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INEQUITY IN REHABILITATION INTERVENTIONS AFTER HIP FRACTURE: A SYSTEMATIC REVIEW

ABSTRACT

Objective To determine the extent to which equity factors contributed to eligibility criteria of trials of rehabilitation interventions after hip fracture. We define equity factors as those that stratify healthcare opportunities and outcomes.

Design Systematic search of MEDLINE, Embase, CINHAL, PEDro, Open Grey, BASE, and ClinicalTrials.gov for randomized controlled trials of rehabilitation interventions after hip fracture published between 1st January 2008 and 30th May 2018. Trials not published in English, secondary prevention or new models of service delivery (e.g. orthogeriatric care pathway) were excluded. Duplicate screening for eligibility, risk of bias (Cochrane Risk of Bias Tool), and data extraction (Cochrane's PROGRESS-Plus framework).

Results 23 published, 8 protocol, 4 registered ongoing randomized controlled trials (4,449 participants) were identified. A total of 69 equity factors contributed to eligibility criteria of the 35 trials. For more than 50% of trials, potential participants were excluded based on residency in a nursing home, cognitive impairment, mobility/functional impairment, minimum age, and/or nonsurgical candidacy. Where reported, this equated to the exclusion of 2,383 out of 8,736 (27.3%) potential participants based on equity factors. Residency in a nursing home and cognitive impairment were the main drivers of these exclusions.

Conclusion The generalizability of trial results to the underlying population of frail older adults is limited. Yet this is the evidence base underpinning current service design. Future trials should include participants with cognitive impairment and those admitted from nursing homes. For those excluded, an evidence-informed reasoning for the exclusion should be explicitly stated.

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INTRODUCTION

Equity in health refers to the prevention of unfair, avoidable differences in health arising from cultural exclusion, poor governance, or corruption.[1-3]Equity in access to healthcare is a founding principle of the National Health Service (NHS).[4] Access is characterised by gaining entry into a healthcare system and the timely delivery of appropriate care.[5] Entering a healthcare system for hip fracture is not a discretionary decision – hospital admission is almost always necessary.[6] However, timely delivery of appropriate care is determined by competing demands for services. In the UK 29% of patients with hip fracture wait longer than the recommended 36-hours for surgery.[7] Access to rehabilitation including bed capacity, formal access criteria, and waiting times exhibits greater variation than access to surgery.[8-10]

Patients enrolled in randomized controlled trials often have better outcomes than those not enrolled in trials.[11] Indeed, trial enrolment presents patients with the opportunity to consider additional access to care. It is possible patients with equal needs do not make equal use of this opportunity.[12] Alternatively, they may not be offered this opportunity as trial access is determined by eligibility criteria. Of interest is whether such eligibility criteria systematically limits access for patient subgroups who may benefit from intervention and who face poor outcomes. Indeed, patients who present from nursing homes with multiple morbidities are often excluded from rehabilitation trials after hip fracture [13] and have higher rates of complications and death.[14-16] These patients may have the most to gain from additional access to rehabilitation through trials.

In 2008, the Darzi Review committed to support local quality improvement efforts through Best Practice Tariffs.[17] Tariffs are assigned *'where the evidence of what is best practice is clear and compelling'* and may lead to local prioritization to maximise reimbursement from Tariffs.[17] The exclusion of patient subgroups from trials results in a dearth of *clear and compelling* evidence to improve care for these patients, limiting the case for a Best Practice Tariff. Therefore, services for these patients may be underprioritized leading to a potentially unfair distribution of disability and death.

The aim of this systematic review is to describe equity factors in randomized controlled trials of rehabilitation interventions after hip fracture. We define equity factors as those that stratify healthcare opportunities and outcomes.[1-3] The primary objective is to determine the role of equity factors in eligibility criteria of trials of rehabilitation interventions after hip fracture, since publication of the Darzi Review. Secondary objectives are to determine the role these factors have in baseline characteristics and subgroup analyses.

