



## Stakeholder position statement on the NICE guideline for depression in adults

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## Background

According to the Mental Health Foundation, four in ten adults report experiencing depression at some time in their life. Moreover, we have seen a stark rise in depression since the Covid-19 pandemic began. The Centre for Mental Health [1] has predicted that almost 20% of the population in England will need either new or additional mental health support as a direct consequence of the crisis – more than 10 million people. The sheer scale of depression and the increasing need for effective interventions should dictate that those charged with developing treatment guidelines follow the most robust methodology in the most transparent way.

The signatories of this position statement bring together major mental health bodies in the UK representing professionals from psychiatry, psychology, social work, counselling and psychotherapy, GPs, pharmacy, nurses and mental health charities and survivor-led organisations. Jointly, we have been raising our serious concerns with the revised version of the 2009 guideline on the Recognition and Management of Depression in Adults that the National Institute for Health and Care Excellence (NICE) first made available to Stakeholders in July 2017[2].

However, consulting the first draft of the revised NICE depression guideline we identified several serious flaws in the methodology underpinning the treatment recommendations. We outlined these in our initial position statement (insert link) and stressed that if these were not addressed in a full and proper revision, the guideline will not be fit for purpose. Moreover, we were concerned that the resulting treatment recommendations would actually impede the care of millions of people in the UK suffering from depression, potentially causing clinical harm.

We briefed a number of Peers and MPs and urged NICE to address these issues in a fully revised version in September 2017. Although successful in getting a second consultation period, to our disappointment, we found that the second iteration produced by NICE in April 2018 addressed none of our key concerns. Thus, we continued to campaign for yet another revision of the draft guideline. In May 2018, a meeting took place between the members of this stakeholder coalition and NICE chaired by an independent methodologist. The meeting was constructive, and NICE committed to revise the guideline for an unprecedented third time. To date over 100 MPs and Peers have supported our campaign by sending three cross-party letters to NICE to urge them to “meaningfully respond to the repeatedly raised concerns and to address all of these adequately”.

The third draft guideline was released for consultation in December 2021 and Stakeholders were invited to submit their comments by the 12<sup>th</sup> January 2022. **The proposed date of its publication is the 29<sup>th</sup> of June 2022.**

Whilst we acknowledge the significant improvement of the draft, we notice, to our renewed disappointment, that the majority of our key methodological issues have not been adequately addressed once again. We thus **remain concerned about the trustworthiness of the guideline if published in its current form.**

This document outlines our revised position statement following the third revision of the draft guideline and our substantial communication with NICE about our continuous concerns with it. It

first provides a summary of our remaining concerns and required amendments. It then outlines the basis for each of these in more detail.

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### **Summary of Serious Concerns & Required Amendment before the Guideline is Published**

We acknowledge the efforts made by the Guideline Committee and welcome the substantial additional work that has been carried out in this third revision. We are particularly pleased about the stronger focus on individualised care and the significant emphasis on the importance of service user choice and shared decision-making throughout the draft guideline.

However, the majority of our key concerns were not addressed adequately. We have stressed repeatedly that all of the key methodological flaws need to be addressed without exception. We therefore maintain that this draft version, although much improved, continues to be of great concern. Whilst this version offers a wider selection of evidence-based treatments for individuals presenting with milder forms of depression for the first time, we fear that a significant proportion of individuals suffering from depression could still be impeded from accessing the right treatment. We are particularly concerned about the care of those who experience more complex and persistent forms of depression. Already disadvantaged in many respects, this group is not likely to receive the most appropriate treatment following the treatment recommendation in this draft.

