

Checklist for submitting comments

- Use this comments form and submit it as a **Word document (not a PDF)**.
- Complete the disclosure about links with, or funding from, the tobacco industry.
- Include document name, page number and line number of the text each comment is about.
- Combine all comments from your organisation into 1 response form. We cannot accept more than 1 response from each organisation.
- **Do not** paste other tables into this table type directly into the table.
- Ensure each comment stands alone; **do not** cross-refer within one comment to another comment.
- Clearly mark any confidential information or other material that you do not wish to be made public. Also, ensure you state in your email to NICE that your submission includes confidential comments.
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Note: We reserve the right to summarise and edit comments received during consultations, or not to publish them at all, if we consider the comments are too long, or publication would be unlawful or otherwise inappropriate.

Comments received during our consultations are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the comments we received, and are not endorsed by NICE, its officers or advisory Committees.

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	Please read the checklist above before submitting comments. We cannot accept forms that are not filled in correctly.
	We would like to hear your views on the draft recommendations presented in the guideline, and any comments you may have on the rationale and impact sections in the guideline and the evidence presented in the evidence reviews documents. We would also welcome views on the Equality Impact Assessment.
	In addition to your comments below on our guideline documents, we would like to hear your views on these questions. Please include your answers to these questions with your comments in the table below. 1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. 2. Would implementation of any of the draft recommendations have significant cost implications? 3. What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.) 4. Please tell us if there are any particular issues relating to COVID-19 that we should take into account when finalising the guideline for publication. See Developing NICE guidance: how to get involved for suggestions of general points to think about when commenting.
Organisation name (if you are responding as an individual rather than a registered stakeholder please specify).	British Association for Counselling and Psychotherapy (BACP)
Disclosure (please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry).	n/a
Name of person completing form	Dr Hadyn Williams, CEO.



Comment number	Document [e.g. guideline, evidence review A, B, C etc., methods, EIA]	Page number 'General' for comments on whole document	Line number 'General' for comments on whole document	Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table. Include section or recommendation number in this column.
1	Guideline	General	General	Context and preparation of response: BACP has prepared this response to the exceptional 2021 third consultation on the revised <i>Guideline for Depression in Adults: Treatment and Management</i> in our role as a professional body for UK counsellors, psychotherapists and coaches. As the largest British professional body for those providing psychological therapies and as laid out in our mission statement (British Association for Counselling and Psychotherapy, 2022), we aim to campaign for the highest standards of care for those experiencing any form of psychological distress, including depression. Moreover, our responsibility to both the British public and our members means that we campaign for a range of treatments to be available through the NHS for those with depression. This commitment reflects the considerable range of evidence of broad equivalence between therapies for depression from trials (for example, Barkham et al., 2021; Richards et al., 2017), meta-analyses (Cuijpers et al., 2020; Cuijpers et al., 2020; Cuijpers et al., 2021; Wakefield et al., 2021), as well as from observational data taken from standardised routine datasets (Gyani et al., 2013; Leonidaki & Constantinou, 2021; Pybis et al., 2017). However, the evidence also shows that it is important to give clients choice about treatment options because doing so improves outcomes, the quality of the therapeutic alliance, engagement in treatment and also reduces drop-out from treatment (Lindhiem et al., 2014; Swift et al., 2018; Williams et al., 2016; Windle et al., 2020). This response has been prepared by members of the BACP Research and Policy Departments and draws on feedback from senior counselling and psychotherapy academic researchers in the UK. Our comments are also informed by reviews specifically commissioned by BACP to assess the revised network meta-analysis (NMA) and economic analysis used in the development of the revised draft guideline. Broadly, we welcome and support the focus on 'client choice' throughout the guideline, as well as the