METHODS

Protocol and registration

The protocol was registered on the International Register of Systematic Reviews (PROSPERO).[18] The protocol and review were reported in adherence to the Preferred Reporting Items for Systematic Review and Meta-analysis statement – Equity extension.[19-23]

Eligibility criteria

We included randomized controlled trials of rehabilitation interventions after hip fracture. Rehabilitation was defined as '*a set of interventions designed to optimize functioning and reduce disability in individuals with health conditions in interaction with their environment*'.[24] We excluded trials of secondary prevention or new models of service delivery unless they included an evaluation of rehabilitation effectiveness. We excluded trials not in English due to financial constraints of employing an interpreter. We excluded nonrandomized studies, and those published before 1st January 2008 to reflect the period after publication of the Darzi Review.[17]

Information sources

We searched electronic databases for published (MEDLINE, Embase, CINHAL, PEDro), unpublished (Open Grey, BASE), and registered ongoing trials (ClinicalTrials.gov) on 30th May 2018. We searched reference lists of systematic reviews identified during electronic database searches. We contacted corresponding authors as required.

Search

We used published terms for the study population (hip fracture),[25] intervention (rehabilitation),[26 27] and study design (randomized controlled trials).[26 27] We supplemented published strategies with one additional term -'exp Rehabilitation' (Supplementary File 1).

Study selection

We imported citations into Covidence for de-duplication and screening.[28] Where registration, protocol, and/or final publication were available for the same trial we retained the most recent source. Two reviewers independently screened abstracts, and full texts of potentially eligible studies, against eligibility criteria (R2, R3). Conflicts were resolved by a third reviewer (R1).

Data extraction

Two reviewers independently extracted data onto templates adapted from published extraction tables (R2, R3).[29 30] Where published trials and secondary analyses of the same trial were available we extracted data from the published trial and data related to subgroup analyses from the secondary analysis. Data extraction included author's name, publication year, country, sample size, sample characteristics, intervention, control, effect estimate.

We extracted data for equity factors in eligibility criteria, baseline characteristics, and subgroup analyses. We defined equity factors by the Cochrane and Campbell Collaboration Equity Methods group's PROGRESS-PLUS framework .[3 23] We extracted justification for eligibility criteria where available.

PROGRESS is an acronym for **P**lace of residence, **R**ace/ethnicity/language/culture, **O**ccupation (e.g. retirement status), **G**ender, **R**eligion, **E**ducation, **S**ocioeconomic status, and **S**ocial Capital.[1-3]

PLUS captures other factors which impact equity namely (1) age (2) disability (3) features of relationships, and (4) time-dependent relationships.[1-3]

Risk of bias

Three reviewers independently assessed risk of bias using the Cochrane Risk of Bias Tool which considers bias in selection, performance, detection, attrition, reporting, and other biases (e.g. usual care group does not reflect clinical practice) (R1, R2, R3).[31] Conflicts were resolved by consensus.

Synthesis of results

We summarized study characteristics, and the extent to which equity factors are considered in eligibility criteria, baseline characteristics, and subgroup analyses, with counts and proportions in text, tables and figures. We defined 'systematic exclusion' as exclusion based on one equity factor in at least 50% of trials. We calculated counts and proportions of eligible patients excluded for equity factors that contributed to eligibility criteria in at least 50% of trials.

Public and patient involvement

Two reviewers led discussions with patients after hip fracture and their carers (n = 8) to inform the review rationale (R1, R4).

RESULTS

Study selection

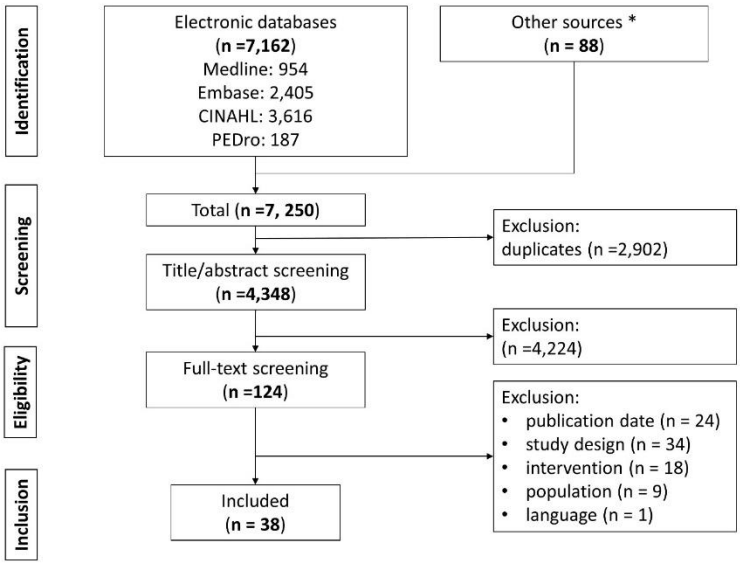
We identified 4,348 articles after de-duplication. We excluded 4,224 on abstract screening. We excluded 85 on full text screening for: study design (n = 34), population (n = 9), intervention (n = 18), language (n = 1), publication date (n = 24), leaving 38 trials included.(Figure 1).

