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Facets of shared decision making on drug treatment for adults with an eating disorder

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Abstract

Shared decision making (SDM) means that clinicians and the patient make decisions about the treatment together. Regarding drug treatment in eating disorders (EDs), such decisions may include psychopharmacological treatment for the ED itself, medications for potential co-morbid psychiatric disorders, pharmacological strategies to alleviate the health consequences of an ED or "pro re nata" (PRN) medication which is given in acute care when required.

Decisions regarding drug treatment in EDs should be specific in terms of the active pharmacological substance, its dose, its route of administration and the duration of treatment. Decisions should be made with regard to the specific health risks of patients with EDs and the entire treatment approach, and should take alternative measures, additional therapies and specific combinations of therapies into account.

The differences in the expectations of patients, carers and clinicians towards drug treatment, the lack of specific suggestions in clinical practice guidelines and the lack of approved psychopharmacological treatment options make SDM necessary, but also a challenge.

However, SDM may be limited due to the patient's impaired insight or limited capacity due to the ED. Thus, the legal framework must be taken into consideration.

Shared decision making

Introduction: Patients have traditionally entrusted decision-making to physicians. However, during the past several decades, patients have demanded increasing participation in decision processes and have also been encouraged to have a more active role in decisions concerning their health, as they are the ones who have to live with the consequences of medical decisions (Lin & Fagerlin, 2014). "Shared decision making" (SDM) means that clinicians and a patient make decisions about the patient's care together, guided by research evidence, the clinical expertise of the clinician and the patient's values and preferences. Thus, SDM is crucially different from the paternalistic approach in which patients are expected to follow the clinicians' advice. SDM is currently considered fundamental to informed consent and patient-centered care (Towle & Godolphin, 1999; Weston, 2001; Friesen-Storms et al., 2015).

As the number of SDM publications in scientific journals has increased in recent years, SDM has been making headway in healthcare policy (Légaré & Thompson-Leduc, 2014). In the United States of America (US), for example, policy driven initiatives such as the Patient-Centered Medical Home and the Affordable Care Act have reinforced the importance of implementing SDM across the health care continuum (Sia et al., 2004). In the United Kingdom (UK), health authorities have engaged clinical champions and patient representatives in national initiatives for SDM and embarked on a process of widely disseminating patient decision aids; and in Germany, patient information and SDM are embedded in social health insurance programs (Coulter et al., 2011; Harter et al., 2011).

Various models with differing advantages and disadvantages in terms of practical applications have been described in the literature (Charles et al., 1997; Charles et al., 1999; Makoul & Clayman, 2006; Coulter, 1997). The integrative model of treatment decision making proposed by Makoul and Clayman (Makoul & Clayman, 2006) highlights essential elements of SDM, including discussion of the problem, the options, the benefits and risks, the individual values of the patients and their preferences, and the patient's ability to follow their treatment plan. It emphasizes that physicians need to share knowledge and recommendations, check and clarify the understanding of patients, and make or explicitly defer decisions and arrange follow-up meetings for SDM.

SDM for drug treatment in EDs: The clinical purpose of SDM is to improve the care of patients by encouraging the production and dissemination of accurate, balanced, understandable

information and increasing patient participation in their care. SDM interventions have been shown to improve patient understanding of the available treatment options, increase the proportion of patients with realistic expectations in terms of benefits and risks, stimulate patient involvement in decision making, and improve agreement between patient values and treatment options (Stacey et al., 2011; Lin & Fagerlin, 2014). Incorporating patient preferences into the decision-making process may also lead to improved patient well-being through improved adherence to treatment, fewer concerns of illness, and higher satisfaction with health outcomes (Greenfield et al., 1988; Kaplan et al., 1989; Lin & Fagerlin, 2014).

The implementation of SDM has gained considerable interest, specifically in areas lacking strong and specific treatment recommendations (Friesen-Storms et al., 2015). This is, unfortunately, the case in EDs. Additionally, there appears to have been no specific research on SDM in drug treatment for EDs, therefore, this article will refer to aspects generally considered to be important in SDM on drug treatment in the current literature. These aspects are to provide up-to-date, evidence-based and independent information on drug characteristics that are relevant to doctors and patients, including information on mechanisms of action, mode and frequency of administration, clinical efficacy, side effects, and safety monitoring (Jongen, 2018). The information in this article will be restricted to what is important and practically applicable.

Medications used in patients with EDs

Drug treatment for EDs: The main ED diagnoses according to DSM-5 are anorexia nervosa (AN), bulimia nervosa (BN) and binge eating disorder (BED) (American Psychiatric Association, 2013). For all three diagnoses, there are only two approved drugs: fluoxetine is approved for the treatment of BN and lisdexamphetamine (LDX) is approved for BED in the US (Himmerich & Treasure, 2018). As there is no single approved drug treatment option for AN, this is the ED diagnosis for which SDM on medication is most challenging. Therefore, SDM in AN will be a main focus of this article.

Compared with other psychiatric disorders, including depression or schizophrenia, having only two approved medications for the entire group of disorders is a severe limitation in the management of EDs. In current textbooks of psychopharmacology, there are ~30 antidepressants and a similar number of antipsychotics available for patients with depression

and schizophrenia, respectively (Benkert & Hippius, 2017; Taylor et al., 2018). The lack of approved psychopharmacological treatment may contribute to the poor outcomes in treatment of EDs. In AN, for example, where no approved drug treatment option is available, outpatient interventions usually fail to achieve weight restoration in the clear majority of patients (Guarda, 2008); only ~30% of patients with AN having recovered after 9 years and the majority of patients with BED remain obese (Eddy et al., 2017). Therefore, there is an urgent need for further treatment options including psychopharmacological treatment. However, randomized controlled trials (RCTs) often fail as a considerable number of patients with AN refuse to participate in an RCT or drop out prematurely. One of the problems facing psychopharmacological research in AN may be the reservations patients have regarding drug treatment in general, particularly for drugs which may increase weight (Miniati et al., 2016).

