

Peer Review File

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Review comments

Reviewer A

The authors are to be commended for addressing a major controversy in treating patients with severe eating disorders. This well conducted scoping review is timely and pertinent for current discussions in the field.

General reply: Dear reviewer, many thanks for reviewing our manuscript and giving us the opportunity to improve it! We appreciate the time and effort you clearly put into this very much and feel that the review process has been very beneficial. Please note that in order to incorporate your suggestions and stay within the maximum word count, we shortened some sentences/passages throughout the manuscript (without changing the content, of course). We are attaching a revised version with tracked changes, however, changes to references are not tracked due to our referencing software.

Several issues should be addressed to strengthen this paper:

Comment 1: The purposes of this review should be clarified in the abstract. As the authors acknowledge in their introduction, palliative care not directed to end of life care is clearly a treatment option for SE-AN patients who refuse coercive life sustaining measures, and this review does not consider this option. To be clear, the authors should explicitly state this omission up front, lest some readers take away the mistaken idea that the only two options for these patients are coercive treatment or end of life care. To address this point, I suggest inserting wording in the abstract to the effect that “Palliative care directed to optimizing quality of life without focusing on end of life care is clearly a treatment option for SE-AN patients who refuse coercive life sustaining measures. However, this review does not consider that treatment option. Here we specifically focus on the provision of palliative care for AN only in the end of life context.” (In the text this constraint is first mentioned in the last sentence of the introduction section).

Reply 1: Thank you for this point, we have added a sentence to this effect to the abstract: “Palliative care outside of the end-of-life context and medical assistance in dying were not reviewed.» (lines 45-46). To stay within the maximum word count for the abstract, we could only state this shortly, and had to make some changes to the rest of the abstract.

Comment 2:

Both the abstract and key findings state that the provision of end of life care is controversial. However, that statement never appears nor is it discussed as such in the text. If the statements remain in the abstract and key findings the authors should

clarify in the text exactly what they think is controversial about providing end of life care to patients with anorexia nervosa. Is the idea that some patients are actually nearing death and facing end of life controversial? That dying patients deserve care? That clinicians should ever accept the fact that these patients are dying? That end of life care would ever replace coerced care? What, specifically, is the controversy about? Wouldn't the authors consider coerced involuntary care to be similarly controversial? If not, why not?

Reply 2: In our view, the controversy is about whether it can be appropriate to provide EOL care in AN instead of coercing life-sustaining measures (and if EOL care can be appropriate, what criteria should be used to decide upon eligibility). We agree that this was not made clear in the results section so far and have included the sentence "Whether providing EOL care in AN instead of coercing life-sustaining measures can be justified and thus appropriate is controversial.» at the beginning of the section on ethical reasoning (lines 303-304), as well as a similar sentence to the summary of main findings at the beginning of the discussion (lines 447-449). That eligibility criteria are controversial is detailed in lines 401-407 and repeated in the summary of main findings at the beginning of the discussion (line 454).

Comment 3:

For the last sentence of the abstract, consider changing the wording to "... the appropriateness or inappropriateness of diagnosis-based ethico-legal exceptionalism such as hard paternalism." Alternatively, "the ethical challenges posed by diagnosis-based...."

Reply : We have written "fundamental normative questions need to be addressed, for example (...) the appropriateness of diagnosis-based ethico-legal exceptionalism such as hard paternalism.» (lines 65-67)

Comment 4:

Line 244. The discussion of futility begins "Except for actively dying patients...". How do the authors define "actively dying" and distinguish that from other types of "dying"? Would actively dying patients qualify for end of life care? What about "actively dying" makes that less controversial?

Reply 4: "Actively dying" refers to a person in the last hours or couple of days of life (see Hui D, Nooruddin Z, Didwaniya N, Dev R, La Cruz M de, Kim SH et al. Concepts and definitions for "actively dying," "end of life," "terminally ill," "terminal care," and "transition of care": a systematic review. *J Pain Symptom Manage* 2014; 47 (1): 77-89.). This phase is clinically and morally different as the point of no return of starvation is passed. Therefore, some important opponents of EOL care for AN (such as Geppert 2015 and Giordano 2019) concede that in actively dying patients, coerced life-sustaining measures would be (physiologically) futile and should be forgone (detailed in table 3, row 2: futility as impossibility). This seemed an important distinction which is why we mentioned it in the beginning of the text on futility. We have added an explanation to this effect in a footnote to line 247 : "The term actively dying refers to the last days or hours of life, characterized by a breakdown of

physiologic functions (95). In persons dying from starvation, a point of no return is reached when the molecular structures necessary for metabolizing nutrients have themselves been metabolized.”

Comment 5:

Line 291. The sentence reads “Others defend the functional approach, arguing that it can (and frequently does) find AN patients incapacitated (131).” To be balanced, shouldn’t there be a sentence saying that others find that patients with AN often retain capacity? See for example: Miller Tate AJ. Presuming incapacity in anorexia nervosa is indefensible: a reply to Ip. *Bioethics*. 2021;35(6):596–601; Elzackers I, Danner UN, Grisso T, Hoek HW, van Elburg AA. Assessment of mental capacity to consent to treatment in anorexia nervosa: a comparison of clinical judgment and MacCAT-T and consequences for clinical practice. *Int J Law Psychiatry*. 2018;58:27–35; Calcedo-Barba A, Fructuoso A, Martinez-Raga J, Paz S, Sánchez de Carmona M, Vicens E. A meta-review of literature reviews assessing the capacity of patients with severe mental disorders to make decisions about their healthcare. *BMC Psychiatry*. 2020;20(1):339.