2	Guideline	General	General	Length of consultation period: We welcome the provision of an exceptional third consultation period and the extension to the consultation of four days in acknowledgement of the festive period public holidays. However, we once again wish to state our view that the time provided for making a response is insufficient to allow proper scrutiny of the documents given their length (over 2500 pages in total) and the great complexity of the analyses conducted.
				While we acknowledge that the duration of the consultation is, as you have highlighted in your response to our comments to the previous consultation, set out in <i>Developing NICE guidelines: the manual</i> , we wish to reiterate that the limited time for document review undercuts the very purpose of the consultation, which is to allow NICE to benefit from robust stakeholder feedback. As before, we strongly recommend that the length of a consultation period should not be standardised but flexible to accommodate for documents of great length/analytic complexity as well as in contexts where the outcomes have huge importance for the population, as in the case of this guideline on depression. We will continue to push for this whenever <i>Developing NICE guidelines: the manual</i> is next updated and consulted upon.
3	Guideline	General	General	Use of the term 'counselling': As with previous versions of the guideline, the use of the term 'counselling' in the guidelines is inconsistent and unclear which is highly problematic.
				Within the profession itself the term counselling refers to a bona fide evidence based activity which requires professional training in a model-based approach from a range of traditions (e.g. person-centred, CBT, psychodynamic and pluralistic). However, within the draft guideline counselling is used to refer variously to the empirically validated protocol developed specifically for depression (PCET or PCE-CfD - Person-Centred Experiential Counselling for Depression); sometimes to any non-directive but bona fide counselling approach; and sometimes to non-directive generic counselling skills used by non-counselling professionals categorised as a non-active treatment - often as a control for another intervention. This confusion and lack of clarity around the use of the term 'counselling' has profound implications for how decisions about recommendations have been made within these guidelines. For example, the committee's comments in Evidence review B in relation to the PRaCTICED trial (Barkham et al, 2021) state that "The committee discussed that the PCET used in this study was not the same as non-directive counselling and therefore this study does not



				provide evidence for the effectiveness of non-directive counselling" (Evidence review B, p146, lines 39-42). As argued in Barkham et al. (2017), it is our view that the committee should include clear and specific definitions of counselling that recognise that counselling includes a wide range of bona fide active and effective counselling treatments covering a range of theoretical modalities - including but not restricted to those such as CBT, STPP and others recommended within the guideline - which are distinct from both a specific counselling protocol (e.g. PCET, CfD) or from a generic intervention seen as a non-active treatment.
4	Guideline	General	General	Failure to include large standardised routine datasets: As we previously commented, the analysis within this revised draft guideline once again privileges RCT evidence and fails to consider evidence arising from the IAPT dataset, a routine outcomes dataset which shows how those with depression fare in response to NHS primary care treatment. The response to our previous comments (p.418 of consultation comments and responses document) states that the committee has not relied solely on RCT evidence but has taken into account "a range of different information, including health economic evidence and contextual information". It also states that RCT evidence supporting the use of a range of psychological therapies and different pharmacological treatments have been included and that the guideline has therefore made recommendations for a range of treatments. The response to our previous comments (same document, p.418) also states that the committee has not included the IAPT data as "they did not consider routine datasets to be better or equivalent to RCT data as one cannot be sure that the populations treated with the different interventions are the same [] For example, examination of IAPT data sets shows that those who received CBT were more likely to have received a previous intervention (typically guided self-help) than those who received other psychological interventions." Discarding data for this reason and considering only data that rigidly meet conditions that fit the committee's methodological design rather than seeking to respond to real world and naturally occurring phenomena by generating designs that fit the real-world data is a strategic failure to grasp the potential provided by the range of research paradigms and by considering both trials methodology and large-scale observational and standardised datasets. The IAPT database, comprising over half a million patients per year, provides substantial and key evidence of how NICE recommendations relating to psychological therapies work in clinical reality.