According to a recent review on psychopharmacological advances in EDs (Himmerich & Treasure, 2018), medications that are currently discussed to potentially help those with AN include atypical antipsychotics, cannabinoid receptor agonists, and N-methyl-D-aspartate receptor agonists. Fluoxetine as a serotonergic antidepressant which is approved for the treatment of BN. Positive study results have also been published for glutamatergic agents and μ-opioid receptor antagonists in BN. However, these medications have not received approval by major agencies for the evaluation of drugs and medicinal products, including the European Medicines Evaluation Agency (EMEA) or the US Food and Drug Administration (FDA). LDX is a prodrug of amphetamine which has been approved by the FDA for the treatment of BED. **Table 1** gives an overview of the medications that are currently discussed to potentially help those with EDs. Despite the lack of approved drug treatment options in EDs, based on the current literature, it appears that >90% of inpatients with EDs are prescribed at least one psychopharmacological medication, >50% are prescribed two or more psychopharmacological drugs (Gable & Dopheide, 2005), and ~50% of inpatients additionally receive "pro re nata" (PRN) medication, which is given additionally when required (Tyrrell-Bunge et al., 2018).

Drug treatment for co-morbid psychiatric disorders: EDs are often accompanied by other mental health disorders, including depression, anxiety, attention deficit/hyperactivity disorder, obsessive compulsive disorder, schizophrenia and personality disorders (Ulfvebrand et al., 2015, Miniati et al., 2018; Link et al., 2017; Martinussen et al., 2017; Himmerich & Treasure, 2018). These disorders often make psychopharmacological treatment with antidepressants or antipsychotics advisable or necessary (Tseng et al., 2017; Himmerich & Treasure, 2018;

Benkert & Hippius, 2017; Leblé et al. 2017).

Patients with BED and BN are significantly more likely to be life-time smokers than healthy controls (Solmi et al., 2016). Patients with EDs who smoke may need drug treatment for smoking, if they are treated in a smoke-free hospital. In the UK, for example, all National Health Service (NHS) trusts introduced smoke-free regulations prohibiting smoking on all NHS sites in December 2006. Therefore, patients with EDs should be offered nicotine replacement therapy to assist them to stop smoking. However, there appear to be no reports on nicotine replacement therapies in patients with EDs, nor of any report on how smoking affects drug treatment in EDs.

Drug treatment for health consequences of EDs: In patients with EDs, not only psychopharmacological drugs are prescribed, but often the health consequences of an ED also require drug treatment. The health consequences of AN include changes in laboratory parameters, including hyponatremia, hypokalemia, hypochloremia, hypomagnesaemia; low red and white blood cell counts indicating malnutrition; a lack of vitamins, including thiamine; a lack of certain nutrients, including iron, and problems of electrolyte balance (Himmerich et al., 2010; Winston et al., 2000; Winston, 2012). Health consequences affecting the cardiovascular system include mitral valve prolapse, supraventricular and ventricular dysrhythmias, long QT syndrome, orthostatic hypotension, low blood pressure and congestive heart failure (Spaulding-Barclay et al., 2016; Meczekalski et al., 2013; Sánchez-Muniz et al., 1991). Many patients with AN suffer from severely impaired bone health in terms of osteoporosis (Meczekalski et al., 2013), which may lead to bone pain and collapsed or fractured vertebral bodies. Severe dehydration, which can result in kidney failure, and hypothermia are also typical consequences of AN (Stheneur et al., 2014; Williams et al., 2008). Refeeding can also cause a prolonged QTc interval, tachycardia, congestive heart failure with edema, and arrhythmias related to hypokalemia (Casiero & Frishman, 2006). Water loading by the patient to manipulate weight to feign treatment success can also cause severe electrolyte disturbances (Winston, 2012).

The health consequences of BN include electrolyte imbalances as a result of purging behaviors (Franke et al., 2010). These electrolyte changes can lead to cardiac arrythmias and heart failure (Sachs & Mehler, 2016). Further potential health consequences of BN include rupture of the esophagus or the stomach during periods of bingeing and purging, inflammation, Barrett's syndrome and adenocarcinoma of the esophagus (Sachs & Mehler, 2016), erosive gastritis, duodenal ulcers (Cuellar et al., 1988), and constipation as a result of laxative abuse (Sachs & Mehler, 2016).

BED often results in obesity and its associated health risks which include high blood pressure, high cholesterol and triglyceride levels, hypophosphatemia and type II diabetes mellitus (da Luz et al., 2018; Weschenfelder et al., 2018).

Therefore, EDs can lead to malnutrition or obesity and can affect fluid and electrolyte balance, the metabolic and the cardiovascular system, the gastrointestinal tract and bone health. Health problems in these areas are often treated with medications, if acute fluid replacement and appropriate nutritional support are not sufficient for their treatment. **Table 2** gives an overview of commonly used drugs for those suffering from the consequences of EDs in these systems of the body.