Reply 5: We agree that the position that at least some treatment refusals by AN patients are competent is very important to the debate and our review. We discuss this in the section on ethical reasoning (lines 327-328 and table 5, row 4, column 3). In the section you are referring to (conceptual questions/DMC), we are not discussing the question whether/how frequently AN patients have DMC, but how DMC should be assessed (which obviously has important repercussions on the question whether AN patients can have DMC) = open conceptual questions surrounding DMC in AN. Your comment made us realize that this was not made clear in the introductory sentence to this passage, which is why we rephrased it to “While there is consensus that DMC can be impaired in AN, it is debated whether AN patients can have DMC for refusing life-sustaining measures. At the heart of this debate is the open conceptual question of how DMC should be assessed in this context (Error! Reference source not found.).” (lines 283-284). So the sentence you’re referring to is not meant to say that AN patients are frequently incompetent, but rather convey the position that we should not deviate from the functional approach to DMC assessment (that is, f.ex., not declare patients incompetent based on an AN diagnosis alone) because the functional approach “works” in the sense that AN patients can be found incompetent using it. We hope the improved introductory sentence makes this context clearer.

Comment 6:

Line 317 ff. In the discussion of autonomy of patients with anorexia nervosa, might it be appropriate to mention and consider the World Health Organization’s Convention on Rights of Persons with Disabilities, endorsed by over 180 countries, which applies to individuals with mental disabilities as well as physical and intellectual disabilities? This declaration seems to come out strongly on the side of autonomy.

Reply 6: In response to your and reviewer B’s comments on the section on legal aspects, we have considerably revised it. In this process, we identified two additional

publications that met inclusion criteria (Clough 2016 and Jackson 2017; they had been picked up by our search but unfortunately not screened due to a clerical error). We included those publications now and updated the flowchart etc. accordingly. Regarding the text on legal aspects, we included the following passage on international conventions:

“The lawfulness of forgoing coercive life-sustaining measures and/or providing EOL care in AN is also discussed under human rights law. Regarding the European Convention on Human Rights (ECHR), coerced life-sustaining measures interfere with patients' rights under Article 3 (prohibition of inhuman and degrading treatment) and 8 (right to respect for private and family life). This can, but need not, be necessary and proportionate to defend their right under Article 2 (right to life) (37, 69, 79–81, 128). In the United Nations Convention on the Rights of Persons with Disabilities (UNCRPD), persons with psychosocial disabilities such as AN are explicitly included. The monitoring committee has interpreted Article 12 (right to equality before the law) as ruling out incapacity judgements as legal grounds for coercion, rendering any coerced life-sustaining measures in AN unlawful (121, 123, 149). This has been contested by authors interpreting Article 12 as a) only ruling out coercion of persons who have DMC while b) calling for respecting the preferences of persons who do not have DMC to the greatest extent possible (109, 143).” (lines 359–371)

Comment 7:

Line 386. Shouldn't the contrary legal opinion also be included here? The right of patients with anorexia nervosa to starve themselves without interference has been upheld in American case law. See Schmidt S (2016). Anorexic woman weighing 69 pounds has a right to starve, court rules, The Washington Post. <https://www.washingtonpost.com/news/morning-mix/wp/2016/11/22/anorexic-woman-weighing-69-pounds-has-a-right-to-starve-court-rules/Schmidt 2016>.

Reply 7: We have added the following sentence: “ We identified six legal cases, mostly from the United Kingdom, in which the courts declared it lawful to forgo coerced life-sustaining measures and/or provide EOL care to a patient with AN (see Supplementary Table 5, column 10) (11, 37, 69, 70, 74–76, 78–81, 123). In another case, the court ordered EOL care to be discontinued in favor of coerced life-sustaining measures (11, 37, 70, 79, 80, 123). Of note, in none of these cases was the patient found to have retained DMC by the court, and rulings were based instead on best interest considerations (see above for the debate on DMC assessment in AN). To promote patients' autonomy, advance directives are proposed (73, 75, 113). However, there is legal uncertainty as to how patients can ensure that their advance directive is not declared invalid on grounds of incapacity (37, 69, 79, 80, 94, 129).” (lines 348–355)

Also, to give an overview, we have added a column to supplementary table 5 (cases of EOL care for AN) detailing court rulings. The article you cited could unfortunately not be included as it does not meet inclusion criterion 7 (scientific journal/publisher), but the case (patient initials A.G., judge Paul Armstrong) has been discussed in two publications that were included and is tabulated in suppl. Table 5 (cases of EOL care for AN). Nevertheless, we are aware that the sensitivity of our search for legal cases is likely low, which we have flagged in the limitations section (lines 523–524)

Comment 8:

Line 402 and line 541ff. Several recent publications based on “lived experience” favor involuntary treatment. However, I am unaware of studies involving family members of deceased patients with severe and enduring anorexia nervosa to ask their opinions and “lived experiences” of involuntary treatment, or of their difficulties in accessing humane end of life care for their departed loved ones. This may be an additional gap in the literature that could be addressed in future research.

Reply 8: That’s a great point, we have added it to the discussion of open research questions (line 513-516): “The outcomes of EOL care in AN need to be studied to allow for a better assessment of the benefits and burdens associated with this option, e.g., comparing the accounts of significant others of patients that died from AN with versus without EOL care.»

Comment 9:

Page 27 footnote 3. To be fair and balanced, the authors should also describe the experiences and viewpoints of the other half.

Reply 9: In response to reviewer B (comment 46), we have deleted footnote 3.

Comment 10:

Line 500. The authors note the absence of “neutral terminology”. Is such a thing possible? Most “neutral” words can easily be misunderstood, misinterpreted, and be made to represent something other than intended by the original authors. Many disputes concerning “wokeness” revolve around these controversies.

Reply 10: We agree that neutral terminology is an ideal that we can/should strive for, but not a goal we can achieve. Therefore, we have phrased the goal as “consented, coherent terminology whose value base is reduced to a minimum and made transparent» (lines 62-63; key findings box; 472-474; 536-537)

Comment 11:

Line 540: With respect to gaps in knowledge, the authors repeatedly refer to the importance of ascertaining the “moral significance” of various view or actions. How would they operationally define and assess these characteristics and evaluate responses in studies?

Reply 11; What we wished to convey is that even with more scientific knowledge, some uncertainty will always be left to deal with in finding ethical solutions to challenging situations in the context of life-threatening AN: “Reducing uncertainty would likely allow care to be better tailored to the individual and reduce moral distress in healthcare professionals. However, data will never tell us the exact prognosis of a given patient or whether she has DMC. (...) Therefore, the underlying normative questions need to be addressed” (lines 484-493). So, the questions surrounding the moral significance (of treatment refusals etc) cannot be answered by research using a positivist approach (including aspects such as operationalization), which is why we’re calling for more ethics research in the discussion (lines 505 and following). Please note that we changed

the wording here to “ethico-legal significance” in the course of our in-depth revision of the section on legal aspects.