#### **Therefore, the following amendments must be made before the guideline is published:**

1. The guideline must enable NHS services to deliver 'parity of esteem'. As for physical conditions, it is imperative to demonstrate that treatment effects are long-lasting. Therefore, NICE should include all long-term follow-up data from trials where it is available and always prioritise treatment recommendations made on the basis of these data. In this draft, selective choices were made about which long-term follow-up data was included to inform treatment recommendations. This is an unacceptable scientific stance and NICE must include and prioritise *all* available long-term follow-up data.
2. Treatment recommendations continue to be solely based on the evidence derived from RCT studies. Creating sound policy requires that we draw on a diverse range of evidence. In response to our critique, NICE conducted a systematic review of qualitative studies on treatment choice. Although important in its own right, it does not address the importance of including service user experience and feedback of the treatments reviewed in this guideline. NICE must review the large amount of existing evidence on service user experience of treatments, and findings must be incorporated into the outcome review to inform treatment recommendations.
3. The draft guideline continues to utilise non-validated categorisations of depression. It is out of step with existing US and European guideline methodologies, leading to erroneous and unhelpful classification of research studies that do not match clinical or service user experiences. NICE must amend the following: (a) reintroduce the traditional classifications of mild, moderate and severe for the review of a new episode of depression, rather than use their own non-validated distinction of less-severe and more-severe depression; (b) adjust the exclusion criteria to allow for higher ecological validity; and (c) combine the evidence review for all more complex forms of depression.

4. The draft guideline continues to use inadequate methods for working out whether a trial has found a clinically significant treatment effect. Full remission or recovery from a severe depression baseline might be difficult or impossible to achieve, yet smaller positive changes might still be clinically meaningful. NICE, therefore, must look at the amount of clinical effect (e.g., partial recovery) from a severe baseline point and not ignore treatment effects because individuals do not fully recover by the end of treatment.

5. The review utilises Network Meta-Analysis (NMA), a statistical analysis that is associated with serious and unique risks. It is an experimental technique with no formal expert consensus yet established on its appropriateness for such a complex type of review. Despite having included direct comparisons in the third draft, NMA is still the primary data analysis. Moreover, the economic modelling carried out is heavily influenced by the NMA results. Treatment recommendations based on this technique need to be viewed with caution. NICE, therefore, must re-analyse the data using standard meta-analyses only and should NMA be used to supplement the findings a validated and reliable model for doing so should be employed.

6. We are very pleased that evidence derived from functioning and quality of life measures have been added in this third draft. It responds to what service users have long called for. However, as with the long-term data, not all available data appears to have been used to inform treatment recommendation. Once again, this is an unacceptable scientific stance and NICE must include all available data in order to circumvent biases based on subjective choices.

7. Treatment guidelines that ignore important evidence as they occur in clinical practice are concerning. NICE must include the available UK-based pragmatic trials and real-world data collected from millions of service users treated for depression within NHS to inform treatment recommendations.

8. The hierarchy of recommended treatments must be replaced with a non-ranked menu to accurately reflect the findings that all included interventions were clinically and cost effective for individuals with first episode of depression.

The basis for each of these required amendments are outlined in detail below:

### **Methodological Focus of Concerns**

This coalition of Stakeholders is driven by and comes from a position of psychotherapeutic neutrality and scientific integrity, just as the development of the guideline should be. In other words, whilst some of the organisations involved may have a particular leaning towards one therapeutic approach or another, our concerns are directed towards the methodology adopted by the guideline development group and specifically their (a) selection, (b) grouping, and (c) analysis and interpretation of the supporting evidence.

The evidence-based medicine paradigm has been shaped by medical science. The overall methodological approach in the guideline inherently favours particular treatments over others through its focus on identifying the most effective treatment, thereby establishing a rank order of treatments. This is not an acceptable scientific stance and requires some adjustment when comparing and contrasting a wide range of treatments including pharmacological, psychological and physical treatments.