Study characteristics

Detailed study characteristics for the 23 published,[32-54] 8 protocol,[55-62] and 4 registered[63-66] trials, and 3 secondary analyses of trials[67-69] are presented in Supplementary File 2.[52]

This review included 4,449 participants (sample size range 11[51] to 400).[55] Interventions included exercise (n = 23),[34-37 39 40 42-50 52 53 55 58 59 63 65 66] physiotherapy (n = 7),[32 41 51 54 56 57 62] occupational therapy (n = 3),[38 56 61] electrical stimulation (n = 1),[33] telerehabilitation (n = 1),[64] and visual feedback on weight-bearing (n = 1).[60] Interventions providers were physiotherapists (n = 20),[32-37 41 43 44 48-50 54 57-60 62 63 66] occupational therapists (n = 3),[38 61 64] exercise trainers (n = 2),[42 46] psychiatrists (n = 1),[40] or a multi-disciplinary team (n = 5).[39 45 52 53 56] Four studies did not specify intervention provider.[47 51 55 65] Intervention settings included hospital (n = 11),[34 35 38-40 45 47 51 55 56 60] home (n = 8),[36 37 42 44 50 58 59 64] hospital and home (n = 4),[32 33 41 52] outpatients (n = 2),[46 54] outpatients and home (n = 4),[48 49 53 62] nursing homes (n = 2),[57 61] and gyms (n = 1).[43] Three studies did not specify intervention setting. [63 65 66]