	Existing evidence from IAPT annual reports (NHS Digital, 2014, 2015, 2016, 2017, 2018)
	demonstrates that patient recovery rates have been virtually equivalent between CBT and
	counselling. Research on different portions of the IAPT dataset in relation to the treatment of
	depression have also reported comparable outcomes between CBT and counselling (Gyani et al.,
	2013; Pybis et al., 2017). In addition, evidence from the PRaCTICED trial (Barkham et al., 2021)
	shows virtually equivalent outcomes. The PRaCTICED trial randomised IAPT patients to PCET or CBT,
	removing the confounding factors that usually make IAPT data inadmissible for inclusion in the development of NICE guidelines, which counters the committee's objections to using the routinely
	collected IAPT dataset.
	collected IAF1 dataset.
	While we recognise that the inclusion of observational evidence in network meta-analysis (NMA) and
	combining randomised and non-randomised evidence can be challenging due to high levels of
	heterogeneity (potentially violating the assumption of transitivity), it is our understanding that in
	the current analysis the selection of studies has not included careful consideration of the risk of
	increased heterogeneity and intransitivity. It is therefore possible that including observational evidence would not be more problematic in terms of heterogeneity than data already included for
	consideration. When including observational data, a sensitivity analysis can be undertaken and more
	details can (and should) be given about any specific characteristics that raise concerns, allowing for
	transparency and greater scrutiny of the analyses. This would allow for a systematic and rigorous
	inclusion of real-world, practice-based data.
	Given all these points, it is our view that IAPT data should be considered alongside RCT data,
	particularly in order to ensure that sufficient consideration is given to high-quality real-world
	evidence that reflects the variety and complexity of patients seeking help for depression and to
	form a more complete, inclusive, and accurate assessment of the comparative effectiveness and
	cost-effectiveness of psychological therapies. As in our previous response, this is not an argument to
	abandon RCT/NMA analyses, but rather to examine the 'weight of evidence' as a whole (Barkham et
	al., 2017) and to consider their results <u>alongside</u> those from relevant routine outcome datasets. In our view, inclusion of IAPT data is crucial when the aim of the NICE guideline is to improve
	treatment of depression in NHS primary care.
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5	Guideline	General	General	Supporting patient choice of treatment: We welcome the new recommendations in this draft of the guideline that patients' ideas and preferences about treatments should be explored (1.3.1). We also welcome the recommendation for clinicians to make a shared decision with the person about their treatment (1.3.5), taking into account that all treatments in Table 1 (1.5.2) or Table 2 (1.6.1) can be used as first line treatments for the relevant severity of depression, and the recommendation that antidepressant medication should not routinely be offered as a first-line treatment for less severe depression unless that is the person's preference (1.5.3). Similarly, we are supportive of the recommendations that commissioners and services should ensure that treatments are made available and that patients can express a preference (1.3.6), as well as the comment on p.67 that "Commissioners and services will need to ensure that a meaningful choice of all NHS-recommended therapies is available". Overall, we are encouraged that these additions to the guideline are broadly supportive of patient choice and we welcome this shift in emphasis.
				Additionally, we welcome the presentation of information regarding delivery, key information and other aspects of treatments for consideration as presented in Table 1 (pp23-30) for less severe depression and Table 2 (pp31-37) for more severe depression as ways of seeking to ensure that relevant information can be discussed between patients and clinicians when considering possible treatments. Similarly, we welcome the attempt at simplification of presentation of treatment options within the visual summaries for less severe depression and more severe depression.
				However, it is our view that listing the contents of the tables in order of recommended use, based on the committee's interpretations of their clinical and cost-effectiveness, undermines the guideline's recommendation to support the collaborative process of shared decision-making which seeks to empower people "to make decisions about the care that is right for them" (NICE guideline on shared decision making), and that offering visual summaries which present treatment options in the same order as the tables also undermines this process.
				First, while there is some evidence that effectiveness of proposed treatments is a consideration for patients, there is limited evidence that patients' preferences for treatment within primary care NHS services are influenced by cost-effectiveness (Churchill et al., 2000; Dorow et al., 2018; Houle et al., 2013; Winter & Barber, 2013). Indeed, research suggests that a number of other potentially contributing factors, including demographic variables such as age, race and sex, as well as aetiological beliefs about depression and previous experiences with depression treatment, either



personally or through friends and family members, may influence patients' treatment preferences for depression (Churchill et al. 2000; Houle et al., 2013; Waitzfelder et al., 2018; Winter & Barber, 2013).

While recommendations relating to cost-effectiveness are of most relevance to commissioners and providers of services, since the guideline's recommendation is that "commissioners and services should ensure that people can express a preference for NICE-recommended treatments, that those treatments are available in a timely manner, particularly in severe depression, and that access to them is monitored" (1.3.6), it is our view that the tables' ranking of treatments also undermines this recommendation since ranking and choice are incompatible. We are concerned that commissioners will be more likely to offer services that match the ranking rather than considering the specific needs within their CCG and that this will undermine patient choice.

Secondly, the committee's interpretation of the findings that has led to this ranking of these treatments is based on flawed analyses which, in our view, render the ranking unreliable and unsupported by the evidence and we therefore challenge this as a method of presenting treatment options to patients (see also specific comments and feedback later in this document relating to the network meta-analysis (NMA) and economic analysis). In addition, while the results of the NMA include comparisons of all active treatments against placebo or TAU, the relative effects between the different active treatments are not presented, thus it remains unclear whether these were directly tested against each other and if any statistically significant differences between them were observed.