Drug treatment for other acute or chronic health problems: Patients with EDs may suffer from health conditions which may not necessarily be related to the ED. However, these conditions may contribute to or complicate the ED and its treatment. An example is type 1 diabetes in patients with AN (Nielson et al., 2002), as the coexistence of type 1 diabetes and AN results in an increased incidence of diabetic complications, including retinopathy and nephropathy, presumably due to blood glucose being difficult to control in those with diabetes and comorbid AN (Brown & Mehler, 2014). In patients with AN and BN, poor diabetic control is often associated with omissions of insulin to avoid weight gain and other failures in adherence to the treatment regime (Szmukler, 1984).

Treatment goals for drug treatment in EDs

Doctors, vs. patients goals: There is a lack of research regarding the question of what psychiatrists, medical doctors, psychotherapists and other clinicians consider their goals in the treatment of patients with EDs. Therefore, it must be assumed that the primary outcomes of RCTs in EDs reflect the clinicians' opinion on meaningful drug treatment outcomes. Usually, a decrease in EDs symptoms is considered a treatment goal. In AN, an increase in body mass index (BMI) and a decrease in AN symptoms are usually the goals of psychopharmacological treatment (Miniati et al., 2016; Dold et al., 2015). However, from a patient perspective, they may feel such a trial and such psychopharmacological treatment were just a way to speed up weight gain for the clinicians' benefit, rather than for helping their thinking and anxiety, and that numbers and weight is all that is important for those 'higher up' (Tyrrell-Bunge et al., 2018).

Patient Reported Outcome Measures (PROMs) and Patient Reported Experience Measures (PREMs): In the context of a quality improvement project on a specialist unit for EDs, Tyrrell-Bunge et al. 2018 surveyed patients with AN on their perspective and treatment goals for psychopharmacological treatment (Tyrrell-Bunge et al., 2018). Over 50% of the patients said they would find medication useful if it helped reduce anxiety or sleep problems. In 83% of patients, weight gain as a possible side-effect of drug treatment for AN was a concern (Tyrrell-Bunge et al., 2018). Therefore, as the fear of weight gain is a symptom of the disorder (American Psychiatric Association, 2013), patients suffering from AN do not want a medication that leads to weight gain which, in contrast, is one of the main treatment goals of the doctors. The psychiatrist and the ward teams should not collude with the disorder and agree with the patient that the side effect of weight gain should be avoided; a medication that helps to reduce the disordered eating behavior and thinking may also offer a reduction of anxiety or help with sleep problems may be a desirable benefit from the patient's perspective (Tyrrell-Bunge et al., 2018).

The inclusion of PROMs and PREMs into the individual treatment goals and into the outcome criteria for RCTs is sensible, as the patient should be aware of the benefit of a treatment prior to deciding to consent to a drug treatment for an ED. PROMs and PREMs assess the efficacy, safety, and experience of care from a patient perspective. Such PROMs and PREMs regarding anxiety and sleep problems in addition to BMI are likely to be of benefit from a patients' perspective and may improve the willingness to consent to psychopharmacological treatment for AN or to participate in an RCT (Tyrrell-Bunge et al., 2018).

Agreeing on common treatment goals and their measurement: A psychopharmacological treatment is only sensible if treatment success is measurable. Therefore, the SDM process should include an agreement on how treatment success will be gauged. Information on available measurements should be shared between the treating physician and the patient. The available measurements and questionnaires are explained below.

Clinical practice guidelines for drug treatment in EDs

Due to the lack of pharmaceutical RCTs in EDs and thus a lack of evidence on psychopharmacological treatment for EDs, clinical practice guidelines (CPGs) for patients with EDs are not able to provide clinicians and patients with optimal treatment recommendations.

They mainly provide generic advice without discussing specific drugs.

The National Institute for Health and Care Excellence (NICE) guidelines, for instance, state that one should not offer medication as the sole treatment for EDs. They advise clinicians to take into account the impact malnutrition and compensatory behaviors can have on medication effectiveness and the risk of side effects, to assess how the ED will affect medication adherence, to be aware of the risks of medication that can compromise physical health due to pre-existing medical complications, and to offer ECG monitoring for patients with an ED who are taking medication that could compromise cardiac functioning. Additionally, NICE guidelines briefly mention EDs and medication misuse (NICE, 2017). However, NICE guidelines do not recommend a specific medication or group of medication for any ED.

"The Management of Really Sick Patients with Anorexia Nervosa" (MARSIPAN) are specific guidelines in the UK for patients with severe AN who are admitted to general medical units. They provide advice to the primary care teams, criteria for admission to both medical units and specialist ED units and to non-specialist psychiatric units, criteria for transfer between services, and advice on the required members of the inpatient medical team. They also include information about the medical, nutritional and psychiatric management of patients with severe AN in medical units, including the appropriate use of the mental health legislation (The Royal Colleges of Psychiatrists, Physicians and Pathologists, 2014). However, these guidelines do not make specific recommendations about drug treatment; they rather give advice whom to involve for treatment decisions.

Aspects of drug treatment in EDs which warrant decisions

Comprehensive treatment strategy: The question of which drug to choose depends on whether treatment is indicated in general, and whether drug treatment should be considered at all. If drug treatment is considered, this psychopharmacological treatment should always be embedded in a comprehensive treatment concept (Benkert & Hippius 2017). Depending on the treatment setting, all parties involved should help to reach a decision on the treatment strategy. In an inpatient ward, for example, this will involve the patient, their carers, medical doctors, psychotherapists, nurses, family therapists, occupational or music therapists, physiotherapists, and pharmacists. The general and comprehensive treatment concept for a patient with an ED must fit the medication in question. D-cycloserine (see **Table 1**), which is not approved for the

treatment of AN has only been tested in a study where patients with AN received additional exposure therapy (Levinson et al., 2015). Therefore, it can only be concluded from this study that D-cycloserine improves the results of exposure therapy for AN, but not that it would lead to weight gain by itself in this patient group.