Moreover, we note that the guideline displays an over-reliance on one type of scientific method and fails to take account of the wide variety of good quality evidence available that uses a variety of

methodologies and designs. Relying entirely on Randomized Controlled Trials (RCTs) represents a seriously restricted model of science. The various limitations of RCTs specifically in the field of mental health have been pointed out repeatedly by experts from many scientific disciplines and positions irrespective of therapeutic modality. Most psychotherapy trials are not sufficiently powered to detect true differences [3], and guidelines that ignore important evidence as they occur in clinical practice are concerning. Thus, there is a need to take account of large standardised routine outcome datasets, such as the Improving Access to Psychological Therapies (IAPT) dataset.

As the Health Foundation and Cochrane Collaboration have stressed, creating sound policy requires that we draw on a diverse range of evidence and that cohort studies as well as qualitative and case study research evidence maximizes the value of reviews to policy and practice decision-making[4, 5]. It also appears to contradict the guidance provided by the NICE manual that stresses the need to include “evidence from multiple sources” (p.67)[6].

Furthermore, by utilising very stringent inclusion criteria, many studies that have been shown to provide an evidence base for many interventions were not considered. Most striking is the omission and therefore non-recommendation of the creative therapies, family therapy and couple therapy for depression, which many service users may benefit from and may want to choose. We also notice the absence of longer-term psychological treatments. All recommended treatment options are brief interventions (with an average of 8 sessions). This is worrying, as research and clinical practice have shown that many individuals with chronic or complex forms of depression have tried short-term treatments without success. There is a danger that the guideline may lead to an exacerbation of the existing revolving-door problem, whilst denying people the choice of longer-term treatments that have been found to be effective.

We recognise that some of these methodological matters should be addressed in the NICE manual which provides guidance and direction to all guideline development committees and technical teams. Sadly, none of our recommendations were considered when it was updated in 2018. As such, the remaining serious methodological flaws in the current draft guideline for depression outlined below relate to the Guideline Committee’s application of methodological practices set out in the current NICE manual.

### **1. The guideline must enable NHS services to deliver ‘parity of esteem’ – long-term follow-up data needs to be included consistently**

‘Parity of esteem’ refers to the legal requirement, set out in the Health and Social Care Act (2012), for NHS bodies to give equal priority to mental and physical health. Depression often manifests as a long-term condition, or becomes a long-term condition if immediate care is inadequate. Depression can also be highly episodic and there is a high relapse rate. For example, 38% of IAPT clients are repeat attenders[7]. It is imperative for research to demonstrate that treatment effects are long-lasting, or indeed to note where effects might appear over the long-term follow-up.

NICE guidelines for long-term physical conditions such as epilepsy and asthma examine treatment outcome data over 1-10 years. We therefore emphasise that the evaluation of treatments for depression must meet the same standards as guidelines for long term physical conditions. This requires the guideline to base recommendations on evidence concerning the long-term effectiveness of treatments over and above recommendations which are made on the basis of short-term outcomes (over 6-12 weeks) and always less than 1 year.

In their communication with us NICE acknowledged the importance of this data and agreed to look for it in all treatment reviews. However, they also stated that the importance attributed to it

remains a judgment by the Committee. This is an unacceptable scientific stance as it creates biases that are based on subjective choices rather than good scientific evidence of treatment effectiveness. We acknowledge, and regret, that very few of the included studies provide long-term follow-up data. However, a proper analysis of long-term follow-up data from *all* trials where it is available should nonetheless always be conducted, and these results should always be *prioritised* when considering treatment recommendations. In this third revision, the Committee appears to have been selective and omitted some important long-term follow-up data without justification.

**We request that all available long-term follow-up data is included and prioritised where available, and that current inconsistencies in this draft version are addressed in order to avoid any subjective bias in favour of a particular treatment approach.**

## **2. The guideline must review evidence on service user experience of treatment**

Ensuring that the views and experiences of those who use the services are properly taken account of, should be the *sine qua non* of a publicly funded body tasked with devising clinical guidelines, particularly as these services are fundamentally shaped by the guidance NICE produces.