We also wish to highlight that despite the emphasis on greater choice of treatment, the current draft recommendations, including the decision to present available treatments in rank-order, have not considered the multiplicity of existing qualitative evidence capturing patients' views and experiences of the different pharmacological and psychological treatments included in the draft guideline. We believe that the inclusion of qualitative evidence on patients' experiences of depression treatment would meaningfully inform the treatment guideline by increasing and prioritising service user voices to further support clinicians and patients engage in shared decisions about treatment.

Finally, the recommendation to present available treatments to patients within a ranking is unacceptable within a guideline where the committee also agreed that "choice of therapy should



				be a personalised decision", noting that "some people may prefer to use a treatment further down the table and that this is a valid choice" (p.67, lines 4-6 & p.68, line 30 - p69, line 2). In our view, the use of ranked tables of treatments is incompatible with supporting patient choice since rankings easily overpower choice and in doing so completely undermine attempts at patient empowerment through shared decision making. It is our view that the valid treatment choices of patients would be better served by the presentation of treatment options listed neutrally, for example in alphabetical order of treatment name. If this were to be adopted, we would also recommend that it be clearly stated in the guidelines that treatments are presented in alphabetical order (for example) and the neutrality of the ordering is highlighted to ensure that ranking or hierarchy is not implied.
6	Guideline	General	General	Failure to include longer-term psychological therapies as a treatment option: All psychological treatments recommended in the guideline are brief/short-term, with recommended duration ranging between 6 and 20 sessions. We notice that the recommendation for those classified as treatment-resistant depression, chronic depression, and depression with personality disorder default back to first or further-line treatment recommendation (i.e. once a again a short-term treatment) instead of recommending a longer-term treatment. Whilst we acknowledge that there is a robust body of research which suggests that the majority of change occurs during the initial phase of treatment, and often within 24 sessions (Robinson et al., 2020), recent research (Nordmo et al., 2021) has demonstrated that this is not true for all patients. Indeed, those experiencing more severe/complex symptoms at intake, who had access to openended psychological therapies, demonstrated slower rates of change, but greater overall benefits when they received longer treatments (an average of 52 sessions). There is also research evidence which supports the use of longer-term psychological therapies (specifically long-term CBT and long-term psychodynamic psychotherapy) for patients diagnosed with treatment-resistant/chronic depression (Fonagy et al., 2015; Leuzinger-Bohleber et al., 2019). Moreover, there are numerous qualitative studies and reviews on patient experience that highlight that GPs, service providers and service-users may perceive short-term treatments as inadequate, including two studies which have been cited in Evidence Review I (Johnston et al., 2007; Mercier et al., 2011, p52). Whilst we welcome the increased focus on patient choice in the guideline, patients' experiences should also be considered in the recommendations, including those patients who want - and need - longer-term treatments, which we feel is not adequately considered and discussed.



7	Guideline	General	General	Impact on generalizability of exclusion of studies not meeting first line treatment or non-chronic depression criteria: It is our understanding that studies with >20% of the sample receiving additional treatment (e.g., antidepressants or psychiatric care), with >20% of patients with chronic depression or with >20% of patients with a personality disorder were excluded from the network meta-analysis (NMA) and therefore excluded from systematic consideration by the guideline committee. The rationale for excluding studies with more than 20% use of antidepressants remains unclear as this is uncommon for meta-analyses of psychotherapy trials for depression (e.g. Cuijpers et al.,
				2020, Cuijpers et al., 2021). Indeed, antidepressant use is highly prevalent with 17% of the UK adult population receiving antidepressants between 2017-2018 (Public Health England, 2020). Furthermore, data suggest that around 80% of people presenting to UK general practices with depression receive antidepressant medication (Kendrick et al., 2015) and in recent years increases have also been observed in the average duration of treatment with antidepressants (Mars et al., 2017; McCrea et al., 2016). In addition, chronic and persistent forms of depression with a minimum duration of two years constitute a substantial proportion of depressive disorders with lifetime prevalence rates estimated to range from 3% to 6% in the Western world (Machmutow et al., 2019). Finally, meta-analytic evidence suggests that comorbid personality disorders are found in almost 50% of patients suffering with depression and are associated with adverse clinical outcomes, including episode duration and recurrence, symptom severity, and poor psychosocial functioning (Friborg et al., 2014; Van & Kool, 2018).
				We recognise that including these studies within the NMA potentially presents challenges relating to homogeneity that would need to be accounted for or addressed in additional sub-group analyses. However, excluding these studies from consideration altogether is hugely problematic since doing so clearly limits representativeness and generalizability and it undermines the applicability of the guideline when recommendations are based on an over-reliance on an NMA that excludes a high proportion of people with depression. The guideline itself is not explicit that it focuses only on evidence relating to first episodes of depression in which there is no adjunctive medication, which is misleading. Given the restrictive evidence base upon which this guideline is based, it is our view that it can only apply to the small percentage of people presenting with a first episode of depression and who are not taking psychotropic medication.