Comment 12:

Line 540. An additional significant gap knowledge gap worthy of further study that bears inclusion concerns the underlying sources of clinicians’ and ethicists’ moral, ethical and clinical biases (their viewpoints and convictions). Since no one is bias free, studying these fundamental differences and their origins is essential for understanding these controversies. How can clinicians and ethicists’ biases concerning end of life care best be characterized? What personality (temperamental, cognitive, emotional) and developmental characteristics of clinicians and ethicists (e.g. for “liberal, tolerant” vs “conservative” modes of processing) lead them to adopt (sometimes strong) opinions one way or the other on these matters? To what extent do clinicians’ and ethicists’ biases originate with early religions training, differences in personal comfort with providing end of life care, medical training, competing intellectual or economic considerations, concerns about potentially negative responses from professional colleagues, family members and patients, and actual bedside clinical experiences with patients and their families? See for example George LS, Epstein RM, Akincigil A, Saraiya B, Trevino KM, Kuziemski A, Pushparaj L, Policano E, Prigerson HG, Godwin K, Duberstein P. Psychological Determinants of Physician Variation in End-of-Life Treatment Intensity: A Systematic Review and Meta-Synthesis. *J Gen Intern Med.* 2023 May;38(6):1516-1525. doi: 10.1007/s11606-022-08011-4. Epub 2023 Feb 2. PMID: 36732436; PMCID: PMC10160244. Also see numerous papers by Pat Croskerry and colleagues on biases in clinical decision-making.

Reply 12: That’s a good point, we added the following sentence to our discussion of further research: “The attitudes of various stakeholder groups need to be measured and compared in representative studies, including possible determinants such as personality traits and religious beliefs.” (lines 508-510)

Reviewer B

The paper offers a timely synthesis of perspectives and is the first of its kind. Methodology is transparent and replicable. The paper uses scoping review to successfully explore whether, when and how EoL care is indicated (excluding non-EoL palliative care) to clarify key concepts, areas of consensus and identify knowledge gaps (open questions). An enormous undertaking.

General reply: Dear reviewer, many thanks for taking the time to review our manuscript in such detail! We feel it has considerably improved in the process and do hope you find the same. Please note that in order to incorporate your suggestions and stay within the maximum word count, we shortened some sentences/passages throughout the manuscript (without changing the content, of course). We are attaching

a revised version with tracked changes, however, changes to references are not tracked due to our referencing software.

Comment 13:

a) Given that grey literature was excluded for pragmatism the work may be better identified as a rapid scoping review?

b) The review also does not report / identify the types of evidence that make up the review in text e.g. lived/living experience, clinician, families, legal etc– consider including this in results.

See: Munn et al. 2018 “report on the types of evidence that address and inform practice in the field and the way the research has been conducted....Rapid review could potentially be conducted for any of the indications listed above for the scoping or systematic review, whilst shortening or skipping entirely some steps in the standard systematic or scoping review process”

Reply 13:

- a) Thank you for this point. We agree that the terminology around scoping review methodology is not completely consolidated at the moment, so different understandings are common. In the methods papers we worked with, including grey literature is not described as necessary for a scoping review, f.ex. Peters 2020 (co-authored by Munn) write “The search strategy for a scoping review should ideally aim to be as comprehensive as possible within the constraints of time and resources”, and the PRISMA extension for Scoping reviews (Tricco 2018) states “Not all scoping reviews will include gray literature (depending on the specific research question and objectives),”. Therefore, we believe that including grey literature is not a definitory characteristic of a scoping review which justifies calling our manuscript a scoping review instead of a rapid scoping review. In addition, we find that including grey literature would not have been feasible in our review even in the absence of the time and financial constraints we experienced. Given the topic and the lack of language restrictions, we would have had to search in at least a couple of hundred languages to conduct a systematic search of grey literature.
- b) Please see our replies to comments 38 and 39, thank you!

INTRODUCTION

Comment 14:

- L 81-6 The numbering unclear if used to delineate diagnostic parameters or citations. Consider rewording / placing citations at the end with a full stop.

Reply 14: We have rephrased to “AN is characterized by emphasis on fear of becoming fat, striving to achieve a lower than normal body weight by starvation (anorexia nervosa restricting subtype) or restriction plus purging (anorexia nervosa binge/purge subtype) (2). It is associated with a range of medical complications (3). With evidenced-based treatments, most persons with AN achieve at least partial remission (4, 5).» (lines 80-83)

Comment 15:

- L95 whose definition of recovery is used here? Reference.

Reply 15: We have harmonized the language to go with the rest of manuscript and added a definition with reference (footnote to line 103): “Following the DSM 5 (2), we define (full) clinical remission as absence of symptoms that are diagnostic criteria for AN, i.e. as return to normal body weight and absence of behavioral symptoms (such as restricted eating) and psychological symptoms (such as intense fear of gaining weight) over a sustained period of time. We define partial clinical remission as return to normal body weight with some remaining behavioral and/or psychological symptoms.»

