

## Development of prescribing safety indicators related to mental health disorders and medications

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**Title:** Development of prescribing safety indicators related to mental health disorders and medications: modified e-Delphi study

**Running Title:** Mental health prescribing safety indicators

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**"In this study no interventions were performed and no substances were administered to human subjects/patients."**

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### ***What is already known about this subject:***

- Prescribing safety indicators can identify patients at risk of medication-related harm.
- There is currently interest in using prescribing safety indicators as a platform for interventions to reduce the burden of adverse events.
- Mental disorders have received little attention in this area, with no single suite of indicators currently available to guide improvement.

### ***What this study adds:***

- The first suite of prescribing safety indicators specifically for mental health disorders and medications has been developed.
- Forty-two prescribing safety indicators with a high potential for causing patient harm have been identified.
- These indicators can be prioritised for development of interventions to improve patient safety.

# ABSTRACT

## Aim

Develop a set of prescribing safety indicators specific for populations with mental disorders and to estimate the risk of harm associated with each indicator.

## Method

A modified two-stage electronic Delphi process was undertaken. The *first stage* consisted of two rounds, where 32 experts from the United Kingdom rated their agreement with a set of 101 potential mental health related potential prescribing safety indicators using a 5-point scale. Indicators that achieved 80% agreement were accepted. The *second stage* comprised a single round, where the panel estimated the risk of harm for each accepted indicator by assessing the occurrence likelihood and outcome severity using two 5-point scales. Indicators were considered high or extreme risk when at least 80% of participants rated each indicator as high or extreme.

## Results

Seventy-five indicators were accepted in the first stage. Following the second stage, 42 (56%) were considered to be high or extreme risk for patient care. The 42 indicators comprised different types of hazardous prescribing, including drug-disease interactions (n=12), drug-drug interactions (n=9), inappropriate duration (n=4), inappropriate dose (n=4), omissions (n=4), potentially inappropriate medications (n=3), polypharmacy (n=1), and inadequate monitoring (n=5). These indicators also covered different mental health related medication classes, including antipsychotics (n=14), antidepressants (n=6), sedative, hypnotics and anxiolytics (n=6), mood stabilisers (n=8), anticholinergic (n=6) and non-specific psychotropics (n=2).

## Conclusion

This study has developed the first suite of prescribing safety indicators specifically for patients with mental disorders, which could inform the development of future safety improvement initiatives and interventional studies.

## INTRODUCTION

Mental disorders are most commonly managed by medications [1] and there has been substantial growth in the proportion of individuals worldwide using medications for mental disorders.[2-5] In view of the considerable impact of mental disorders on the affected individuals, [6] their families, the community and the economy,[7] encouraging rational and safe prescribing of psychotropic medications is of major significance. However, there are various challenges when prescribing for patients with mental disorders,[8] including the risk of adverse reactions associated with psychotropic medications,[9] the high prevalence of psychotropic polypharmacy,[10, 11] unlicensed psychotropic prescribing [12, 13] and the use of high-risk psychotropic medication,[9] coupled with the high prevalence of physical comorbidity and associated polypharmacy in people with mental disorders which increases the risk of drug interactions with non-psychotropic medications.[14] Consequently, research evidence suggests that prescribing errors, inappropriate prescribing and preventable medication-related harm are common in this population.[15-17] This underlines the significance for examining the safety of prescribing in this vulnerable patient group in order to identify areas for improvement.

Prescribing safety indicators are statements describing potentially hazardous prescribing and inadequate medication monitoring practices that place patients at risk of harm.[18] These indicators offer an opportunity to assess and improve prescribing safety by identifying patients at risk of adverse drug reactions and medicines-related harm to prompt further investigations before actual harm occurs.[19] In 2017, the World Health Organisation (WHO) launched their third Global Patient Safety Challenge “*Medication Without Harm*”, which aims to reduce the global burden of severe and avoidable medication-related harm by 50% over five years.[20] The potential for prescribing safety indicators to be used as part of different approaches towards reducing medication related harm has led to growing interest in their use. In England and Wales, sets of prescribing safety indicators are currently being used nationally to inform safer prescribing.[19, 21] In the United States, prescribing safety indicators have been used in a multimethod quality improvement intervention to improve medication safety in primary care.[22] Prescribing safety indicators have also been used for the development of pharmacist-led information technology intervention for medication errors (PINCER) [23] which is currently being rolled out nationally across England to electronically search clinical records to identify patients at risk of hazardous prescribing and to act accordingly. It is projected that this intervention would reduce medication-related harm, hospital admissions and associated costs to the National Health Service (NHS).[24] Accordingly, the United Kingdom (UK) Department of Health and Social Care highlighted the need to develop more prioritised and comprehensive suites of indicators that involve other types of medicines associated with high risk of harm.[25, 26]