Multidisciplinary competence: In EDs, specialists of several medical disciplines are involved. For a psychiatrist, it is appropriate to prescribe psychopharmacological drugs, including olanzapine, fluoxetine or LDX (see **Table 1**). However, the consequences of an ED, for example, treatment-resistant osteoporosis as a consequence of AN or type 2 diabetes as a consequence of BED, may warrant the prescription of insulin-like growth factor 1 or insulin (see **Table 2**). Therefore, an endocrinologist is appropriate to prescribe these medications. Prescriptions should also be supervised by a pharmacist who understands the medications prescribed for a patient to evaluate potential interactions between drugs.

In inpatient or day-hospital settings, nurses usually contribute substantially to SDM on medication. In addition to their medical knowledge, nurses are able to provide information on the availability of a medication on the ward, how it needs to be stored, how it can be given to a patient, and what the local guidelines for prescription and documentation entail.

Dosage and timeframe: The doses of medications used in EDs may vary from the doses used in other disorders. Olanzapine is such an example; it is not approved for the treatment of AN but for schizophrenic disorders. The recommended starting dose for acute treatment of schizophrenia is 10 mg/d (Benkert & Hippius, 2017), whereas the majority of studies investigating olanzapine in patients with AN (Kafantaris et al., 2011, Brambilla et al., 2007, Bissada et al., 2008, Attia et al., 2011), initiated olanzapine treatment at 2.5 mg/d and increased this dose slowly to 5 or 10 mg/d (for review see Himmerich & Treasure, 2018). However, in clinical practice in adolescent psychiatry, the starting dose is often 1.25 mg/d (Spettigue et al., 2008). Therefore, a dosage between 1.25 and 10 mg/d is often used for the treatment of AN. Regarding the dosage, it should be noted that prescribing guidelines, including the British National Formulary (BNF) cite caution for people with a slower metabolism and female patients. Thus, in patients with AN a slow up-titration schedule of 1.25 mg/d increments each week for adolescents and 2.5 mg/d for adults up to a maximum of 10 mg/d for both adolescents and adults is recommended. The same caution applies to down-titration (Joint Formulary Committee, 2018). Thus, plans need to be made on the starting dose, the up-titration schedule, the dose for acute therapy and maintenance and down-titration. In relation to the treatment dose,

the timeframe for the different dosages needs to be determined.

However, due to the lack of evidence for the majority of medications used for the treatment of EDs, it is difficult to obtain sufficient information concerning the dose and the necessary treatment duration form the scientific literature. Strictly speaking, evidence-based guidelines for the pharmacological treatment of EDs are only available for LDX and fluoxetine (Himmerich, Treasure 2018).

Administration and dispensing: As shown in **Table 1** and **Table 2**, there is a variety of routes of administration for medications to treat EDs and their health consequences. Olanzapine, for example, an antipsychotic that has been investigated to treat AN (Himmerich & Treasure, 2018) can be administered orally or intramuscularly. Insulins are injected subcutaneously, and estrogens can be applied orally or as transdermal patches. Severe electrolyte disturbances may require intravenous application of potassium or magnesium, and constipation may be treated by rectal glycerine application (see **Table 2**). Decisions also have to be made on dispensing, depending on whether the patient can take the medication autonomously, whether they are – due to their illness – restricted in taking their medication regularly, or whether the administration route is reserved for professional administration, for example an intravenous application. A patient with an ED may need the help of a nurse, a physician or a pharmacist for regular intake of their medication.

Information to be shared

Evidence and measurement of treatment success: To share evidence on drug treatment in EDs is a challenge for clinicians, as fluoxetine is the only EDs medication that is approved in most countries. For AN, there is no approved drug treatment, as mentioned above. Therefore, the prescribing psychiatrist must summarize the evidence from single studies in a comprehensive manner.

If a psychiatrist wants to discuss olanzapine with a patient with AN, they could, for example, explain in an intelligible manner that scientific literature suggests that olanzapine is the atypical antipsychotic with the highest likelihood to restore weight and treat important psychological and emotional symptoms in patients with AN in a safe manner: i) olanzapine was superior to placebo with regard to weight gain in four published RCTs (Kafantaris et al., 2011, Brambilla

et al., 2007, Bissada et al., 2008, Attia et al., 2011) and in one not yet published but recently completed large, multisite RCT in patients with AN (mentioned in Davis & Attia, 2017); ii) olanzapine may be the most efficacious of antipsychotics examined for the treatment of AN due to its known beneficial influence on anxiety (Tollefson & Sanger, 1999; Temmingh & Stein, 2015) and sleep (Kluge et al., 2014); and iii) it affects the serotonergic, dopaminergic and histaminergic neurotransmission and thus may have a beneficial effect on the self-regulatory, the hedonic and the homeostatic system which have all been shown to play a crucial role in the pathophysiology of EDs (Himmerich & Treasure, 2018).