Comment 16:

- L 97-109 – important points but needs rephrasing – aspects unclear e.g.

a) are you alluding to QoL goals in SE-AN RCT as consistent with a palliative model of care? The two could be conflated.

b) Need to describe what was unique about this RCT – unclear how it relates. Are you also inferring that care that is better aligned with needs and preferences (e.g. trauma informed, neuro and gender affirming) such as allowing people to set their pace for change and goals has not been accessible or well-defined

c) Consider making it more explicit that palliative care does not equate to EOL care and that it is a flexible spectrum of care. This is a common misconception. Might also introduce that the earlier spectrum of palliative care is not considered here in this review. It relates exclusively to EoL care which is typically brief.

d) L108 might add and this is opposed by others

Reply 16:

a) We agree that what constitutes “palliation” in mental healthcare (“or palliative psychiatry”) is a matter of open debate. Mental healthcare focussing primarily on QOL has in fact been termed “palliative psychiatry in a broad sense” (Westermair, Anna L.; Buchman, Daniel Z.; Levitt, Sarah; Perrar, Klaus M.; Trachsel, Manuel (2022): Palliative psychiatry in a narrow and in a broad sense: A concept clarification. In: *Aust N Z J Psychiatry* 56 (12), S. 1535–1541. DOI:

10.1177/00048674221114784.), but we feel it’s outside the scope of our review to discuss this conceptual question as its focus is on EOL care which is well-defined. Actually, the lack of conceptual clarity about what “palliation” means in mental healthcare/AN was the reason for restricting the scope of the review to EOL care.

b) This was supposed to refer to the sentence before that, but we agree that this was not clear. We have rephrased to “one possibility could be shifting the goal of care away from weight normalization and clinical remission towards harm reduction and improved quality of life (12–14). This was studied in a seminal RCT showed high retention rates and improvements in quality of life (12).» (lines 104-106).

c) We have written “Palliative psychiatry also includes end-of-life (EOL) care. EOL care is a portion of palliative care that is directed towards persons nearing death (17)» (lines 108-110). Also, in response to comment 1 (from reviewer A), we

have added a sentence to this effect to the abstract: “Palliative care outside of the end-of-life context and medical assistance in dying were not reviewed.» (lines 45-46), so that readers are aware of the scope of our review right from the start. This is repeated at the end of the introduction: “The review does neither consider the provision of palliative care for AN outside of the EOL context …” (lines 123-124)

- d) We have rephrased to “EOL care has been proposed as alternative model of care for extremely ill AN patients (14, 18–20) but strongly opposed by others (21–23). Leading eating disorders experts have called for the development of guidelines, eligibility criteria, and protocols (24).»(lines 110-113)

Comment 17:

o The introduction is very brief. May wish to explain the impetus for the review and explore some of those issues in context. Consider in the introduction exploring ‘Benefit outweighing harm’. Life at any cost? Even if this is at further loss of QoL i.e. treatment trauma, PTSD. Where some have found comfort in suicide during or immediately following treatment. Also Some background about legal aspects currently placed in results section could be explicated here in the introduction/background

Reply 17: Yes, as the results sections is very long, we tried to keep the introduction short to stay within the maximum word count for the manuscript. We explore the points benefit/burden ratio and life at any cost/sanctity of life in the results/ethical reasoning (lines 302-304 and table 5, row 2 column 2 and 3 and row 3, column 3). But we agree with your recommendation to transfer part of the legal background to the introduction and have implemented it:

“Despite these risks, patients with AN are often very reluctant to seek the life-saving treatment of weight gain, which is critical to the success of treatment (11). Here, coercion can come into play. In US legislation, for example, coercion rests on the assumption that the individual either lacks decision-making capacity (DMC) regarding treatment for his/her AN (guardianship) or is a danger to himself/herself and/or gravely disabled (civil commitment). Guardianship and certification differ in terms of the type of treatment that can be provided under each statute (medical care vs. psychiatric care), as well as the venue for that treatment. Guardians can make decisions regarding a ward’s emergent medical care (such as artificial nutrition). Once the ward is no longer medically unstable, coerced inpatient psychiatric care and further nutritional rehabilitation can only be authorized by the courts under civil commitment laws (12).

However, despite the risk of morbidity and mortality from untreated AN, there is often reluctance to use coercion. Such concern may be well founded in that such treatment may not necessarily be recognized in retrospect as helpful, especially by individuals with SE-AN whose ultimate goal is quality rather than quantity of life (13).» (lines 88 – 102).

Comment 18:

o If including papers post searches then need to include Treem, Yager and Gaudiani Sept 2023 and any other papers if they meets inclusion. this may otherwise be

interpreted as bias.

Reply 18: Are we correct in assuming that you are referring to footnote 3 here? We have deleted this in response to your comment 46.

Comment 19:

L259 authors state – treatment refusal which is a symptom of AN – would be helpful to include qualitative accounts of treatment refusal by way of introduction – why is it that treatment is so unacceptable to people, beyond being a symptom of the disorder i.e. “Treatment is worse than the disease, especially when ‘cure’ or a quality life are unlikely”. Exclusion of this perspective has been cited by those with living experience as dismissive i.e. “that is your anorexia talking” and is cited as harmful. See Elwyn, see Asaria , See Downs et al 2023

Reply 19: We agree that qualitative accounts on why treatment can be unacceptable to patients are highly important. However, the section you’re referring to deals with futility, more specifically how the term can be understood and whether it can apply to AN. So the sentence you’re referring to states that some authors argue that futility (understood as an unacceptably low chance of clinical remission) does not apply to AN as the reason for the poor chances is treatment refusal which is treatable and thus reversible (see also table 3, column 1, row 3). We unfortunately did not identify any qualitative study on patient’s views of futility. We give an overview of what little studies have been done on patient attitudes towards EOL care and related concepts in the section on stakeholder attitudes (lines 372 and following) and have stressed this lack of research in the discussion (lines 508-510).

Comment 20:

P8 L 169 might add to ‘strengths’ that multiple language papers were included, also state how many non-English language publications were included and if authors responded re translation.

Reply 20: Thank you for pointing this out! We have added this information here: “19 publications included in full-text screening were not written in English (7%) of which 12 were written in another language the screeners are fluent in (German or French). The full-texts of the remaining seven publications were translated to English using DeepL®. If they could not be excluded unambiguously based on this translation, the corresponding authors were asked to verify the accuracy of the translation (n = 3 with a 67% response rate) prior to the final decision on in- or exclusion. Ultimately, seven non-English language publications were included (6% of the included publications).» (lines 167-172)

Also, we have added “Strengths of this study are its wide thematic and methodological scope, the systematic literature search including four databases and complementary search strategies, the lack of restrictions regarding language or year of publication, and the in-depth qualitative analysis of included publications.» (lines 520-523)

Comment 21:

P7 L122 consider rephrasing sentence too long.