				It is our view that if such studies cannot be incorporated reliably and with confidence into the NMA, that the committee should recognise that this is a shortcoming of the NMA methodology and therefore should find another way of using the high-quality evidence that has been excluded. We note that the committee acknowledges the importance of not excluding such evidence in Evidence review B where it is stated that "the committee were aware that a number of important and well-known, often pragmatic trials, were excluded from the NMA typically because the samples in the trials were <80% first-line treatment or <80% non-chronic depression. The committee used their knowledge of these trials in the round when interpreting the evidence from the systematic review and making recommendations" (p147). However, it is not clear what is meant by "in the round", a term which does not inspire confidence or convey any sense of rigorous scientific endeavour. There are no details about which studies were considered in this way and no information about how such consideration might have been undertaken systematically. The lack of transparency undermines legitimate scrutiny of <i>all</i> the evidence that the committee has considered when arriving at decisions and recommendations. In our view it is essential that provision is made for the inclusion of such high-quality evidence that is more representative of the wider population of people suffering from depression, but that it is done so in a manner than supports transparency and rigour. Furthermore, excluding well-designed pragmatic studies and restricting inclusion criteria so strictly is another example of the committee holding rigidly to a methodological design that we must challenge, rather than seeking to adapt the methodology to real world clinical practice. In our view, the resulting guideline therefore cannot possibly meet the needs of the majority of patients presenting with depression.
8	Guideline	General	General	Consideration of Network Meta-Analysis (NMA): It is our understanding that from a technical point of view the analysis is robust; appropriate statistical models have been used and all software codes are provided in the supplementary material. However, we have also identified several limitations in other parts of the NMA procedure, particularly in the evaluation of the required assumptions and the selection of the interventions (we detail specific comments relating to these below). It is our view that these limitations, as well as the overall uncertainty of the results, have been overlooked to some degree and the findings have been over-interpreted. Therefore, it is our opinion that the recommendations within the guideline based on these findings are unreliable.



Inclusion criteria for populations and interventions: The NMA has very broad inclusion criteria for the population under investigation with the only restriction being treatment for adults, and the only differentiating characteristic being the severity of depression. At the same time the review considers any possible type of intervention as equally applicable for all patients within these populations. Specifically, it is reported in the protocol that "for interventions in the NMA it is assumed that any patient that meets all inclusion criteria is, in principle, equally likely to be randomised to any of the interventions in the synthesis comparator set" (review protocols document, p.18), which we understand to be an expression of the fundamental assumption of transitivity in NMA, meaning that all included interventions could, in theory, be included in the randomisation. In our view this is an unsupported assumption in relation to the treatment of depression, suggesting that age and severity of depression are the only characteristics that are considered when deciding whether an intervention is appropriate for an individual. Research evidence suggests that decisions about appropriateness for treatment depend on several factors, including: avoidance of specific side effects, clinicians' experiences of treating similar patients, clinicians' training and supervisory experiences, empirical evidence of the effectiveness of treatments, client preferences, and clients' experiences with previous treatments for depression (Amsterdam et al., 2016; Cohen & DeRubeis, 2018; Raza & Holohan, 2015; Zimmerman et al., 2004).

Some interventions have been excluded without any reasonable justification. Specifically, the protocol reports that "to be included, pharmacological interventions needed to be licensed in the UK and in routine clinical use for the first-line treatment of depression" (Review protocols document, p12), but later on it states "Note that if necessary for connectivity in the network specific drugs that are excluded and 'any antidepressant' or 'any SSRI' or 'any TCA' nodes will be added where they have been compared against a psychological or physical intervention and/or combined with a psychological or physical intervention but they will not be considered as part of the decision problem" (Review protocols document, p.12). This suggests that some interventions have been included based on data-driven criteria relating to comparators, contravening best practice recommendations and guidance for conducting NMA that clearly state that the choice of interventions should be based on clinical criteria and on the plausibility of 'joint randomisability' (Caldwell et al., 2005; Chaimani et al., 2021; Salanti, 2014;). Selection should be based on clinical criteria set out in the protocol, including all studies meeting the pre-defined criteria, rather than a data-driven approach which can lead to bias and render the findings unreliable.