In setting out its approach to Patient and Public Involvement (PPI), NICE refers to policy contained in the Health and Social Care Act 2012; the NHS Constitution; Putting People at the Heart of Care 2009; and Essential Standards of Quality and Safety. These policies collectively enshrine the right of service users to be fully involved in decisions affecting their care.

While the Committee has consulted service users as part of the guideline development process, it has ignored the wealth of published evidence providing insights and knowledge of hundreds of service user and carers about their experience of treatments.

Sound policy requires that we draw on a diverse range of evidence, including qualitative research and service-user feedback. A synthesis of the evidence would enhance understanding of service user experiences. This is a position held by several bodies including the American Psychiatric Association, the Cochrane Collaboration and the Health Foundation.

In addressing our critique, NICE decided to carry out a systematic review of qualitative studies on *treatment choice*. Whilst this provides important insight into service users' experience of service user choice or the lack of it, it does not address the pivotal aspect of service user experience of the pharmacological, psychological, psychosocial and physical treatments reviewed in this guideline.

There is an important distinction to be made between making general decisions on which psychotherapeutic interventions are the most effective, and making contextually-sensitive decisions on which interventions will be effective and appropriate for which service users. We do not believe the present focus of the systematic review adequately addresses these latter considerations, and thus will not provide sufficient guidance for clinicians about making contextually sensitive referrals.

As such, we uphold the **need to add a full systematic review of primary studies that focused clearly on service user experiences of treatments**, employing formal methodology for synthesis such as meta-ethnographic synthesis, meta-synthesis or formal grounded theory as recommended in the NICE manual[6]. **Findings from such a review must also be incorporated into the broader approach to quantitative review and treatment recommendations rather than being left as a stand-alone section.** This would strengthen this guideline in terms of a focus on individualised care without discrimination. It would furthermore support an evidence-driven approach to support joint decision-making where individuals have not expressed a preference over a particular one.

### 3. Categorisation of depression must reflect good evidence

The current draft guideline is out of step with US and European guideline methodologies, leading to erroneous and unhelpful classification of research studies which do not match clinical or service user experiences. In particular, we express our concerns with (a) the adopted dichotomisation of depression into 'less severe' and 'more severe' in the evidence review of treatment of a new episode of depression, and with (b) the adopted separation of the more complex forms of depression into distinct groups.

We remain very concerned that these two key methodological issues have not been changed. Given that the treatment recommendations are based on these unvalidated distinctions of depression, their generalisability and applicability to clinical practice is highly questionable.

#### **The distinction between less severe and more severe depression**

The Committee devised a method for dichotomising study populations into 'more severe' or 'less severe'. This approach has no scientific validity and overrides the categorisations of severity used by well-established measures as well as established methods of calculating the clinical significance of treatment effects. This dichotomy is also relied on for the Network Meta Analysis. Indeed, the Guideline Committee admit that this dichotomisation was driven by their wish to conduct a Network Meta Analysis, which is an inappropriate form of reverse engineering, particularly as dichotomization inflates effect sizes.

We further are concerned about the stringent inclusion/exclusion criteria for the two treatment reviews for new depression episodes. Many bona fide RCTs were excluded as their study populations reported > 20% of patients with chronic depression, > 20% of patients with a personality disorder, and > 20% receiving additional treatment. Research has shown that 45% of patients diagnosed with depression are also suffering from a comorbid personality disorder. In addition, usage of antidepressants is highly prevalent, with 17% of the adult population in the UK (7.3 million people) taking antidepressants between 2017-2018. Not only is it rather uncommon for meta-analyses of psychotherapy trials for depression to exclude studies with more than 20% use of antidepressants, exclusion of these and other criteria limits the representativeness and generalisability of the results.

#### **The distinction between complex forms of depression**

There is no evidence that warrants the distinctions between chronic depression, treatment-resistant depression, depression with personality disorder and psychotic depression. By doing so, this guideline provides erroneous and unhelpful classification of research studies with the consequence that treatment recommendations may also be erroneous.