Figure 1: **Study selection**



Risk of bias within studies

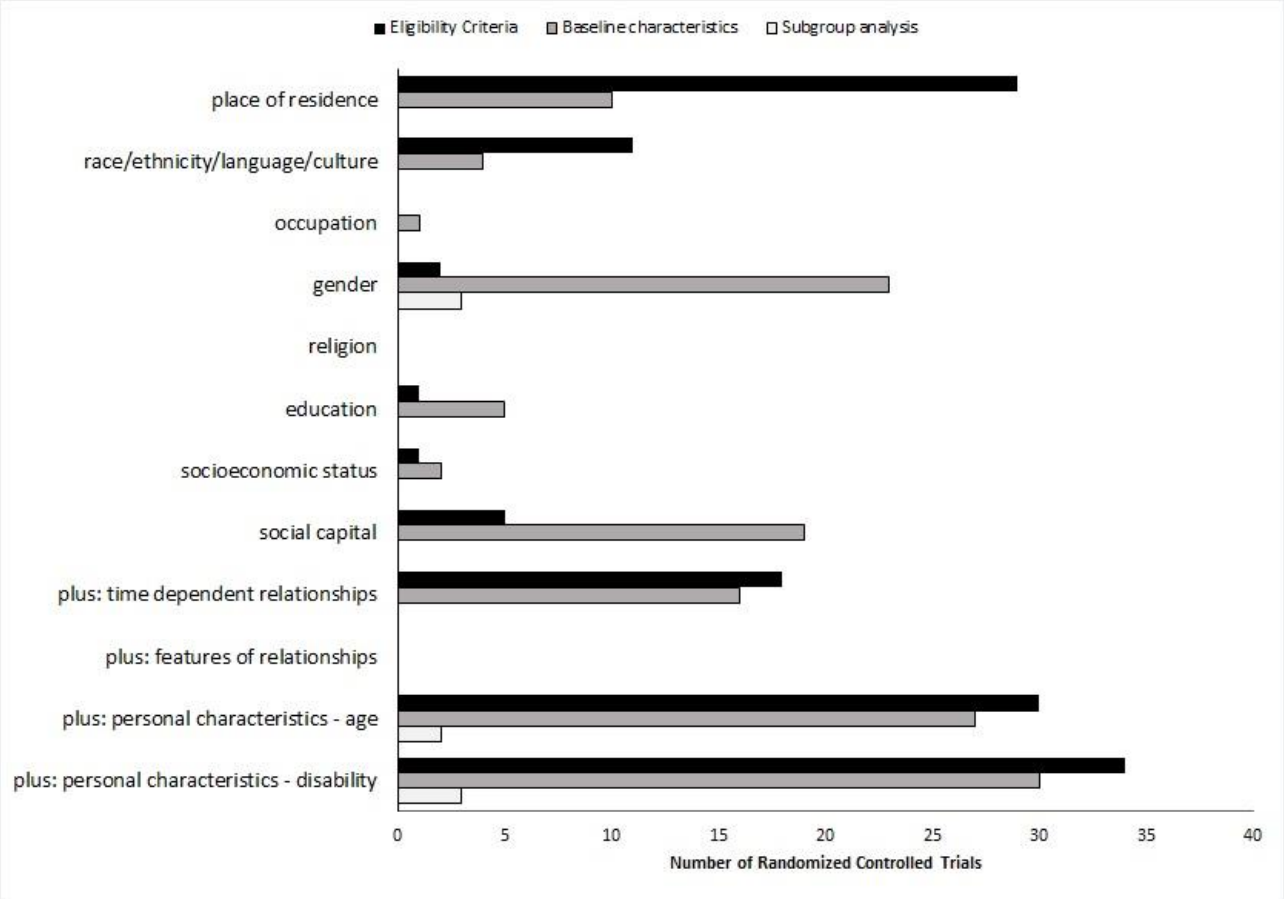
Detailed risk of bias assignments are presented in Supplementary File 3. Lack of blinding of personnel and participants was the most common reason for high bias assignment (n = 17).[33 35 37 40 41 45 48 50 52-58 60 62] Additional reasons for high bias assignment included: allocation concealment (n = 1),[52] blinding outcome assessors (n = 1),[45] and incomplete outcome data (n = 1).[52]

Synthesis of results

Eligibility criteria

At least one PROGRESS-PLUS factor contributed to eligibility criteria in 34 (97.1%) trials (Figure 2, Tables 1-2).[32-46 48-66] Potential participants were excluded based on PROGRESS factors - place of residence, race, gender, education, socioeconomic status, and/or social capital and PLUS factors – time-dependent relationships, age, and disabilities. One trial did not specify eligibility criteria.[47] Occupation, religion, and features of relationships did not contribute to eligibility criteria.

Figure 2: Contribution of equity factors to eligibility criteria, reporting of baseline characteristics, and subgroup analyses in randomized controlled trials of rehabilitation after hip fracture



Justification for eligibility criteria

Fifteen (42.9%) trials included justification for at least one eligibility criteria.[32 36 38 39 41 42 46 50 52 55 57 58 60 64 65] Potential participants were excluded based on prefracture nursing home residence,[38] timing of discharge from rehabilitation,[38] time since fracture,[38] aged less than 60-years or greater than 85-years, organ failure,[38] history of lower limb disorder,[38] comorbidities that could affect gait,[60] or cognitive impairment,[38] to mitigate their potential to reduce the intervention effect. Potential participants were excluded based on language, vision, or hearing disabilities,[39] and/or other comorbidities[32 36 38 39 41 42 50 52 57 58 64 65] as they may limit intervention participation. Potential participants were excluded based on poor social support due to the cognitively vulnerable nature of the population.[55] Potential participants were excluded based on cognitive impairment due to limited capacity for consent.[46]