Reply 21: We have rephrased to “Our aim was to portray the current body of knowledge on EOL care for AN, clarify key concepts, and identify knowledge gaps (rather than provide a definitive, quantitative answer to a narrow question such as the effect of EOL care on standardized measures of quality of life). Therefore, scoping review methodology was most appropriate (23)» (lines 126-129)

Comment 22:

P7 L 128 English expression - do currently not?

Reply 22: We have rephrased to “As standard registries such as PROSPERO currently do not accept Scoping Reviews» (line 130)

Comment 23:

L133 thematic focus? Subject or topic? What does this mean? (could be confused with thematic analysis which the paper did not use).

Reply 23: We wanted to convey that we chose databases that cover the areas of research that were most suitable for our review question (such as clinical medicine, psychiatry, psychology).

Comment 24:

L140? eventual shortcomings? Do you mean you returned few results? Subsequent shortcomings? ”

Reply 24: We developed the search strategy with much care. However, although our sensitivity assessments were positive, we cannot guarantee that our search did not miss relevant publications (we don't know what we don't know). Thus, our database search eventually has shortcomings. To compensate for them, we employed various other, non-database search forms. As far as we know, this is common procedure in systematic literature searches.

TABLE 1

Comment 25:

Wondering how (c) stakeholder attitudes and opinions is different to patients, sig others and HC professionals in (f) are these not stakeholders?

Reply 25: You're right, we have harmonized the language and provided an ostensive definition of stakeholders in the notes (table 1).

Comment 26:

Exclusion 1 b) are you suggesting saturation? This is confusing.

Reply 26: We excluded publications when the only content relevant for our review was cited from other sources (we included those sources then). We give the example of reference 38, Vandereycken W. Whose competence should we question? Eur Eat Disord Rev 1998; 6(1):1–3. Here, only the following passage is relevant for our review question: “The same questions arise with respect to ‘passive euthanasia’ or ‘palliative care’. O'Neill and coworkers from Shef@eld in the United Kingdom (1994) have reported on the case of a 24-year-old women who had had anorexia nervosa since the age of 16.

After several hospital admissions, the multidisciplinary team regarded her as incurable. The patient was then transferred to a hospice and managed symptomatically for pain due to a complication of her osteoporosis. She died within a week of admission. The authors conclude that this is an example of a good standard of palliative care being generalized to patients other than those with cancer. A similar case was reported in Canada (Hebert and Weingarten, 1991). A 22-year-old woman with an 8-year history of anorexia nervosa with numerous hospitalizations and every known form of treatment was admitted in a state of extreme emaciation and cardiovascular collapse. As before she resisted every effort directed at weight gain and pulled out the infusion line as she has done in the past with nasogastric tubes. After a discussion with the ethics committee and the patient's parents, the physicians decided not to start further treatment and the patient died the next day. In their conclusion, the authors state: 'Forced feeding in anorexia nervosa is usually appropriate if patients are in danger of imminent death by inanition, but when a life of suffering is sustained only by more and more aggressive measures it may be appropriate to withdraw life-saving nutritional support'. In the debate on this case the question was raised 'whether the values of nutrition expressed by an anorexic patient can ever be the basis of competent decisions'. Does this imply that compulsory treatment should be continued until she is competent (again)?' However, the author only summarizes two publications and does not add any new content. Therefore, we excluded this publication (and included the two referenced publications).

Comment 27:

Exclusion 2b) involuntary hospitalisation is likely at EOL why exclude?

Reply 27: We excluded publications on involuntary hospitalisations as sole intervention because (only) hospitalizing somebody is not a sufficient response to acute danger to life – the relevant question that needs to be addressed is whether, during an involuntary hospitalisation, life-sustaining measures will be undertaken (or whether EOL is to be offered). We tried to make this clearer by changing the wording to “involuntary hospitalization alone» (table 1). We offer a justification for this in lines 202-208: “To improve readability, concepts and arguments were sorted into the dichotomy of providing either coerced life-sustaining measures or EOL care. Thus, we did not consider the options of providing voluntary life-sustaining measures (as this is outside the scope of our review), forgoing both coerced life-sustaining measures and EOL care (as this does not seem defensible) (59) or providing both at the same time (as they seem mutually exclusive). Neither of these options was discussed in the publications included in the review.”

Comment 28:

Exclusion 2e – the decision to exclude articles with foci of MAiD can this occur at EOL? Is this a pragmatic decision?

Reply 28: We excluded MAiD for conceptual reasons. First, in many countries, MAiD is seen as incompatible with palliative care such as EOL care (see Radbruch L, Lima L de, Knäul F, Wenk R, Ali Z, Bhatnagar S et al. Redefining Palliative Care-A New Consensus-Based Definition. J Pain Symptom Manage 2020; 60 (4): P754-764.:

“palliative care (...) neither intends to hasten nor postpone death”. Second, MAiD necessitates, at least in part, a different ethical justification than EOL care (act of commission rather than act of omission). Because of those differences, we believe that the issue of MAiD for AN necessitates a separate review.

Comment 29:

Exclusion 4b – is there an example for this? How was it decided that the co-morbidity is unrelated?

Reply 29: When designing the study, we had included this reason as much of the literature on Palliative/EOL care for persons with other mental disorders such as schizophrenia is focussed on persons with a life-limiting somatic condition AND the mental disorder. However, in our review, no publication was excluded for this reason which is why there is no example.

Comment 30:

Exclusion 4c) BN excluded yet there is high overlap with AN and BN included in SEED

Reply 30: Correct, we only included publications on anorexia nervosa. While we agree that there is considerable overlap on the symptom level, we feel that the diagnostic criteria are sufficiently clear to justify reviewing literature the disorders separately. Also, we feel it is relevant that danger to life in AN typically stems from severe underweight, whereas in BN, it typically stems from purging. While both can result in acutely life-threatening situations, the medically indicated treatment is different, as is patients’ reaction to it (persons with BN typically do not oppose having their electrolytes corrected – neither do persons with bingeing-purging type AN). This results in differences in ethical reasoning and legal challenges, which in our view further justifies only reviewing literature on AN.

Comment 31:

Inclusion 7B) books by scientific publisher – interesting that My Life as a Male Anorexic was not picked up (Routledge) and also Touyz et al book – Management of SE-AN and Robinson 2009 SEED – management of complex presentations.

