH were associated with significantly higher anticoagulant prescription (aRR vs ischemic stroke: ICH, 3.14; 95% CI, 2.21–4.04 and SAH, 4.64; 95% CI, 2.40–5.72).

Discussion
This article analyses trends in the prevalence and treatment of risk factors before stroke during 15 years. Hypercholesterolemia increased significantly over time, and previous MI and TIA fell. Prescribing of antiplatelets and cholesterol-lowering treatments significantly increased during the study period. A minority of patients with AF was prescribed anticoagulants; this did not significantly improve over time and was least likely in older people. Overall, one third of first strokes occurred in people who were not prescribed treatment for a previously diagnosed risk factor.

Anticoagulants are effective for the prevention of AF-related stroke; a 2007 meta-analysis found that anticoagulation was substantially more effective than aspirin.17 A UK consensus statement published after the SLSR data was collected recommended that aspirin is no longer used for stroke prevention in AF.18 Anticoagulant prescribing for AF remained low throughout the study period, and was the lowest in older patients, among whom AF was most prevalent. UK research found significantly lower primary prevention use among older people, despite advancing age being the most important risk factor for vascular disease.19 The SLSR did not record contraindications to anticoagulants, although US research found low warfarin use even among those with no contraindications.6

These results provide an example of delay in implementing evidence-based practice.20 Guidelines recommending anticoagulation for AF were published in the early 1990s.21 Barriers to anticoagulant use have been examined in qualitative research and include perceived high rates of bleeding, particularly in the elderly, and clinicians’ perceptions that patients would not agree to treatment.22 However, a randomized controlled trial in people aged >75 found that warfarin was more effective than aspirin in preventing stroke, with no increase in hemorrhage.23
Figure 1. Trends in risk factors diagnosed before-stroke prevalences with 95% CI, and variation by ethnic group. CI indicates confidence interval; MI, myocardial infarction; and TIA, transient ischemic attack.
The SLSR data suggest that there is room for improvement in the use of anticoagulation in AF.

Consistent with previous reports, this study found that AF was substantially less prevalent in black than in white patients with stroke. This difference was not caused by underdiagnosis: a similar discrepancy was found on ECG on hospital admission. This difference may be explained by lower AF prevalence in black people in the general population and ethnic differences in the pathogenetic role of AF in stroke.

Randomized controlled trials of anticoagulation in AF were conducted overwhelmingly in white populations; only 6% of participants were nonwhite. Additionally, tools for identifying patients with AF at highest risk, CHADS2, and CHA2DS2-VASc, do not incorporate ethnicity and have not been validated in black populations. A US observational study found increased warfarin-related intracranial hemorrhage in black compared with white patients. These data question whether the balance of benefit and harm with anticoagulation may vary among different ethnic groups.

Previous studies have found that ethnic minority populations have inadequate access to health care. We found no difference in risk factor treatment between ethnic groups, except for hypertension, with significantly more black patients treated than white patients. Here, we did not assess risk factor control, but merely whether treatment was prescribed. UK observational studies have reported significantly worse control in black patients compared with white patients.

There was a reduction in patients with untreated risk factors from 40% in 1995–1998 to 17% in 1999–2002, followed by increases until 2010, although the overall trend was not significant. This change from 1995–1998 to 1999–2002 was principally caused by a large increase in hypertension treatment from 52% to 74%. This improvement was not sustained; rates reduced to 55% by 2007–2010. The reason for these changes is unclear, but migration in the source population may have contributed. According to census data, from 1991 to 2001, the number of black African residents increased (7%–15%) and the number of white fell (72%–63%).

In the SLSR, deprivation was not associated with significant differences in risk factors or prescribed treatments, and was not responsible for ethnic differences in risk factors. This contrasts with the US research, which reported that income differences explained much of the difference in risk factor prevalence between white and black patients.

Risk factor prevalences are susceptible to changes in diagnostic cutoffs over time. UK hypertension guidelines have recommended similar cutoffs during the study period (>160/100 or >140/90 mm Hg with other risk factors); diagnostic criteria for diabetes mellitus were lowered in 1999 from a fasting blood glucose ≥7.8 to ≥7.0 mmol/L. European guidelines on hypercholesterolemia were published in 1998, recommending a diagnostic cutoff of total cholesterol ≥5, or low-density lipoprotein-cholesterol ≥2.5; subsequent revisions recommend treatment based on overall cardiovascular risk. The large increase in hypercholesterolemia is likely to be explained by increased detection.
Strengths and Limitations

This study was population based, with multiple notification sources, including hospitalized and community patients with stroke. Risk factor diagnoses were collected from patient medical records. Although bias may occur through changes in documentation practice during the time period, this was mitigated by using both hospital and primary care records. This study did not collect individual blood pressure or serum levels.
cholesterol values; therefore, the results represent rates of detected risk factors and omit those who were unaware.