Potential participant exclusion counts and proportions

Eighteen trials provided counts of potential participants excluded for criteria occurring in at least 50% of trials.[32-36 38-42 44 46 48 50 51 54] Seven studies excluded 760 of 3,952 (19.2%) potential participants admitted from a nursing home.[34 35 38 42 44 48 50] Eleven studies excluded 740 of 6,549 (11.3%) potential participants with cognitive impairment.[32 33 36 38-42 44 46 51] Six studies excluded 380 of 3,892 (9.8%) potential participants younger than the minimum age.[35 46 48 50 52 54] Eight studies excluded 262 of 2,870 (9.1%) potential participants with mobility/functional impairment.[32-34 41 50-52 54] Two studies excluded 38 of 1,268 (3.0%) potential participants treated nonsurgically for hip fracture.[32 54]

Baseline characteristics

At least one PROGRESS-PLUS factor was reported in baseline characteristics in 23 published trials and 8 trial protocols (Figure 2, Tables 1-2).[32-55 57-62] Religion and features of relationships were not reported.

Subgroup analyses

At least one PROGRESS-PLUS factor contributed to subgroup analyses in 1 (2.9%) published trial[52] and 3 (8.8%) secondary analyses of published trials (Figure 2, Table 1-2).[67-69] Subgroup analyses for gender, age, depression, balance confidence, nutrition, and cognition were planned in one protocol (Figure 2, Table 1-2).[59] Further details on subgroup analysis are presented in Supplementary File 4.

DISCUSSION

Summary of evidence

This review aimed to describe equity in randomized controlled trials of rehabilitation interventions after hip fracture. For more than 50% of the 35 trials, we identified exclusion of potential participants based on nursing home residency, cognitive impairment, mobility/functional impairment, minimum age, and/or nonsurgical candidacy. Where reported, this equated to exclusion of 2,383 of 8,736 (27.3%) potential participants based on equity factors. Nursing home residency and cognitive impairment were the main drivers, accounting for 1,500 excluded potential participants.

Strengths and Limitations

We used published search terms reviewed by a research librarian. We searched for published, unpublished, and registered trials to reduce the risk of publication bias. We used broad eligibility criteria, and duplicate screening for eligibility, bias assignment, and data abstraction to reduce the risk of selection bias. We used Cochranes recommended appraisal tool[31] and framework for synthesis of equity factors.[1-3] We did not search conference websites for proceedings which may have led to the exclusion of relevant trials. We searched for articles based on study design which

may have led to the exclusion of secondary subgroup analyses of trials. We excluded articles not published in English and trials of secondary prevention or new models of care which may incorporate components of rehabilitation. Exclusion of trials published before 1st January 2008 may have led to an underestimation of the proportion of trials with exclusion based on PROGRESS-PLUS factors as earlier reviews reported exclusions based on minimum age, gender, comorbidities, cognitive impairment, and mobility impairment.[27 70] We defined equity factors by the PROGRESS-PLUS framework which does not incorporate medical inequities resulting from care quality. We did not extract the number of trials which incorporated public and patient involvement. Trials with involvement may see fewer cases of inequity.

Interpretation

Researchers define eligibility criteria to ensure feasibility while reducing potential for harm or exploitation of vulnerable potential participants.[72] These criteria are often accompanied with a rationale when seeking ethical approval. This rationale rarely appears in protocols or publications. It is therefore unclear whether exclusions are employed based on (i) potential for benefit, (ii) feasibility of participation, (iii) feasibility of outcome measurement or (iv) target population.

Potential for benefit

In this review, 29 (82.9%) trials excluded potential participants based on cognitive impairment. This criterion does not seem appropriate as one in three patients with hip fracture have cognitive impairment.[13] Planning services around reported intervention effectiveness is challenging as findings are not generalizable to a substantial proportion of the population. Further, patients with cognitive impairment demonstrate improved mobility, functional, and cognitive outcomes with intensive rehabilitation after hip fracture.[13 73] Subgroup analysis for one trial in this review indicated greater improvement in mobility for those with lower than those with higher executive function.[52] Therefore, patients with cognitive impairment may have potential for benefit from additional access to rehabilitation enrollment in trials offer.

One trial justified exclusion based on cognitive impairment - to mitigate their potential to reduce the intervention effect.[38] This may be addressed with regression adjustment and subgroup analyses. Capacity for consent was also cited to justify exclusion based on cognitive impairment.[46] This was overcome in two trials in this review.[34 55] When patients were unable to provide consent, it was requested from persons responsible for their medical decisions[34] or a *suitable informant*.[55] Therefore, we recommend any trial in the context of hip fracture should include those with cognitive impairment, and where they are excluded an evidence-informed reasoning should be stated.