Reply 31: Regarding “My Life as a Male Anorexic”: Correct, this was not picked up by our search. We have now looked into the table of contents and the abstract and did not find anything on EOL care (or palliation, futility, terminality or end-stage), so it seems to us that this book does not meet our inclusion criteria. Was there a specific reason for which you felt the book should be included?

Regarding Touyz – Management of SEAN: The following chapters are included in our review:

Woodside, D. Blake; Twose, Richelle M.; Olteanu, Alexandra (2016): Hospital admissions in severe and enduring anorexia nervosa: When to admit, when not to admit, and when to stop admitting. In: Stephen W. Touyz, Daniel Le Grange, J. Hubert Lacey und Phillipa Hay: Managing severe and enduring anorexia nervosa: A clinician's guide. Hg. v. Stephen W.

Touyz, Daniel Le Grange, J. Hubert Lacey und Phillipa Hay. New York, NY: Routledge/Taylor & Francis Group, S. 191–204.

Yager, Joel; Carney, Terry; Touyz, Stephen W. (2016): Is involuntary (compulsory) treatment ever justified in patients with severe and enduring anorexia nervosa? An international perspective. In: Stephen W. Touyz, Daniel Le Grange, J. Hubert Lacey und Phillipa Hay: Managing severe and enduring anorexia nervosa: A clinician's guide. Hg. v. Stephen W. Touyz, Daniel Le Grange, J. Hubert Lacey und Phillipa Hay. New York, NY: Routledge/Taylor & Francis Group, S. 205–221.

Kaplan, Allan S.; Miles, Amy (2016): The role of palliative care in severe and enduring anorexia nervosa. In: Stephen W. Touyz, Daniel Le Grange, J. Hubert Lacey und Phillipa Hay: Managing severe and enduring anorexia nervosa: A clinician's guide. Hg. v. Stephen W. Touyz, Daniel Le Grange, J. Hubert Lacey und Phillipa Hay. New York, NY: Routledge/Taylor & Francis Group, S. 223–230.

Regarding Robinson – Management of complex presentations: Correct, this was not picked up by our search. We have now looked into the table of contents and the abstract and did not find anything on EOL care (or the related concepts we searched for), so it seems to us that this book does not meet our inclusion criteria. Was there a specific reason for which you felt the book should be included?

Comment 32:

Asaria 2023 JoED also not picked up but Elwyn was?

Reply 32: The Elwyn article was published on January 5th, 2023, the Asaria article on July 3rd. Our search closed on April 15th, which is why the former is included but the latter is not.

Comment 33:

Exclusion table: exclusion criterion 1: only mentioning EOL care for AN (n = 28) – are you saying you would exclude if it didn't discuss other EDS? This is not consistent with table 1?

Reply 33: Thank you for pointing this out, this was indeed poorly phrased. We have changed the phrasing in supplementary table 2, row 2, to match table 1 (“exclusion criterion 1: mentioning, but not discussing EOL care for AN (n = 28)”). Publications that were excluded for this reason typically simply stated something like “EOL care is discussed in this context” without giving any further information/analysis, so they would not have contributed anything to the review.

Comment 34:

L185 remove brackets – that is –

Reply 34: We have exchanged brackets for M dashes as requested (line 184-187).

Comment 35:

L204 some typographical issues make difficult to read

Reply 35: Are you referring to the interpunctation around the reference? We have changed this to “forgoing both coerced life-sustaining measures and EOL care (as this does not seem defensible) (52)» (lines 204-205) and hope this increases readability.

Comment 36:

L207 define ‘principlism’ as it relates to the paper (other terminology such a normative question also should be defined as they are used)

Reply 36: We have added a footnote to line 209 (“Principlism is a normative framework developed by Beauchamp and Childress (53) that is based on the ethical principles of respect for autonomy, beneficence, non-maleficence, and justice. Normative means relating to value judgements (rather than facts alone).» In addition, we have added a footnote to line 289 explaining hard paternalism: “Applying the definition of Dworkin (114), hard paternalism refers to coercing patients that have DMC, whereas soft paternalism refers to coercing patients that lack DMC»

Comment 37:

225 – terminality reference 57 (Gaudiani et al) is this in response to Gaudiani et al 2022...

Reply 37: Unfortunately, we’re not quite sure what you are saying. Reference 57 is Draper 1998 and line 225 does not have a reference. If you’re referring to reference 75 (Riddle 2022), yes, this was a response to Gaudiani 2022.

RESULTS

Comment 38:

May assist reader if include a brief description of the included material from supplementary table – for example the results encompassed perspectives from XX peer reviewed sources (legal journals, ED journal), XX books by a scientific publisher etc etc. This provides helpful context to orientate the reader. Also consistent with Munn et al 2018

Reply 38: Thank you for this suggestion, we have added the following: “Through two-step screening, we identified 117 publications eligible for inclusion (Figure 1), of which 104 were articles from scientific journals and 13 chapters in books from scientific publishers.” (lines 213-215)

Comment 39:

It would also be helpful to introduce whose voices and how many were represented in the dichotomies e.g. families, LE, MHN, psychiatry, medicine, ethicists. This could even have a uniform format e.g. 26 accounts X LE, X carers, X public opinion, X ethicists, legal etc. useful contextual reference for the reader and affords interpretation and synthesis of tabulated text. Some quantifying may be necessary if a notable difference is observed e.g if there were fifteen accounts in support and three opposing. Or equal opposition to support.

Reply 39: We agree that it would be helpful to include such information, and have done so in the section on attitudes (lines 372 and following). For the review as a whole, however, this unfortunately seems unfeasible, as the included literature is too diverse. Some papers report on the voices of study participants, others detail the authors' opinions/viewpoints. Many authors do not comment on how they identify, whereas others have various identities (f.ex. McKinney as person with lived experience and researcher). Most publications include several types of account (f.e.x, case report with quotes from significant others and legal reasoning). Also, with articles with several authors, it cannot be traced back whether a given passage reflects the opinion of every author or just some of them. In addition, some papers are co-authored by persons with different identities (such as Down 2023), and some authors seem to have shifted their position over the course of several publications (such as Geppert and Giordano). Thus, it unfortunately seems impossible to extract whose voices are represented in the literature reviewed in a coherent and reproducible way.