During SDM, the clinicians should also share information on how treatment success will be measured. Using the example of olanzapine treatment for AN, treatment outcomes could be the BMI, ED and general psychopathology, treatment adherence, and patient and carer quality of life. BMI can easily be measured using a measuring tape and a scale. Questionnaires to gauge ED psychopathology, the Yale-Brown-Cornell Eating Disorders Scale (YBC-EDS) or the Eating Disorder Examination-Questionnaire (EDE-Q) could be used. The YBC-EDS is an interview assessing core preoccupations and rituals associated with EDs. It allows for assessment of the severity of symptoms independent of the content of the symptom experienced or exhibited (Mazure et al., 1994). The EDE-Q is a questionnaire assessing key behavioural features and associated psychopathology of EDs, which includes four subscales: Restraint, weight concern, shape concern, and eating concern (Luce & Crowther, 1999). General psychopathology could be assessed using, for example, the Brief Psychiatric Rating Scale (BPRS) which assesses 24 different psychiatric symptoms (Overall & Gorham, 1962).

Potential side effects and safety measures: In addition to beneficial aspects, potential side effects and measures to control measures also need to be explained. In the case of olanzapine prescription for AN, clinical outcome measures of adverse effects could be oriented towards the World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Schizophrenia (Hasan et al., 2013), as olanzapine is approved for the treatment of schizophrenia. However, clinicians must also consider CPGs, including the NICE guidelines, which state the specific risks for prescribing medication in patients with EDs (see above; NICE, 2017). Potential side effects can affect the metabolic system and thus require regular physical examinations including the measurement of weight, blood pressure, pulse and body temperature. Further possible side effects include disturbances of conduction within the heart which are measurable by ECG. As stated in the NICE guidelines, medication can compromise

physical health due to pre-existing medical complications. Disturbances in laboratory parameters are examples of such medical conditions, and olanzapine can lead to additional changes requiring the regular measurement of clinical-chemical parameters of electrolytes and the fluid balance, of the kidney and liver function, and of blood count. With regard to extrapyramidal side effects, certain scales such as the Simpson-Angus Extrapyramidal Side Effects Scale (SAS; Simpson & Angus, 1970) and the Barnes Akathisia Rating Scale (BARS; Barnes, 1989) are available. Similarly, sleepiness is a frequent symptom in patients with AN, (Lauer & Krieg, 2004; Della Marca et al., 2004) and a common side effect of antipsychotics, specifically olanzapine (Fang et al., 2016). Thus, a standardized measurement of sleepiness using the Epworth Sleepiness Scale (ESS; Johns, 1991) may be considered. To cover a broad range of side effects, clinicians could use the UKU-Side Effect Rating Scale (UKU-SERS; Lingjærde et al., 1987) which is a general rating scale for the registration of unwanted side effects of psychotropic medication.

Table 3 provides a synopsis of important aspects of SDM on the prescription of medication in adult patients with an ED.

Specific aspects of SDM in EDs

Illness-related impairment in decision making: From a neurobiological perspective, decision making is a highly complex process involving multiple cortical areas and various neurotransmitter systems. Examples of involved brain areas include the orbitofrontal, the anterior cingulate, and dorsolateral prefrontal cortex. These are connected with each other as well as with other subcortical structures, including the limbic system, and are involved in different aspects of decision-making. For example, the orbitofrontal cortex is linked with limbic structures and involved in the process of emotional and reward-based decision making, whereas the dorsolateral prefrontal cortex and the anterior cingulate cortex are vital in intellectual and rational decision making (Rosenbloom et al., 2012). Food-related decisions do not only involve intellectual and rational decision making but are predominantly associated with an emotional and reward-based component which may be specifically impaired in patients with EDs (Frank et al., 2016).

On the neurotransmitter level, dopamine plays a crucial role in reward-based and value-based decision making (Saddoris et al., 2015). Patients with AN, have been shown to have increased

dopamine receptor affinity which can affect reward mechanisms and thus impair reward-based decision making (Frank et al., 2005).

Other neurotransmitters and hormones that have been reported to show alterations in patients with EDs include serotonin, norepinephrine, glutamate, opioid, cannabinoid, histamine, ghrelin, leptin, insulin, and glucagon-like peptide-1, and these changes are likely to influence decision making (Himmerich & Treasure, 2018). These signaling molecules are involved in emotion and appetite regulation, self-perception and cognition. Thus, it is understandable why an intense fear of weight gain is a core symptom of AN and why the majority of patients with AN do not want a medication that would lead to weight gain (Himmerich et al., 2018).

It is also well known that the hypothalamus-pituitary-adrenal (HPA) axis is activated in AN. This may contribute to the above-mentioned neuroendocrine effects in AN, as the activated HPA axis interacts with limbic structures, including the insular and prefrontal cortices (Bou Khalil et al., 2017). These interactions may be responsible for curbing food intake during emotional stress (Ulrich-Lai et al., 2015). An activated HPA axis has also been shown to influence decision-making across different settings and circumstances (Guillaume et al., 2013; Singer et al., 2017).

Therefore, patients are at risk of making decisions that are influenced by their illness (Arcelus et al., 2011). As a result, following the patient's thinking risks the patient being left to a life ruled by the ED or succumbing to mortality in severe cases.

Legal aspects: For patients who have impaired insight or limited capacity in decision making, drug treatment can be given under a relevant legal framework. In the UK, two pieces of legislation are relevant to drug treatment in EDs, namely the Mental Health Act (Department of Health, 2015) and the Mental Capacity Act (Department of Health, 2005). Patients who refuse treatment or lack the capacity to consent to treatment and are at risk of danger to themselves or others may be considered for compulsory treatment. This is particularly relevant in AN due to the severity of the illness which can affect the patients' decision-making capacity and its association with a high mortality rate (Arcelus et al., 2011). However, the decision regarding whether the ED is of a nature and degree which precludes the patient from making informed decisions relating to their treatment can be difficult and, thus should not depend on the subjective clinical judgement of the psychiatrist. Therefore, in the UK, this decision is made jointly by an Approved Mental Health Practitioner, who takes the lead in this decision, and

usually a social worker, two independent psychiatrists and the closest relative of the patient (Department of Health, 2015).