It is not possible to draw conclusions from this study about primary prevention uptake in the general population. The stroke population is more likely to contain people with multiple and inadequately treated risk factors. Indeed, the number of people with a first stroke reduced over time, which could be consistent with improvements in prevention. This study does provide evidence, however, that a substantial number of patients with stroke were not prescribed optimal treatment for previously diagnosed risk factors.

## Conclusions

There have been significant improvements in the use of appropriate antplatelet and cholesterol-lowering treatments; however, almost one third of strokes occurred in patients with diagnosed but untreated risk factors. Anticoagulant prescription in AF remained low throughout the study period and was the lowest in older people. These results highlight a need for continued research into interventions to improve uptake of primary prevention.

## Sources of Funding

This article presents independent research commissioned by the National Institute for Health Research (NIHR) under its Program Grants for Applied Research funding scheme (RP-PG-0407-10184). The views expressed in this article are those of the authors and not necessarily those of the National Health Service (NHS), the NIHR, or the Department of Health. The SLSR has also received funding from the Northern & Yorkshire NHS R&D Program in Cardiovascular Disease and Stroke, Guy’s and St Thomas’ Hospitals Charitable Foundation, the Stanley Thomas Johnson Foundation, the Stroke Association, and Department of Health Healthcare Quality Improvement Partnership.

## Table 3. Association of Demographics and Stroke Subtype With Prescribed Preventative Medication

<table>
<thead>
<tr>
<th>Age (as ordinal)</th>
<th>Hypertension</th>
<th>Hypercholesterolemia</th>
<th>MI (Antiplatelet)</th>
<th>AF (Anticoagulant)</th>
<th>AF (Antiplatelet)</th>
<th>TIA (Antiplatelet)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65 y</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65–74 y</td>
<td>1.1 (1.02–1.17)</td>
<td>1.12 (1.03–1.19)</td>
<td>1.04 (0.79–1.24)</td>
<td>0.41 (0.2–0.82)</td>
<td>1.12 (0.81–1.42)</td>
<td></td>
</tr>
<tr>
<td>75–84 y</td>
<td>1.05 (0.97–1.13)</td>
<td>1.18 (1.1–1.24)</td>
<td>1.05 (0.81–1.25)</td>
<td>0.77 (0.44–1.3)</td>
<td>1.16 (0.87–1.43)</td>
<td></td>
</tr>
<tr>
<td>≥85 y</td>
<td>0.95 (0.84–1.05)</td>
<td>1.21 (1.1–1.28)</td>
<td>0.89 (0.6–1.16)</td>
<td>0.19 (0.08–0.41)</td>
<td>1.26 (0.96–1.53)</td>
<td></td>
</tr>
<tr>
<td>Male*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.09 (1.03–1.15)</td>
<td>0.89 (0.76–0.99)</td>
<td>0.88 (0.71–1.05)</td>
<td>1.35 (0.93–1.91)</td>
<td>0.92 (0.75–1.1)</td>
<td>0.94 (0.76–1.11)</td>
</tr>
<tr>
<td>White*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1.17 (1.1–1.23)</td>
<td>0.93 (0.8–1.05)</td>
<td>0.92 (0.66–1.16)</td>
<td>0.8 (0.37–1.49)</td>
<td>0.94 (0.65–1.25)</td>
<td>0.87 (0.64–1.11)</td>
</tr>
<tr>
<td>Other</td>
<td>1.06 (0.92–1.18)</td>
<td>1 (0–1.15)</td>
<td>0.7 (0.35–1.11)</td>
<td>1.17 (0.29–2.77)</td>
<td>0.87 (0.37–1.46)</td>
<td>1.06 (0.66–1.4)</td>
</tr>
<tr>
<td>Unknown Ischemic*</td>
<td>1 (0.76–1.22)</td>
<td>Not estimable</td>
<td>1.07 (0.6–1.43)</td>
<td>1.5 (0.47–3.11)</td>
<td>0.97 (0.48–1.48)</td>
<td>0.39 (0.07–1.01)</td>
</tr>
<tr>
<td>ICH</td>
<td>0.79 (0.69–0.89)</td>
<td>1.03 (0.82–1.18)</td>
<td>0.88 (0.4–0.99)</td>
<td>3.14 (2.21–4.04)</td>
<td>0.45 (0.24–0.74)</td>
<td>1.12 (0.8–1.38)</td>
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<tr>
<td>SAH</td>
<td>0.74 (0.55–0.93)</td>
<td>0.85 (0.37–1.21)</td>
<td>0.45 (0.08–1.11)</td>
<td>4.64 (2.45–7.2)</td>
<td>0.3 (0.02–1.06)</td>
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<tr>
<td>Undefined</td>
<td>0.83 (0.72–0.95)</td>
<td>1.08 (0.91–1.21)</td>
<td>1.04 (0.78–1.26)</td>
<td>0.71 (0.28–1.41)</td>
<td>1.19 (0.9–1.46)</td>
<td>1.14 (0.84–1.42)</td>
</tr>
<tr>
<td>5-y advance in time</td>
<td>1.01 (0.98–1.04)</td>
<td>1.09 (1.03–1.15)</td>
<td>1.15 (1.07–1.22)</td>
<td>1.21 (1.01–1.45)</td>
<td>1.18 (1.09–1.26)</td>
<td>1.11 (1.03–1.19)</td>
</tr>
</tbody>
</table>