Comment 40:

Conceptual questions. It would be helpful to introduce all of the key ideas that will follow as the subsequent sections are not introduced at all? For example, ethical reasoning are these also open questions? Legal aspects in the results sections? Is this background? If so, it belongs in the introduction/ background before results?

Reply 40: That's a good point, we added an introductory sentence as proposed: "The main categories were conceptual questions, ethical reasoning, legal aspects, stakeholder attitudes, practical aspects, outcome, and stakeholder needs. We synthesize the literature on them in what follows.» (lines 221-223)

Comment 41:

L310 contest (oppose) may be clearer than contend.

Reply 41: "They" in what is now line 293 refers to "proponents of EOL care" (line 290). So with the sentence you're referring to, we wanted to say that proponents of EOL care contend (as in argue) that EOL care improves patients QOL.

Comment 42:

L312 non-maleficence could the authors provide examples of 'burden'.

Reply 42: We give some examples in table 5, row 3, column 3 ("Coerced LSM are invasive and burdensome and violate patients' dignity»). We agree that there are many burdens associated with coercive measures and that these are very important. Here, we review literature on the ethical debate about EOL care, so we summarize only what has been written on the burdens of coercion in terms of arguments in favor of EOL care (which is far less than has been written in terms of arguments against coercion outside of the question of whether EOL care can be appropriate).

Comment 43:

L360 "once the ward is no longer medically unstable"? assuming typo here?

Reply 43: “Ward” is supposed to mean “patient that has been placed under guardianship” here (not “unit in a hospital”). Does that answer your question?

Comment 44:

L377 “whose deficits are more likely global” – need to define / be specific. This may not be so in the context of Kiely, Conti and Hay’s “global impoverishment” as theoretical criteria of SE-AN for testing.

Reply 44: We were referring to symptoms such as desorganized thinking or flight of ideas. These are likely to impair decision-making regardless of which decision has to be made, whereas AN symptoms such as fear of gaining weight impair only decisions in the context of nutrition, exercise, etc.

Comment 45:

L398 & 404 – interesting that adolescents (13-25years) are included as there are likely unique ethico-legal considerations for this group where WHO considers adolescent developing brain to age 25 and also possibility of developmental ‘stunting’ to the AN if illness traversed (unremitting) across developmental stages.

Reply 45: We included these studies because our search did not have restrictions regarding patient age (but explicitly stated the age(s) so that the reader is made aware; the same goes for suppl table 5: cases of EOL care for AN). We agree with your assessment that adolescents constitute a special case and believe this is reflected, f.ex., in the support for “higher age” and “long duration of AN” as eligibility criteria for EOL care (line 416). We decided not to discuss this point further as the included literature discussed EOL care for AN nearly exclusively with regard to adult patients.

Comment 46:

If you are to include reference 151 post-searches then other post-search papers should be included as this is otherwise a source of bias

Reply 46: We agree and have deleted footnote 3.

Comment 47:

L406 – Suggest an overarching statement it is otherwise very confusing - three Swiss studies, sharing the same fictional vignette surveyed MH nurses (2022; 153) and psychiatrists views (2021; 131 and 2019; 154) over three years.

Reply 47: We have added an overarching statement as suggested and rephrased the passage in an effort to make it more concise: “Four studies surveyed mental healthcare professionals. In a survey among senior psychiatrists in the United Kingdom (38), O’Neill et al.’s case report on hospice care for a 24-year old AN patient (63) received little support (median score of 23 on a visual analogue scale from 0 to 100; n = 43). Three studies (138, 157, 158) of mental healthcare professionals in Switzerland used the fictional case vignette of a 37-year old patient with a 26-year history of AN, multiple failed high-quality treatment attempts, and a current BMI of 9.5 kg/m², who was deemed to have DMC for her refusal of further treatment. Most respondents believed further curative treatment to most likely be futile (73% of n = 453 psychiatrists) and would not be surprised if the patient

died within six months (87% of n = 454 psychiatrists) (158). Consequently, the majority would prioritize quality of life over life expectancy (82% of n = 452 psychiatrists and 91% of n = 30 mental health nurses) (157, 158) and agreed that palliative sedation could be appropriate (73% of n = 24 mental health nurses) (157). While the majority would forego coerced treatment in such a case (62% of n = 454 psychiatrists and 73% of n = 24 mental health nurses), a substantial minority reported they would coerce treatment (21% of n = 454 psychiatrists) (138, 157), indicating either disbelief in the stated DMC of the patient or hard paternalism (discussed above under Ethical Reasoning). " (lines 379-394).

Comment 48:

L422 consider re-wording

Reply 48: We have rephrased to “Practical aspects pertain to deliberating about EOL care including eligibility criteria and to providing EOL care. The overarching recommendation is to make voluntary treatment aiming at sustaining life and (at least partial) clinical remission available at all times (20, 28, 55, 63, 72, 86, 106, 119, 136). Procedural recommendations for deliberating about and recommendations for providing EOL care were highly consistent and are depicted in Table 6.”(lines 396-401)

Comment 49:

L432 which weight – could be confused with body weight change word - maybe credence?

Reply 49: We agree that this phrasing might be misunderstood, thank you for pointing this out. “Weighing” (of arguments/principles/values) is a fixed expression in clinical ethics, so we would like to keep this word. We have added “moral” to make the context clearer: “which moral weight should be given to the patient’s preferences, healthcare professionals’ assessment, and societal values?» (lines 405-407).

Comment 50:

L448 unacceptable quality of life was there discussion on what this meant and how this was measured? Could be a research implication in future directions heading.

Reply 50: That’s a good point, we have added it to the discussion of open research questions (line 516).

Comment 51:

L451 this is deemed necessary to treat the patient to competence for an advance directive – consider re-phrasing. Consider including (a) (b) (c) to separate the points.

Reply 51: Thank you for this suggestion, we have changed the phrasing as suggested (lines 423-426).

Comment 52:

L460 need a definition of stakeholder

Reply 52: We have now provided an ostensive definition in the notes to table 1.