In addition to being out of step with European and US guidelines, we are particularly concerned that it will be out of step with the clinical understanding of the groupings in the UK, especially with respect to chronic depression, and will thus lead to confusion instead of providing helpful guidance.

We therefore **request for NICE to address these concerns by (a) adopting the traditional classifications for the review of a new episode of depression; (b) adjusting the exclusion criteria to allow for higher ecological validity; and (c) combining the evidence review for all more complex forms of depression.**

In the future, NICE also needs to look at whether the overall categorical system of mental disorders really fits with service user experience or whether a more trauma-focused approach would better fit



service user experience. In the meantime, the current guideline must at least be in line with the best clinical and research evidence.

#### **4. The guideline must use appropriate methods for determining treatment effect**

The current draft guideline has used inadequate methods for working out whether a trial has found a clinically significant treatment effect. Having raised this point, we are pleased that the third draft of the guideline includes continuous changes in scores on depression scales in every review question. However, we remain concerned that full recovery is still a critical outcome in this draft and that partial recovery, as we had advised, has not been added. It furthermore appears that the decisions for treatment recommendation have been influenced by these recovery rates. Moreover, the economic analysis focuses primarily on full remission.

Full remission or recovery from a severe depression baseline might be difficult or impossible to achieve, yet smaller positive changes might still be clinically meaningful. Treatment which helps some service users move from severe depression to mild or moderate depression (i.e., 'partial recovery'), for example, would be worth recommending. Failing to do so risks the wellbeing of service users who may otherwise be denied these potentially transformative changes.

This is of critical importance because persistent, severe and complex forms of depression represent a large component of the population of people with depression, yet there are very few treatments which have been found to help. In order to identify clinical practices which can relieve the severe and ongoing suffering within this population, the guideline review must look at the amount of clinical effect from a severe baseline point and not ignore treatment effects simply because clients do not fully recover by the end of treatment.

**The guideline review, therefore, must look at the amount of clinical effect (e.g., partial recovery) from a severe baseline point and not ignore treatment effects because clients do not fully recover by the end of treatment.**

#### **5. The guideline must not base its primary recommendations on results of Network Meta-Analysis**

The current draft guideline uses statistical analyses (i.e., network meta-analysis, NMA) that are associated with serious and unique risks over and above that of standard meta-analyses that need careful addressing when employing it [8-10]. The Guideline Committee disagrees yet offers no scientific basis for their disagreement. NMA is an experimental technique with no formal expert consensus yet established on its appropriateness for this type of review. It relies on particular conditions, which, if not met, render the outcome unreliable. It is not the role of NICE to provide an experimental platform for methodological technicians. This type of methodology must first be subject to critical discussion and consensus forming within the scientific field through peer-reviewed publications and debate.

Use of the methodology in national guidelines should also be subject to formal stakeholder consultation, which has not yet taken place. NICE has over-reached its function in undertaking this experimental technique and making it the basis of a national guideline impacting millions of people experiencing distress. This approach represents a serious deviation from accepted methodologies, is not supported by several experts in the field, has not been subject to a proper stakeholder consultation and should not be used.

The main assumption underpinning the validity of NMA is that the indirect and mixed comparisons are only valid when the studies included in the synthesis are similar in their distribution of effect modifiers[8]. These include not only severity at baseline, number of previous episodes and quality of study, which the draft guideline tried to address, but also sample size, age, sex, socio-economic factors, therapist factors, as well as treatment dose and administration of treatment, which the draft did not address. The NMA analyses carried out include a large amount of studies comparing 81 interventions and combinations of interventions, which differed considerably in all these variables, thus violating the transitivity or consistency assumption[11]. The variable distribution and thus contribution of the different treatments included in the statistical analyses is highly problematic. Thus, findings might not depict a representative range of treatment, thereby biasing an effect estimate compared with those with more studies[10].