However, there are practical challenges in administering medication against a patient's will. For example, some of the medications are only available in oral form and can be difficult to administer to refusing patients. For those that are available in intramuscular form, it can also be challenging as muscle atrophy is common in severe AN. Currently, there has been no research on the effect of compulsory drug treatment on patients with EDs, to the best of our knowledge. Therefore, it is important that patients are involved as much as possible in the decision-making process with relevant information (**Table 3**) provided to them; and the decision must be made in their best interest, balancing the risks and benefits of such treatment even if it is to be given without consent under legal frameworks.

Discussion

Summary: In summary, SDM is fundamental to informed consent and patient-centered care in EDs. There are currently immense difficulties in SDM in EDs, including limited research, the lack of approved psychopharmacological treatment options, and insufficient advice on the specific pharmacological drug treatment options from CPGs. Drug treatment in EDs is not restricted to the few discussed potential psychopharmacological treatment for EDs (**Table 1**), but also includes psychopharmacological treatment for comorbid disorders and drug treatment for the consequences of the ED (**Table 2**). Here, we have emphasized how important it is that clinicians and patients share their goals for the patients' care and information on the history, symptoms, results of examinations, diagnoses and the characteristics of the medication in question; we have developed a synopsis of the most important aspects of SDM in drug treatment for patients with EDs (**Table 3**).

However, this article only describes a collection of clinical issues that warrant clarification and in-depth research. Therefore, the following section aims to provide some trenchant comments from those involved in SDM in EDs, which may promote further discussion surrounding SDM for drug treatment in EDs.

The psychiatrist's perspective: From the perspective of a psychiatrist, SDM is a challenge in EDs due to the lack of evidence derived from RCTs. Although the SDM literature demands that

the clinicians share information on evidence, this evidence is almost not existent in EDs, with the exception of fluoxetine in BN and LDX in BED (Himmerich, Treasure 2018). AN, as an example of an ED, is characterized by ego-syntonic self-starvation, denial of illness, ambivalence towards treatment, treatment refusal and high drop-out rates (Guarda et al. 2008). Therefore, SDM with a patient who does not want to gain weight often feels like compromising with the disorder rather than helping the patient to lead an autonomous and self-paced life. CPGs, including the NICE guidelines, do not fully support the doctors' reasoning to prescribe a medication; by contrast, they elicit and promote anxieties, as they only remind the doctors of the difficulties and risks rather than making positive recommendations. Therefore, SDM may feel like an obstacle that prevents psychiatrists from helping their patients with EDs, specifically if patients require PRN medication for a variety of consequences of the ED rather than accepting the one medication that may help to tackle the cause of these physical and mental consequences.

In addition, psychiatrists are aware of the severe side effects of drug treatment having observed them during clinical practice, including massive weight gain leading to serious health risks (Himmerich et al., 2015), rhabdomyolysis (Himmerich et al., 2006) or live-threatening psychotic symptoms (Himmerich et al., 2003); no one individual wants to take full responsibility for these events. In addition, it is unlikely that a patient would want someone to make decisions on taking such serious risks on their behalf. Therefore, SDM is without any alternative. From a psychiatrist's perspective, the question is not whether or not to use SDM, but rather what degree of responsibility are patients and their clinicians willing and able to accept during the process of SDM.

The internist's perspective: Patients with EDs, particularly those with AN, can be admitted to the emergency department or a medical ward for treatment of conditions that can be related to their ED or unrelated, e.g. infections, cardiovascular complications, or metabolic disturbances (Rome & Ammerman, 2003). Treatment can become difficult for several reasons, however, the most aggravating factors are legal uncertainties and medical teams not being set up to deliver specialized multidisciplinary care.

Upon admission, patients are often unwell or unresponsive, and they are treated in their best interest. As soon as their condition improves, they often request discharge or limitations to their treatment; this puts the physician in a difficult position, as the complications arising from an ED can be potentially life-threatening, depending on the degree of their severity and nutritional status, and would ideally require prompt and adequate treatment, e.g. electrolyte replacement.

In order to decide whether the patient has the ability to make such a decision, a capacity assessment needs to be completed. Often, patients do have the capacity and, even when aware of the potentially life-threatening condition, they do not wish to receive treatment. Even in cases when the capacity assessment leads to the conclusion that the patient is lacking capacity, legal frameworks can make the administration of treatment difficult. In the UK, the physician has to decide whether to admit a patient with an ED, if it is necessary, in their best interest and as the least restrictive measure, against their will under the Mental Health Act (Department of Health, 2015) or under the Mental Capacity Act (Department of Health, 2005). However, neither of those legal frameworks allows the immediate administration of medication against the patient's will, and the physician is only allowed to monitor the patient's condition. Having a patient legally admitted to a medical ward can negatively affect the patient-physician relationship and can hinder an SDM process.

Another difficulty in the management of patients with ED on a general medical ward are the often limited resources and the non-specialized physicians and therapists. In the UK, the MARSIPAN guidelines (The Royal Colleges of Psychiatrists, Physicians and Pathologists, 2014) recommend that hospitals which can admit severely ill patients with EDs identify a consultant physician with interests in managing EDs and nutrition to optimize inpatient care for those patients. However, this is not feasible for every hospital. For general physicians in emergency departments or on medical wards, it can be difficult to assess the severity of the condition of patients with EDs and to decide on appropriate treatment. Often, physicians can only offer treatment or dietitian's review and advice.