Comment 53:

L468 und =and

Reply 53: Thanks for spotting this, we have corrected the typo.

Comment 54:

It is interesting that (to my reading) faulty conceptualisations of AN, lack of funding and access to care has not arisen in the introduction, discussion nor in the concept tables of dichotomies. These are very clearly articulated in articles included such as Elwyn and Sharpe et al. Could the authors comment?

Reply 54: We agree that access to affordable care is a highly relevant issue in AN. In our manuscript, you may find it

- In table 3 (concept of futility), column 1, row 3: “(Coerced life-sustaining measures cannot be futile in AN…)because patients have not had access to high-quality treatment (93)»
- In the section on ethical reasoning: “**Justice.** Opponents of EOL care argue that it endangers patients’ access to care aiming at clinical remission (133, 86) and violates their right to be treated regardless of compliance and costs (133, 100) which is already infringed on by lack of affordable high-quality care (35, 139–142).» lines 330-333).
- In table 5 (ethical reasoning) column 2, row 5: “As treatment failures stem from lack of resources and/or expertise, society has an obligation to provide those instead of EOL care (35, 139–142). Patients have a right to be treated regardless of compliance and costs (133, 100). EOL care is an excuse for professionals to get rid of cumbersome patients (133, 67, 88). EOL care suggests that AN treatment is futile in general, endangering access to care (133, 86).”

We agree that the issue of access has not taken a prominent spot in the introduction/discussion. As the debate we’re reviewing here is very complex, we had to focus on some issues. When deciding what to prioritize, we feel its important that affordability has not been discussing with regard to EOL care in the literature included in our review (only with regard to treatment aiming at clinical remission). This makes sense to us – as the general justifiability of EOL care is controversial, access and affordability are not priorities. Only when the justifiability of EOL care is settled will these issues become important. As EOL care is the focus of our review (not problems with care for persons with AN in general, however important), we decided to not make access/affordability a major issue in the introduction or discussion.

Comment 55:

Table 5

For ease of reading consider formatting - dotted line or a line / alternating grey /white to show connection between columns for to the opposing reasonings

Also include number of accounts in table e.g AN is never terminal n=12

Reply 55: Thank you for this suggestion, we added dotted lines in tables 3-5 as proposed.

Regarding quantifying the accounts, we see your point. However, due to reasons similar to those in reply 39, this is unfortunately not feasible. Would we count accounts of individual persons? This is not feasible in multi-author papers, and some authors have expressed views consistent with different positions at different points in time (such as Geppert and Giordano). Would we count publications? This is not feasible as most publications contribute passage to different positions, and also because many publications repeat arguments in order to critique them – would the repeated argument be counted? – we coded only the content of passages, regardless of whether the author(s) opposed or endorsed it (see methods, lines 201-202). Would we count coded text passages? This would inflate the contribution of long papers that repeat their arguments over concise papers such as commentaries without necessarily reflecting differences in the validity/relevance of an account/argument. Thus, we believe that trying to quantify the number of accounts would yield a very unreliable result, that may nonetheless look reliable to the reader. To avoid this confusion, we would like to not quantify the number of accounts.

Comment 56:

Table 6 is not connected with the text? Is in relation to which section?

Note – All included tables need in text explanation

Reply 56: Thank you for spotting this – the reference to table 6 had unfortunately not been up to date. It's updated now and in line 401.

Discussion

Comment 57:

P 31 L493 regarding 'open' conceptual questions . State concretely

Reply 57: We have repeated “open” here so that the passage now reads “several conceptual questions remain open and that it touches on fundamental normative questions. Regarding open conceptual questions, key terms such as terminality, futility, and decision-making capacity (DMC) in AN are used by different authors in very different ways, often without making this explicit.» (lines 460-463)

Comment 58:

L537 language – consider changing ‘weigh’ to prioritise, like wise - ‘weight should be given to the patient’s preferences - credence?

Reply 58: We agree that this phrasing might be misunderstood, thank you for pointing this out. “Weighing” (of arguments/principles/values) is a fixed expression in clinical ethics, so we would like to keep this word. We have added “moral” to make the context clearer: “which moral weight should be given to the patient's preferences, healthcare professionals' assessment, and societal values?» (line 503-504).

Comment 59:

L543 do you mean to cite Elwyn here (i.e. ref 92 compared with 2015 ref 93) ?

Reply 59: Both references have been (co-)authored by persons with lived experience (Elwyn and McKinney) – we have added the Elwyn reference now (line 507).

Comment 60:

P 32 a summary of recommendations i.e. future research would be useful

Reply 60: We have provided a discussion of open research questions in lines 505-518).

Other thoughts to Consider

Comment 61:

- Recent injections of research dollars are predominantly allocated to primary prevention. The enduring group are again underserved and overlooked – stigma. This warrants mention in future directions i.e. advocating for the needs to enduring patients. Open questions – hypotheses for testing

Reply 61: While we may personally agree that persons with SEAN are underserved in many countries (how much varies widely between countries, and we do not know to which country you are referring here), we feel that advocating for their needs in the discussion conflicts with our overarching goal for this review. This was to provide a as-neutral-as-possible overview over a controversial debate, namely the one about EOL care for AN. We feel that the debate really needs a foundation that as many people as possible can agree on, and we hope that our review may contribute to this. To do this, it needs to be as neutral as possible to be acceptable to as many people as possible.

Comment 62:

- Did the search adequately capture the impact of qualitative accounts of coercive treatment / treatment trauma as a barrier to engagement?

Reply 62: While we agree that trauma from treatment as barrier to engagement is a very important issue, it was not the focus of our review which was EOL care. So we did not search for/include any accounts/arguments against coercion in AN, but only those in the context of life-sustaining measures/EOL care. Inside the scope of our review would have been, f.ex., qualitative studies on whether patients would prefer potential traumatization by treatment over probable death in EOL care (or not) or studies on traumatization as barrier to engagement with EOL care, but we did not identify such studies. We have stressed this lack of research in the discussion (lines 505-518). In addition, potential traumatization came up in the ethical reasoning, more specifically in non-maleficence based arguments for EOL care (lines 313-315 and table 5, row 3 column 3).