Relative risks with 95% confidence intervals; columns show results from a logistic regression model with the risk factor as the dependent variable.

AF indicates atrial fibrillation; ICH, intracerebral hemorrhage; MI, myocardial infarction; SAH, subarachnoid hemorrhage; and TIA, transient ischemic attack.

*Reference category.

## Disclosures

None.

## References


Ethical approvals
Dr Iain Marshall  
Clinical Academic Fellow  
King’s College London  
Capital House 9th Floor  
42 Weston Street  
London  
SE1 3QD

23 June 2011

Dear Dr Marshall

Study title: A qualitative study into the beliefs of people with hypertension about cardiovascular risk

REC reference: 11/LO/0907

The Proportionate Review Sub-committee of the NRES Committee London - Wandsworth Research Ethics Committee reviewed the above application on 15 June 2011.

Ethical opinion

The following issues were discussed with you.

A. The sub-committee queried the disclosure of possible bad practice by GPs. You clarified that in the unlikely event that the study uncovers evidence of harmful practice (which could put the participant or other patients at risk), you would break confidentiality and take appropriate action as per GMC Good Medical Practice guidance. This might include reporting to any of the practice senior partner, the Primary Care Trust, the GMC, or other relevant body depending on the individual circumstance. You would inform the participant if you took this action. If the interview uncovers general areas where practice could be improved, but where patients are not at any particular risk, you would not break confidentiality. However, you will present the overall results of the study to the practice (a written summary) after the analysis, and will mention any areas where practice could improve, without identifying any participants.

B. The sub-committee queried the disclosure of poor compliance/concordance by patients’. You explained that in the event participants’ reveal poor compliance/concordance to their medication, you would not break confidentiality. However, you would discuss blood pressure medications in general with them after the interview. You would ask them to make arrangements to see their own GP, or the cardiovascular specialist nurse at the practice in the first instance to discuss specific further action.

C. The sub-committee queried the taping (electronically recording) of interviews. You clarified that the electronic recordings will be deleted after the analysis of transcriptions is complete. It may be necessary for you to return to the recordings during the analysis itself to clarify any points unclear from the transcription.

D. You proposed the following changes to the patient information leaflet. (replacement confidentiality section from part 2)

Will what I say be confidential?
· Yes. We plan to publish a summary of what people have told us in the interviews.
However, we will not use your name or any other details which could be used to identify you.

- In the unlikely event you tell the interviewer information which suggests you or others are at serious risk (e.g. dangerous practice by a doctor), we would have to take further action and report it. This is not expected to happen, and we would tell you beforehand.

On behalf of the Committee, the sub-committee gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

**Ethical review of research sites**

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see “Conditions of the favourable opinion” below).