The patent's perspective: From the perspective of the patient, the discussion of any form of treatment can cause anxiety for several reasons. It is often the case that the ED leads to a patient developing self-imposed rules and coping mechanisms, which influence their food intake or energy expenditure; these are challenged in both outpatient and inpatient treatment settings, which can cause distress. There can be a reluctance to change or engage with treatment, which may be related to denial of the illness or the negative stigma associated with EDs, or the anxiety felt when faced with parting from the 'safety' of what they know.

Decisions regarding psychopharmacological treatment are equally anxiety-provoking. In the case of AN, in addition to the potential stress caused by taking the drug itself, patients may feel a sense that the most important treatment outcome from the view of healthcare professionals is weight gain, rather than providing support with the psychological or behavioral issues that cause

distress. Patients are faced with and have to bear the consequences of decisions surrounding medication, for or against inpatient treatment and around the mental health act. In contrast to the psychiatrist, this is not their area of interest or expertise. Therefore, patients often rely on the information given by other patients to obtain a second opinion on these matters. This introduces another challenge for SDM, particularly in an inpatient setting, as relationships established with other patients can encourage unhelpful thinking or behaviours reinforcing to the ED, introduce a sense of 'competition', or lead to decision-making based on the experiences of others. It is therefore important that SDM is sensitive to patient concerns and that the potential benefits of drug treatment, including reduced anxiety, improved sleep and the potential increased ability to engage with therapy, are also explained. This highlights the need for further evidence-based information to encourage patient inclusion, discussion and ultimately cooperation. The use of advanced directives could also be discussed for consideration, which can be made by a patient when they are well in the event of relapse.

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Table 1: Medications that are currently discussed to potentially help people with EDs based on (Himmerich & Treasure, 2018; Dold et al., 2015; Levinson et al., 2015; Andries et al., 2014; Benkert & Hippius, 2017). The table shows the different drug classes, the active substances, their possible route of administration and their daily doses for the treatment of EDs in adults by oral administration as a tablet and their approval status. Natrexone has been tested using single doses prior to exposure therapy. Abbreviations: EDs, eating disorders; NMDA, N-methyl-D-aspartate; US, United States of America.

	Drug class	**Active substance**	**Available route of administration**	**Dose**	**Approval status**
Anorexia Nervosa	Antipsychotic	Olanzapine	Oral and intramuscular	2.5-10 mg/d	Not approved
		Aripiprazole	Oral and intramuscular	5-15 mg/d	Not approved
	Cannabinoid receptor agonist	Dronabinol	Oral	5-15 mg/d	Not approved
	NMDA receptor agonist	D-Cycloserine	Oral	50-250 mg	Not approved
Bulimia Nervosa	Serotonergic antidepressant	Fluoxetine	Oral	20-60 mg/d	Approved
	Glutamatergic agent	Topiramate	Oral	12.5-200 mg/d	Not approved
	μ-Opioid receptor antagonist	Naltrexone	Oral	250 mg prior to exposure	Not approved
Binge Eating Disorder	Amphetamine	Lisdexamfetamine	Oral	30-70 mg/d	Approval in the US

Table 2: Currently used or investigated medications to treat health consequences of EDs in adult patients (Jagielska et al., 2016; Misra & Klibanskia, 2011; McCallum et al., 2006; Winston et al., 2012, Winston, 2000; Santonastaso et al., 1998). The table provides an overview of the problem area, potential health consequences, treatment strategies, active substances that may be used, and route of administration. With the exception of oral vitamin and electrolyte replacement, most of these medication strategies are only used when dietary measures fail. This table does not aim to provide a comprehensive summary, but to demonstrate the variety of drugs that may become necessary to treat the health consequences of EDs. Abbreviations: EDs, eating disorders; VRA, vasopressin receptor antagonist; GI tract, gastro-intestinal tract; GERD, gastroesophageal reflux disease; emerg., if emergency treatment is necessary; NSAID, non-steroidal anti-inflammatory drug.

	Health problem	**Drug class/treatment strategy**	**Active substance**	**Route of administration**
Malnutrition	Vitamin deficiency	Multivitamins	Vitamins	Oral (e.g. Forceval®)
	Vitamin B deficiency	Vitamin B Compound	B vitamins	Oral (e.g. Vitamin B Compound Strong®)
	Thiamine (vitamin B1) deficiency	Thiamine replacement	Thiamine	Oral, i.v.
	Iron deficiency	Iron replacement	Iron	Oral
Disturbances of the fluid and electrolyte balance	Dehydration	Fluid replacement	Water and electrolytes	Oral, i.v.
	Water loading	VRAs in severe cases of water loading with hyponatraemia	Conivaptan, Tolvaptan, Lixivaptan	Oral, i.v. emerg. (VRAs not tested in EDs)
	Hyponatremia	Sodium replacement	Sodium	Oral, i.v. emerg.
	Hypokalaemia	Potassium replacement	Potassium	Oral (e.g. Sando-K®), i.v. emerg.
	Persistent hypokalaemia	Magnesium replacement	Magnesium	Oral, i.v. emerg.
	Persistent hypokalaemia and vomiting	Proton pump inhibitors	Omeprazole	Oral, i.v.
	Hypochloraemia	Sodium chloride, Saline solution i.v.	Sodium chloride	Oral, i.v.
	Hypocalcaemia	Calcium substitution	Calcium, vitamin D	Oral: Calcium and vitamin D, i.v. calcium emerg.