Evaluation of transitivity: A sensitivity analysis excluding the pharmacological interventions was performed as an evaluation of transitivity. The transitivity assumption, however, should be evaluated prior to performing the NMA by examining the similarity of the network nodes when included in studies making different comparisons and by comparing the distribution of the potential effect modifiers. If conducted, these evaluations have not been reported. It appears that transitivity has not been formally evaluated or, if evaluated, has not been reported, making it impossible to assess whether a key assumption for conducting NMA has been met. If the evaluation has not been conducted, this calls the results of the analysis into question (Salanti et al., 2014). If conducted but not reported, this undermines transparency and does not allow for proper scrutiny of the analyses undertaken, weakening confidence in the reliability of the findings.

Heterogeneity: The decision to perform separate analyses for participants with less severe depression and more severe depression seems reasonable given the expectation of differences between the two populations and we acknowledge that broad inclusion criteria potentially make findings more applicable to the wider population. However, in our view there remains considerable heterogeneity across the two groups which necessitates stricter inclusion criteria. It is our understanding that separate sub-group analyses can be conducted in cases where data has greater heterogeneity but that this involves considerable additional complexity, however we consider this to be an important issue that the committee should resolve.

In addition, the selection of studies for analysis has ignored the fact that non-pharmacological interventions might also be very heterogeneous because their efficacy depends on several unmeasured characteristics, such as the experience of the clinicians, previous medications, and so on. Whilst it is difficult to include data and take such characteristics into account in the analysis, these should be considered and acknowledged when drawing conclusions (Cipriani et al., 2013; Kriston, 2013).

In our view, the robustness of the findings that inform the guideline recommendations would be strengthened had stricter inclusion criteria for studies been applied to the NMA and had the committee also then systematically considered excluded studies separately from the NMA which also contribute high quality evidence in order to inform recommendations (see also our earlier point in this feedback relating to excluded studies). As we have previously stated, the committee's over-reliance on NMA to assess and consider trials evidence has considerable limitations which could be mitigated by the inclusion of data from routine datasets as well as ensuring the systematic

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consideration of trials data that does not meet the NMA inclusion criteria, but which still meets quality standards. We therefore repeat our call for the committee to consider the weight of evidence from a wider and more inclusive view of available high-quality data.

Evaluation of inconsistency: Evaluation of inconsistency in NMA is required in order to avoid inaccurate or invalid conclusions (Chaimani et al., 2021; Cipriani et al., 2013,). In this guideline, consistency was evaluated only globally comparing the model fit of the consistency model with the unrelated mean effects model. Since there is very little direct evidence in the analyses, such a method would not show any inconsistency even where this is present, meaning that this evaluation is unreliable.

For instance, for less severe patients, 34 classes were available for the primary outcome (depression symptomatology) which form 561 possible comparisons. Although it is not reported in the text how many of these comparisons have available data, it seems from Figure 1 (Evidence Review B, p.17) that, roughly, there should be around 50 and most of them should only have 1 study. Consequently, with so limited direct evidence, a global evaluation for inconsistency would not provide anything useful. It is unclear why the node-splitting approach that compares direct and indirect estimates has not be conducted and we are unsure why there are tables comparing direct evidence with NMA results (which is not an appropriate way to evaluate inconsistency) but not tables comparing direct with indirect results. The committee states that, "It is important to note that these comparisons have been performed in addition to the NMA inconsistency checks (where direct and indirect evidence is compared)" (Evidence Review B p.39). It is unclear if this refers to the model fit approach or to some comparisons not reported in the manuscript. In terms of comparing direct and indirect evidence, it would be much more informative to present them together in a forest plot to give insight on how much precision is gained with the NMA as reported in "strength could be borrowed across interventions in the same class, therefore improving precision of effects" (Review Evidence B document, p.11). For instance, Tables 14 and 15 show that for some comparisons, precision was lost and this is probably due to the increased heterogeneity and the lack of sufficient direct evidence.