**Conditions of the favourable opinion**

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission (“R&D approval”) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

**Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at [http://www.rdforum.nhs.uk](http://www.rdforum.nhs.uk).**

Where a NHS organisation’s role in the study is limited to identifying and referring potential participants to research sites (“participant identification centre”), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

- The sub-committee requested the proposed changes detailed by you (above) be actioned.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Confirmation should also be provided to host organisations together with relevant documentation.
Approved documents

The documents reviewed and approved were:

<table>
<thead>
<tr>
<th>Document</th>
<th>Version</th>
<th>Date</th>
</tr>
</thead>
</table>
| Evidence of insurance or indemnity | 04 August 2010
| GP/Consultant Information Sheets  | 1       | 27 May 2011     |
| Interview Schedules/Topic Guides | 1       | 07 June 2011    |
| Investigator CV                  | 27 May 2011 |
| Letter of invitation to participant | 1       | 27 May 2011     |
| Other: Supervisor’s CV           | 27 May 2011 |
| Other: Reply Slip                | 1       | 20 May 2011     |
| Participant Consent Form         | 1       | 27 May 2011     |
| Participant Information Sheet    | 1       | 27 May 2011     |
| Protocol                         | 1       | 01 March 2011   |
| REC application                  | 69420/216135/1/663 | 20 May 2011 |

Membership of the Proportionate Review Sub-Committee

The members of the Sub-Committee who took part in the review are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document “After ethical review – guidance for researchers” gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

11/LO/0907 Please quote this number on all correspondence
With the Committee’s best wishes for the success of this project

Yours sincerely

Dr Murray Bain
Chair

Email: atul.patel@imperial.nhs.uk

Enclosures: List of names and professions of members who took part in the review

“After ethical review – guidance for researchers”

Copy to:

Supervisor Dr Christopher McKevitt
Dept Health & Social Care Research
7th floor,
Capital House,
SE1 3QD

R&D Dr Anne Grant,
Lambeth PCT
Research Support Unit Southwark PCT
2nd Fl Woodmill, Neckinger
London
SE16 3QN

Sponsor Keith Brennan
King’s College London
London
SE1 1UL
NRES Committee London - Wandsworth

Attendance at PRS Sub-Committee of the REC meeting on 15 June 2011

Committee Members:

<table>
<thead>
<tr>
<th>Name</th>
<th>Profession</th>
<th>Present</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Murray Bain</td>
<td>Senior Lecturer / Consultant Paediatrician</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Dr. Adrian Draper</td>
<td>Consultant Chest Physician</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Mr Roy Sinclair</td>
<td>Pharmacist</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Mrs Alexandra Williamson</td>
<td>Lay Member</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

Also in attendance:

<table>
<thead>
<tr>
<th>Name</th>
<th>Position (or reason for attending)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mr Atul Patel</td>
<td>PRS Co-ordinator</td>
</tr>
</tbody>
</table>
Dear Dr Marshall

Project Title: A qualitative study into the beliefs of people with hypertension about cardiovascular risk
R & D Reference: RDLam612

Thank you for your assistance providing the documentation for the scrutiny of this project.

I am satisfied that this study meets with the requirements of the Research Governance Framework. It has been approved by the research lead for the respective NHS organisation.

Approval is given on behalf of NHS Lambeth on the understanding that you adhere to the conditions on the attached document. The end date of the project is listed as 02/08/2012.

If you require any further information, please contact Ali Alshukry on 020 7525 0264.

Yours sincerely

Dr Anne Grant
RG & M Manager
South East London NHS
Bexley, Bromley, Greenwich, Lambeth, Lewisham & Southwark
Patient literature for the qualitative study
Dear xxx

We’d like to invite you to help with some research about high blood pressure.

A researcher from King’s College London is running an interview study at the practice. The study is trying to find out more about people’s experiences of high blood pressure.

Taking part would involve coming to talk to the researcher for about 45 minutes. We’ve also sent a leaflet about the study, with our contact details if you have any further questions.

Taking part is entirely voluntary. Whether you choose to take part or not will have no effect on your medical care.

If you are interested, please fill out the reply slip and return it directly to King’s College London. We’ve enclosed a stamped addressed envelope. The researcher will then get in touch to arrange a time for the interview.

Yours sincerely,

Dr Tyrrell Evans, on behalf of Paxton Green Group Practice

version 1, 27/5/2011
Study information leaflet (version 2, 1/7/2011)

Patient views and experiences about high blood pressure medication and future health

Part 1 – Key points

• We would like to interview people with high blood pressure. We would like to find out about your experience with high blood pressure, and the medicines used to treat it.
• This study is taking part at Paxton Green Health Centre from July 2011 to July 2012.
• If you agree to take part, we will ask you to come to the health centre to talk with a researcher from King’s College London for 45 minutes about your views.
• The study involves only this one interview. The study does not involve any medical tests, or change to your usual treatment. The researcher will not be able to see your medical records at any stage.
• It is up to you to decide to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

Part 2 – Further information

What is the purpose of this study?