Feasibility of participation

Trials may exclude potential participants as pragmatically they could not be supported to participate in the intervention within budget and/or time constraints. These constraints are important issues in any research but have implications for a trial's potential cost-benefit when generalisability is limited. Where this occurs, and an intervention demonstrated efficacy, the design needs to be adapted (if possible) to maximise equity and evaluated through additional trials or service evaluations. These additional steps delay patient benefit. We reported exclusions on language, vision, or hearing disabilities,[39] and/or comorbidities[32 36 38 39 41 42 50 52 57 58 64 65] as they may limit participation in the intervention. One trial countered 'may not be able to participate' through engagement of staff and relatives to establish a controlled and protected environment which resulted in a low attrition rate.[40] Careful consideration of intervention design is required prior to exclusion based on a perceived lack of potential for participation. Further, it may be argued a *perceived* lack of potential is an insufficient justification for exclusion, and an evidence-based reasoning be stated.

Feasibility of outcome measurement

In the current review, 25 (71.4%) trials excluded potential participants with mobility/functional impairment. It is not clear whether feasibility of primary outcome measurement contributed to this exclusion criterion. For example, one trial which excluded participants unable to walk 10 metres prefracture selected the Short Physical Performance Battery.[62] This trial included additional self-reported mobility measures, falls, and frailty obtainable in potential participants unable to walk 10 metres prefracture.

Target population

Inconsistencies in eligibility criteria may point to a lack of consensus of how best to define the target population. For example, 30 (85.7%) trials excluded potential participants based on a minimum age. Minimum ages included 55 -, 60 -, 65- , or 70- years highlighting a lack of consensus as to an appropriate minimum age, if one is needed at all. This minimum age may reflect efforts to capture a target population of 'frail older adults' to improve consistency in the probability of outcomes across participant groups. However, a recent cohort study indicated a 50% increase in walking aid use 1-year after hip fracture for adults aged less than 60 years.[77] In addition, one trial included in the current review reported improvements in functional outcomes among adults aged 60-79 years compared to those aged greater than 79 years.[67] Therefore, excluding potential participants based on a minimum age reduces access for patients who may benefit from the intervention and who face poor outcomes.

In some cases, exclusion of potential participants based on a target population may be justified. For example, it may be reasonable for a community-based intervention to be trialled in participants who reside in the community. In the current review, 21 trials included post-acute rehabilitation. Of these, 19 were completed in the community (home, outpatients, senior's gym). Only 2 trials were completed in nursing homes. It could be argued these interventions contribute to relative discrimination denying access to additional rehabilitation for those with higher needs.[78] Indeed, in the UK only 70% of hospitals have access to physiotherapy follow-up in nursing homes where therapy input is already limited across residents.[7] Systematically excluding those who likely incur the greatest healthcare costs will fail to generate the health economic evidence base required to change healthcare funding for these individuals.

Conclusions

We identified systematic exclusion of potential participants from rehabilitation trials after hip fracture based on equity factors that stratify healthcare opportunities and outcomes. We suggest randomized controlled trials of rehabilitation after hip fracture should be designed considering equity of access to the additional care trial enrolment provides. In particular, we suggest trials should have a clearly defined target population and consent process with broad eligibility criteria (inclusive of potential participants with cognitive impairment and those admitted from nursing homes) to maximise generalisability to the underlying population of frail older adults. Primary outcome measures should facilitate participation to reduce bias from missing data by considering their accessibility, and both floor and ceiling effects. We propose researchers target a range of treatment settings (community and nursing homes) to further reduce potential inequities. For each exclusion criteria, an evidence-informed reasoning for the exclusion should be explicitly stated. This reasoning should indicate a clear potential for harm (e.g. mobilisation in participants treated conservatively), or a specific description of why excluded potential participants could not be supported to participate within budget/time constraints.

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For full reference list please see supplementary file 5

Table 1: Contribution of PROGRESS-PLUS equity factors to eligibility criteria, reporting of baseline characteristics, and subgroup analyses in randomized controlled trials of rehabilitation after hip fracture.