It is our position, and in line with Canadian Agency for Drugs and Technologies in Health[12], that findings from indirect or mixed comparisons (NMA) should only be used to supplement evidence derived from direct comparisons. Moreover, given that the economic modelling is heavily influenced by the NMA (and therefore its limitations), we are similarly concerned about the trustworthiness of the outcome of the economic analysis of treatments. We therefore reiterate that until there is consensus and evidence of the validity of such a statistical analysis for this type of complex dataset that combines three different modalities of treatment, the primary method to synthesise the evidence should be through direct comparison (standard meta-analysis).

**NICE must reanalyse the data using standard meta-analyses only and should NMA be used to supplement the findings, a validated and reliable model for doing so should be employed.**

## **6. The guideline must take proper account of non-symptom outcomes**

We are very pleased that the Guideline Committee included functioning and quality of life measures in the current draft guideline as previous iterations had an extremely narrow focus on symptom outcomes and failed to take into account other aspects of service user experience which have long been called for.

We regret to learn that of those studies included in the reviews, only a few had reported on these outcomes. However, we regret even more that the Guideline Committee once again decided to adopt an inconsistent approach whereby some of these findings were taken into consideration when interpreting results and formulating treatment recommendations for some treatment modalities, but not for others. Again, this is not an acceptable scientific approach.

Service users express a preference for improvements in quality of life over symptom change. The principle of patient-centred care, enshrined in the NHS Constitution and other NHS policies, demands that NICE take account of what service users actually want from treatment. As such, we **request that NICE stresses the importance that (a) future studies report on such outcomes, and (b) for existing studies to publish these findings where the data was collected.**

## **7. The evidence from UK pragmatic trials needs to be considered fully, not partially**

Treatment guidelines that ignore important evidence as they occur in clinical practice are concerning. The exclusion of available UK-based pragmatic trials and real-world data collected from millions of service-users treated for depression within the NHS in the very setting where the evidence from the guideline must closely be followed, cannot be justified.

The guideline makes reference to these studies, however, only appears to consider these partially to aid interpretation of clinical and cost effectiveness (and, once again, inconsistently). This is not adequate and **we request the full inclusion of such important and most relevant evidence into the treatment guideline.**

#### **8.The hierarchy of treatment options must be replaced with a menu**

Given a current record-setting demand, and the considerable waiting times for treatment in many parts of the UK, it is crucial to ensure that evidence-based treatment is available to anyone who needs it. This guideline has a direct impact on centralised NHS workforce planning, as well as localised decision making by commissioners. It will have a direct impact on which trainings Health Education England will fund to support increasing capacity in England's IAPT service, where so much of this rising demand is felt.

We are, therefore, pleased about the stronger focus on individualised care and the significant emphasis on the importance of service user choice and shared decision-making throughout this third iteration of the treatment guideline.

Notwithstanding the methodological concerns pertaining to the analyses, the findings of the NMAs and cost analysis for individuals with first episode of depression stress that the treatments included were all found to be clinically and cost effective.

As such, we do not see the necessity for the continuation of a hierarchical order, but the need to offer a menu (non-ranked) of treatment options needs to be made available. Removing the hierarchical ranking of treatments is a simple way to enable capacity-building in the NHS mental health workforce and provision of a range of treatments across services, and we strongly recommend doing so.

#### **Conclusion**

If these remaining serious methodological flaws are not adequately addressed in the guideline, the treatment recommendations cannot be relied on and will impede the care of millions of people in the UK, potentially causing clinical harm to some. During the meeting between this coalition of stakeholders and NICE, NICE representatives suggested that some of these concerns could be addressed in the next revision of the guideline. Whilst we hope that NICE will indeed improve their methodological approach in future guidelines, we maintain that the remaining issues need to be addressed now and not postponed. NICE guidelines have a significant influence on UK policy as well as internationally and therefore, publishing this guideline in its current form would have a very damaging impact on service users, services, the health professional work-force and research practices.

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