• It is important to get good information when deciding to start treatment for high blood pressure. However, we currently don’t know whether patients are given the best information in a clear way.
• This study aims to find out about peoples’ experience of medicines for high blood pressure. We are interested in what good or bad effects you feel their medication might have on you. We also would like to know about your views about your future health.
• We hope the study will help improve the information available about high blood pressure for patients, and give doctors and nurses a better understanding of their patients’ point of view.
• The researcher is a GP who works in a local practice and is an academic fellow at King’s College London in the department of Primary Care and Public Health Sciences. The study is being undertaken for educational purposes, and the results will form part of his PhD thesis.

Will what I say be confidential?

• Yes. We plan to publish a summary of what people have told us in the interviews. However, we will not use your name or any other details which could be used to identify you.
• In the unlikely event you tell the interviewer information which suggests you or others are at serious risk (e.g. dangerous practice by a doctor), we would have to take further action and report it. This is not expected to happen, and we would tell you beforehand.

Why have I been invited to be involved in this study?

• Your GP practice has sent you this invitation as, according to their records, you have had treatment for high blood pressure.

What does the study involve?

• The study involves an interview with a researcher which will take around 45 minutes. We hope to interview around 25 people in total.
• The researcher will ask you questions about your experiences of high blood pressure and the medicines used to treat it. The researcher will also be interested in your views about what the
likely effects high blood pressure could have on your health in future.
• The interview will be tape-recorded to make sure our study shows accurately what people have said.

Where and when will the interviews take place?
• The interviews will be at Paxton Green Surgery. They can take place during the day or on some evenings. If it is difficult for you to make it to the surgery, the researcher can visit you at home if you prefer.
• Although the interview will be at your GP practice, the researcher will not be able to access to your medical records.

Who has reviewed the study?
• This study has been reviewed and been approved by the Wandsworth NHS Research Ethics Proportionate Review Sub-Committee.

Are there advantages to taking part?
• You are unlikely to benefit personally. However, we hope that you will enjoy sharing your experiences.
• We hope the study will improve the information given to others with high blood pressure in future.

Will there be any disadvantages to taking part?
• There should be no disadvantage to taking part, other than spending around 45 minutes of your time. We don’t expect you will find the questions asked distressing, or particularly sensitive.

What if I have any concerns?
• You can contact the researcher or the lead member of the clinical team at any time using the details on the bottom of this leaflet. We will be happy to discuss your concerns or put you in touch with someone else who may be able to help.

How will I find out the results of the study?
• We would be delighted to send you a summary of our findings if you would like one.
• We hope to publish the results of this study in medical journals, and give presentations about it at local, national and international conferences.

Contact details:
If you would like further information please do not hesitate to contact us.

Main contact:
Dr Iain Marshall (Clinical Academic Fellow)
King’s College London
9th Floor Capital House
42 Weston Street
London, SE1 3QD
Tel. 0207 848 6603 (Mondays, Thursdays and Fridays)
E-mail: iain.marshall@kcl.ac.uk

GP practice contact:
Dr Tyrrell Evans
Paxton Green Health Centre
1 Alleyn Park
London, SE21 8AU
Tel. 0208 670 6878
Email: paxton@paxtongreen.nhs.uk
D

Topic guide for semi-structured interviews
Semi-structured interview topic guide for interviewer

Introduction (5 minutes)

• Thank you for taking part
• Check the participant has received and read the information leaflet
• Discuss the interview: lasts about 45 minutes, covers experiences with blood pressure, future health, and information – the topics shouldn’t be intrusive or distressing.
• Let me know if you want to take a break, or there are any questions you prefer not to answer.
• Mention that the interview is confidential. If they agree their own GP will be told they took part, but not about what they said.
• Mention that the interviewer has no access to medical records
• Ask if any questions
• If happy to proceed, ask to sign consent form.

Participant introduction (5 minutes)

• Tell me a bit about yourself
  o Age
  o Occupation
  o Country of origin, and self-described ethnicity
  o How long living in the area
  o General health (check about high blood pressure, how long since diagnosed, and if on any treatment)

Main interview (35 minutes)

Future health

• What effects do you think that high blood pressure could have?
  o [Further probe]: short and long term effects, and good and bad effects? Effects in the past? Possible effects in future?
  o [Further probe - if stroke/cardiovascular disease not mentioned by participant]: Have you heard about a link between high blood pressure, and stroke or heart attacks?
• [Taking each effect identified by the participant in turn]: how likely do you feel this is to happen to you?
  o [Further probe if needed]: do you feel these are certain to happen? Unlikely? Likely? How likely or unlikely?