	Exclusion criteria			Baseline characteristics*			Subgroup analysis†		
	n	**(%)**	**references**	**n**	**(%)**	**references**	**n**	**(%)**	**references**
Total	35	(100)		31	(100)		34	(100)	
PROGRESS-PLUS factors‡									
Place of residence									
admitted from nursing home	18	(51.4)	34 35 37 38 41 43 44 48-50 53 54 57-59 61 62 65	7	(22.6)	32 34 36 41 46 53 55			
admitted from assisted living				6	(19.4)	32 34 36 39 41 46			
admitted from community	1	(2.9)	51	8	(25.8)	32 34 36 39 41 46 53 55			
admitted from hospital/rehabilitation				2	(6.5)	53 55			
outside trial catchment area	11	(31.4)	32 36 43-45 48-51 53 54						
discharge to nursing home	7	(20.0)	41 48 49 54 61 62 64	2	(6.5)	35 42			
discharge to community	1	(2.9)	41	2	(6.5)	35 42			
discharge to rehabilitation				2	(6.5)	35 42			
definition not specified				2	(6.5)	54 59			
Race/ethnicity/ language/culture									
white				3	(9.7)	36 42 46			
language barrier	11	(31.4)	32 35 36 38-40 46 53 54 57 64						
definition not specified				1	(3.2)	59			
Occupation									
employment status				1	(3.2)	40			
Gender									
gender	2	(5.7)	42 51	23	(74.2)	32-38 40 41 44-50 52-54 57 59-61	3	(8.8)	59 67 69
Education									
none				3	(9.7)				
primary				4	(12.9)				
secondary				4	(12.9)				
tertiary				5	(16.1)	36 40 42 45 47			
low technology literacy	1	(2.9)	64						
definition not specified				2	(6.5)	57 59			
Socioeconomic status									

insurance				1	(3.2)	34			
income				1	(3.2)	47			
internet at home	1	(2.9)	64						
Social capital									
living with other people	1	(2.9)	61	12	(38.7)	36 37 39 46 48-50 52-54 57 59			
marital status				7	(22.6)	37 40 42 45 47 59 61			
no social support	3	(8.6)	41 55 64	4	(12.9)	34 41 46 53			
use of rehabilitation services	1	(2.9)	36	1	(3.2)	60			
use of home/community services				3	(9.7)	41 46 53			
PLUS: **time dependent relationships**									
time since fracture	5	(14.3)	36 42 43 58 62	8	(25.8)	36 37 39-41 43 52 61			
time since admission	1	(2.9)	59						
time since surgery	5	(14.3)	33 37 40 55 66	2	(6.5)	33 44			
time since hospital discharge	2	(5.7)	63 65						
time since rehabilitation discharge	2	(5.7)	36 38						
time on study ward	1	(2.9)	55						
readmit within 2 weeks of discharge	1	(2.9)	60						
expected rehabilitation duration	4	(11.4)	52 60 61 63						
actual rehabilitation duration				1	(3.2)	60			
length of hospital stay				6	(19.4)	35 38 39 42 45 55			
PLUS: **age**									
age				27	(87.1)	32-54 57 59-61	2	(5.9)	59 67
minimum age	30	(85.7)	32-37 40 42-46 48-50 52-66						
maximum age	2	(5.7)	43 66						
PLUS: **disability**									
Disability (See Table 2)	34	(97.1)		30	(96.8)		3	(8.8)	

*excludes 4 registered randomized controlled trials and 3 secondary analyses of randomized controlled trials

†excludes 4 registered randomized controlled trials

‡religion and features of relationships did not contribute to eligibility criteria, reporting of baseline characteristics, or subgroup analyses in any randomized controlled trial of rehabilitation after hip fracture

Table 2: Contribution of the PLUS equity factor of disability to eligibility criteria, reporting of baseline characteristics, and subgroup analyses in randomized controlled trials of rehabilitation after hip fracture.