	Hypophosphataemia	Phosphate supplementation	Phosphate	Oral (e.g. Phosphate-Sandoz®)
	Hypomagnesaemia	Magnesium supplementation	Magnesium	Oral, i.v. emerg.
Endocrine and metabolic disorders	Obesity	Antidepressant and μ-opioid receptor antagonist	Bupropion and naltrexone	Oral (Mysimba®)
		GLP-1 analogue	Liraglutide	Subcutaneous injection (Saxenda®)
	Type 2 diabetes	Oral hypoglycemics, e.g. Biguanides	Metformin	Oral (e.g. Glucophage®)
		Insulins	Rapid-, short- or long-acting Insulins	Subcutaneous injection (e.g. Humalog®, Lantus®)
	Hypercholesterolaemia	Statins	Atorvastatin	Oral (e.g. Lipitor®)
GI tract problems	GERD	Antacids	Sodium alginate, sodium bicarbonate, calcium carbonate	Oral (e.g. Gaviscon®)
		Proton-pump inhibitors	Omeprazole	Oral
	Abdominal discomfort	Antispasmodics	Mebeverine	Oral (e.g. Colofac®)
		Gastroprokinetics	Metoclopramide	Oral (e.g. Maxolon)
	Constipation	Non-absorbable sugar laxative	Lactulose	Oral
		Hyperosmotic laxatives	Glycerine	Rectal
Cardiovascular diseases	Persistent hypotension	Glucocorticoid	Fludrocortisone	Oral
Impaired bone health	Osteoporosis	Minerals and vitamins	Calcium and vitamin D	Oral (e.g. Adcal-D3®)
		Hormones	Oestrogens	Oral, transdermal
			Insulin-like growth factor-1 (e.g. Mecasermin)	Subcutaneous
		Bisphosphonates	Risedronate	Oral
Pain	Pain associated with osteoporosis/GI pain	NSAID	Paracetamol	Oral
Axiety and sleep	Anxiety and sleep disturbances	Antihistamines	Promethazine	Oral, i.m., i.v., rectal

disturbances	Sleep disturbances	Nonbenzodiazepine hypnotic agents	Zopiclone	Oral

Table 3: Synopsis of important aspects of SDM on drug treatment in adult patients with an ED based on (Makoul & Clayman, 2006; Stacey et al., 2011; Lin & Fagerlin, 2014; Himmerich & Treasure, 2018; Benkert & Hippius, 2017; Taylor et al., 2018; National Institute for Health and Care Excellence [NICE], 2017; The Royal Colleges of Psychiatrists, Physicians and Pathologists, 2014; Joint Formulary Committee, 2018). For further references, see text. The information may be obtained in preparation for or during an SDM meeting. Such a meeting may be a ward round meeting, a Care Programme Approach meeting or a separate meeting. Abbreviations: SDM, shared decision making; MHA, Mental Health Act; GP, General Practitioner.

Legal aspects needing clarification prior to SDM
• Legal framework of the treatment (voluntary vs. compulsive treatment, e.g. under MHA) • Capacity of the patient
Individuals involved in the SDM process
• Patient • Carers • Physicians (medical doctors of different specialties) • Nurses (mental and physical health nurses) • Therapists (psychotherapists, occupational/art/music therapists, physiotherapists) • Dietitians • Pharmacy • GP team, home treatment team, specialist treatment team • If necessary, representatives of insurances or health services
Information to be shared by patient with help of clinicians
• Individual treatment goals • Current problem(s) and/or symptom(s) they want help with • Their values and preferences • Information about current risk-taking behaviours, including vomiting, laxative abuse, water loading • Mental and physical health problems, social and family history • Current and previous medication and nutritional supplements • Smoking status, use of illicit drugs • Dietary habits that may influence drug metabolism (e.g. grapefruit juice)
Information to be shared by family, GP and home treatment team
• Previous and current difficulties at home • Experience with previous medicinal treatments • Available support for prescription, administration and intake of medication
Information on health and current treatment of the patient to be shared by the clinicians
• General psychopathology and eating disorder psychopathology • Physical health problems (gastro-intestinal tract, metabolic system, cardiovascular system, bones, kidneys, brain) • Body weight, blood pressure, pulse, body temperature • Changes in laboratory parameters

• Results of ECG and other examinations • Refeeding problems • Current medication, nutritional supplements and treatment • Clinical observations, including adherence to meal plan and risk-taking or disorder-related behaviours • Summary of history taking, physical examination, symptoms detected, clinical observations made and diagnoses suggested or established
Information on the treatment options to be shared by the clinicians
• Treatment goals of the clinicians • Available treatments • Medicinal, naturopathic and psychological treatment alternatives • Advice from guidelines • Evidence from scientific literature • Own clinical experience • Benefits • Side effects and risks • Interactions with current and potential future drugs and treatments • Measurements of treatment success and side effects • Realistic perspective
Decisions to be made
• Common treatment goals • Comprehensive treatment concept • Problem(s) or symptom(s) that need drug treatment • Prescriber (prescribing within limits of competence) • Medication • Application • Administration • Length of treatment • Monitoring and precautionary measures • Measurement and documentation of treatment success and side effects • Follow-up meeting to evaluate impact of decision
Duties of the clinicians during SDM process
• Clarification and documentation of decisions • Checking and documentation of the understanding of the patient • If necessary, explicit postponement of the decision • Arrangement of follow-up meetings to check implementation and impact of decision

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