Treatment for high blood pressure

• Do you have a regular treatment?
• How and when do you take your treatment?
  o [Further probes]: Have there ever times that you forget? Are there times that you decide not to take? Have there ever been times that you change the dose/number of tablets? Do you use any other treatments – e.g. herbal?
• What effects do you feel that your medication could have?
  o [Further probe]: short and long term effects, and good and bad effects? Effects in the past? Possible effects in future?
  o [Further probe - if stroke/cardiovascular disease not mentioned by participant]: Do you feel that high blood pressure medication has an effect on stroke or heart attacks?
• [Taking each effect identified by the participant in turn]: how likely do you feel this is to happen to you?
  o [Further probe if needed]: do you feel these are certain to happen? Unlikely? Likely? How likely or unlikely?

Information

• Do you remember getting any information when you were diagnosed with high blood pressure?
  o [Further probes]: from your doctor or nurse? Written or spoken information? From others – friends/family? About high blood pressure itself, and about the treatment?
• Did you find this useful? What were the good and bad parts of it? Could it be improved?
• How important is getting information for you?
• What do you feel are the most important things to tell others in future who are considering starting a treatment?

Conclusion

• Thank you for coming, and for taking part
• Would you like us to send you a copy of the study results? [Ask for an email address or postal address if they do.]
Search strategies for the systematic reviews

E.1 Systematic review from Chapter 6

1. Qualitative Research/
2. Nursing Methodology Research/
3. Questionnaires/
4. exp Attitude/
5. Focus Groups/
6. discourse analysis.mp.
7. content analysis.mp.
8. ethnographic research.mp.
9. ethnological research.mp.
10. ethnonursing research.mp.
11. constant comparative method.mp.
12. qualitative validity.mp.
13. purposive sample.mp.
14. observational method$.mp.
15. field stud$.mp.
16. theoretical samp$.mp.
17. phenomenology/
18. phenomenological research.mp.
19. life experience$.mp.
20. cluster samp$.mp.
21. or/1-20
22. hypertension/
23. 21 and 22

E.2 Systematic review from Chapter 7

1. heart[MESH]
2. stroke[MESH]
3. cardiovascular diseases [MESH]
4. hypertension [MESH]
5. cardiac [All Fields]
6. coronary [All Fields]
7. heart [All Fields]
8. stroke [All Fields]
9. cardiovascular [All Fields]
10. vascular [All Fields]
11. hypertension [All Fields]
12. or/1-11
13. risk [MeSH Terms]
14. risk [Title/Abstract]
15. or/13-14
16. communication [MeSH Terms]
17. Patient Education as Topic [MESH]
18. Health Education [MESH]
19. communication [All Fields]
20. presentation [All Fields]
21. or/16-20
22. clinical presentation [All Fields]
23. 21 not 22
24. 12 and 15 and 23
Characteristics of excluded studies

There follows a non-exhaustive list of key studies which were excluded from the systematic review in Chapter 7, with reasons for their exclusion. These are studies which the reader might have expected to be included, but were excluded for often subtle deviations from the selection criteria.

- Thomson et al., 2007: The intervention decision aid was primarily a risk communication intervention, but the control arm was not sufficiently similar to usual care, comprising a study doctor who made a firm recommendation on the basis of a decision analysis tool.

- Sheridan et al., 2006: This study otherwise met the inclusion criteria, but did not evaluate any of the specified outcomes.

- Sheridan et al., 2011: The decision aid studied did prominently feature risk communication, however, it also included a ‘coaching’ element, which aimed to persuade the patient to take action.

- Goodyear-Smith et al., 2008: This study did not evaluate any outcomes of interest for the review; only reporting the outcome of hypothetical decision made to use a treatment (which resembled a statin, but was not named this).

- Thomson et al., 2006: This paper provided some very brief comments from users of a decision support tool only, but not sufficient for any detailed analysis and to be included in the qualitative part of the review.

- Lalonde et al., 2006: This study compared a simple risk communication booklet versus an extended educational decision aid. This study was excluded since both arms appear to include identical risk information; the RCT is in essence evaluating the effect of adding comprehensive education to risk communication.
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