	Exclusion criteria			Baseline characteristics*			Subgroup analysis†		
	n	**(%)**	**references**	**n**	**(%)**	**references**	**n**	**(%)**	**references**
Total	35	(100)		31	(100)		34	(100)	
PLUS: Disability									
Patient-related									
cognitive impairment	29	(82.9)	32 33 36-42 44 45 48 49 51-66	21	(67.7)	32 34-37 39-41 46-48 50-52 54 55 57 58 61 62 67	2	(5.9)	52 59
no capacity for consent	9	(25.7)	35 44 46 51 52 54 57 61 65						
unwilling/unable to participate	4	(11.4)	32 35 56 63						
mobility/functional impairment	23	(65.7)	32-37 41-45 50-52 57-60 62-66	24	(77.5)	33 34 36 37 39 41 44-46 48-55 57-62 67	2	(5.9)	52 68
low activity tolerance	2	(5.7)	41 52						
balance confidence/falls				9	(29.0)	32 35 41 46 50 57 58 61 62	1	(2.9)	59
medical condition limiting exercise	11	(31.4)	32 36 39 41 50 52 57 58 62 64 65						
depression	4	(11.4)	36 44 53 64	9	(29.0)	36 37 39 42 46 54 58 62 67	1	(2.9)	59
severe mental illness	2	(5.7)	53 64						
alcoholism	4	(11.4)	32 43 44 53						
drug abuse	1	(2.9)	53	1	(3.2)	40			
smoker				1	(3.2)	40			
psychosocial problems				2	(6.5)	55 61			
visual disability	5	(14.3)	32 36 39 52 58	1	(3.2)	46			

hearing disability	4	(11.4)	32 33 39 58						
communication disability	2	(5.7)	58 64						
comorbidities‡§	18	(51.4)	32 33 35-37 40 42-44 56 58 60 63-66	16	(51.6)	32 36 37 39-44 46 51-53 57 60 62			
nutrition				2	(6.5)	46 58	1	(2.9)	59
BMI				9	(29.0)	32 33 37-40 44 52 62			
medications				5	(16.1)	39 41 46 52 58			
Injury-related									
multiple fractures	5	(14.3)	35 48 49 56 66						
bilateral hip fracture	3	(8.6)	36 39 45						
complications¥**	5	(14.3)	33 39 40 58 66 33 39 66	7	(22.6)	36 37 40 42 46 52 62			
pathological hip fracture/ cancer	10	(28.6)	32 34 36 37 42 46 48-50 56 57 59 66	2	(6.5)	36 42			
terminal illness/reduced life expectancy	14	(40.0)	33 35-37 45 46 48 50 53 55 57 61 63						
nonsurgical candidacy	19	(54.3)	32-35 37 40-42 44-46 50 53-55 57-59 65						

ADL = activities of daily living; BMI = body mass index

*excludes 4 registered randomized controlled trials and 3 secondary analyses of randomized controlled trials †excludes 4 registered randomized controlled trials ‡exclusion based on neurological disease,[36 37 42 43 58 64-66] cardiac disease,[33 36 37 42 44] previous hip surgery,[32 35 40 42 58] pulmonary disease,[36 42 44] renal disease,[32 37 42] other progressive disease,[43 44] history of stroke,[37 40] amputated lower limb,[43] bone disease,[42] history of lower limb trauma,[38] hip surgery for infection/arthritis,[56] lower limb sensory neuropathy,[37] body weight greater than 120 kg,[60] conditions that increased the risk of falling,[42] gait impairment not related to hip fracture,[63] organ failure,[38] systemic disorders,[40] creatinine clearance of <15mL/min,[32] hypercalcemia,[32] primary hyperparathyroidism or sarcoidosis,[32] liver cirrhosis[42] and/or acute vertigo.[58] §baseline characteristics include cardiac disease[40 42] endocrine disease[36 40 42 46 52], bone disease[42 46 62] osteoarthritis[36 46], 'other comorbidities' (no other information provided)[32 37 39-44 46 51-53 57 60 62] ¥ exclusion based on cardiac and [33 39 40 58 66] respiratory[33 39 66] complications ** baseline characteristics include complications[62] cardiovascular complications[36 37 42 46 52], pulmonary complications[36 42 46 52] neurological complications[46 52] gastrointestinal complications[42 52] urogenital complications[52 62], lower limb complications[42 52], renal complications[40 42]