This issue of the lack of local consistency was raised by us in our previous consultation feedback to which the response was "It is not true that assessing for global inconsistency means that we cannot draw conclusions on local inconsistency. The terms "local" and "global" inconsistency refer simply to the methods for testing inconsistency. Both methods rely on relaxing the consistency assumption



for one or all loops in the network, so both methods aim to assess the same thing (i.e. the failure of the consistency assumption in a statistical sense)" (consultation comments and responses document, p32). However, it is our understanding that this is incorrect. In the current analysis, it was assessed whether the consistency model fits the data better than a model that relaxes the consistency assumption. This is an implicit way to evaluate the plausibility of consistency and it cannot show whether there are specific comparisons for which direct and indirect evidence disagree.

The previous response from NICE relating to our concerns also stated that "finding no evidence of global inconsistency is reassuring as it means there is no evidence that the consistency assumption fails to hold across all loops" (consultation comments and responses document, p.32). This statement ignores completely the limited direct evidence available and the presence of uncertainty in the results that both reduce substantially the ability of all approaches to detect statistically important inconsistency.

Finally, the previous response to our concerns acknowledged that "local tests could be run in addition, although in networks of this size it is highly likely that spurious results would be found, due to multiple testing which would then be over-interpreted and unhelpful" (Consultation comments and responses document, pp. 32-33). Instead of performing "unhelpful" comparisons between direct and indirect evidence, comparisons between direct evidence and NMA results were performed – a wrong way to evaluate inconsistency because direct evidence and NMA evidence are not independent – with implicit statements that these comparisons also give insight about inconsistency. The number of local inconsistency tests would be equal to the number of direct comparisons, so we question why multiple testing would be a problem in that case, while at the same time it is deemed acceptable to compare direct evidence with NMA.

Overall quality/confidence of the evidence and GRADE: Formal evaluation of the confidence in the evidence using one of the two available approaches, the GRADE-NMA (Puhan et al., 2014; Salanti et al., 2014;) or the CINeMA framework (Nikolakopoulou et al., 2020) has not been performed. This was a methodological concern that we raised in our previous consultation response that has not been adequately addressed and is a serious omission that undermines credibility and confidence regarding the possible risk of bias. Results on the different GRADE domains are reported but it is unclear how these assessments have been integrated with the numerical results to draw conclusions. For example, no additional analysis has been conducted to assess the impact of study



				risk of bias. This could be done either by excluding risk of bias studies or by using the risk of bias as covariate in a meta-regression model. In terms of indirectness, only general conclusions are reported and no study-level evaluation seems to have been performed. We are not satisfied that the limitations of the analyses as set out above have been sufficiently accounted for by the committee in drawing up their recommendations and, in our view, the findings from the NMA have been relied upon too heavily, particularly those findings upon which conclusions have been drawn about the relative effectiveness of one intervention against another. Such ranking is not sufficiently or robustly supported in these findings given the limitations and overall uncertainty of the results and is unhelpful in terms of the contextual reality.
9	Guideline	General	General	Economic analysis: Having carefully assessed the economic analysis, we welcome the transparency of the methodology used for both the economic literature review and the economic modelling, including the exclusion and inclusion criteria for the analyses. We also welcome the finding from the modelling that counselling is recognised as a cost-effective option for the treatment of both less severe and more severe depression, and that the modelling demonstrates that potentially there is a case for a wide range of interventions given that expected net monetary benefits for most of them are very similar. However, we note that the models also show high levels of uncertainty around all interventions, and relatively modest differences in overall quality of life gains, cost per QALY gains and net monetary benefits between most interventions. We recognise that this uncertainty is not a limitation of the economic modelling, but rather a limitation of the available evidence, reflecting that virtually all counselling/psychotherapy trials studies are underpowered for cost-effectiveness analysis (Cuijpers et al., 2016). This again supports our call for more methodological diversity in the types of evidence used - including the IAPT dataset - to inform and contribute to the development of NICE guidelines. Nonetheless, it is clear from the analyses undertaken by NICE that there is considerable uncertainty around differences in effectiveness and cost effectiveness between different treatment options. In this context, we support the committee's recommendation for - and emphasis on - individual patient treatment preference from a range of treatments. However, it is our view that offering choice of treatment from a menu of options offered in a questionable ranking based on uncertain and severely limited findings from economic analyses and network meta-analysis (NMA), undermines



the committee's recommendation to support patient choice. It is our view that genuine patient choice and shared-decision making with clinicians would be better supported by treatment options that have been shown to be effective being offered in a more neutral format, such as an alphabetical list.
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