Whilst there are a number of prescribing safety indicator sets that have been developed for different populations and settings, such as primary [18, 27-30] and secondary care,[31, 32] a recent systematic

review indicated that a suite specific to psychotropic medications and populations with mental illness has not been developed. This review also reported that existing mental health-related indicators described in the literature do not fully represent all known areas of risk in psychiatry, that many indicators had international origins and were not specifically validated by experts to reflect prescribing within the UK context.[3] [33] Therefore, the aim of this study was to develop a suite of prescribing safety indicators specific for populations with mental disorders and to estimate the risk of harm associated with each indicator.



# METHODS

## Study design

A modified electronic Delphi (e-Delphi) technique was used to develop the prescribing safety indicators. The Delphi technique is a structured consensus method that uses a series of questionnaires or rounds “*to obtain the most reliable consensus of opinion of a group of experts*”.[34]

Ideally, indicators of health care quality need to be based on strong scientific/clinical evidence.[35] However, robust supporting data is often scarce.[35-37] Therefore, combining expert opinion and scientific evidence using consensus methods, such as with the Delphi method, is a common approach to developing prescribing quality and safety indicators.[18, 27, 31, 32, 38]

The e-Delphi process in this study involved two stages adapted from similar work to develop prescribing safety indicators in primary care.[18] The *first stage* consisted of two rounds to develop and agree on a set of prescribing safety indicators related to mental health disorders and medications. The *second stage* included a single round which aimed to identify the most clinically significant indicators based on the severity of harm and likelihood of them occurring in clinical practice. The main modification from the original Delphi approach was not limiting data collection to open questions in the first round as potential indicators were identified from the literature. However, participants were allowed to suggest new indicators in the first round, as well as comment on those presented.

## Identifying potential indicators

A previous comprehensive systematic review which identified 245 potential mental health-related prescribing safety indicators [33] was used as the major source of indicators to propose to participants in this study. Indicators from this review were combined with other new potential prescribing safety indicators identified after reviewing several resources such as the British National Formulary (BNF), Martindale, AHFS Drug Information, Stockley’s Drug Interactions (all accessed via Medicines Complete[39]), relevant NICE guidelines,[40] the Maudsley Prescribing Guidelines in Psychiatry,[9] the Psychotropic Drug Directory [41] and searching safety alerts produced by national agencies such as the Medicines and Healthcare products Regulatory Agency (MHRA)[42] and the US Food and Drug Administration (FDA).[43] Further potential indicators were identified from the clinical experience of two mental health clinical pharmacists within the research team (RNK and JN).

Indicators were defined as mental health-related if they included (a) mental disorders according to the International Classification of Diseases (ICD-10) [44] and the Diagnostic and Statistical Manual of

Mental Disorders (DSM–5);[45] (b) medications that could be used to treat or prevent mental disorder (i.e. psychotropics) ; or (c) medication that can be used to treat or prevent side effects of the psychotropics[33] (e.g. anticholinergic medications for the treatment of sialorrhoea and extrapyramidal symptoms caused by antipsychotics).[46]

A refined list of potential indicators was then constructed using the lists identified from the above sources by applying predefined inclusion and exclusion criteria,[27] (Box 1) to restrict the indicators to UK practice and to select only potentially hazardous prescribing practices that could cause significant risk of harm. Two mental health clinical pharmacists applied the criteria, using existing guidelines/literature and professional opinion. The refined list was then circulated between the research team to recommend any necessary modifications.

The final list of indicators that were included in stage 1, contained 101 potential prescribing safety indicators. The indicators were not specific for a patient age group unless specified within the indicator. Most of these potential indicators (n=61/101, 60.4%) were identified from existing sets of indicators.[33] However, 55.7% (n=34/61) of these indicators identified from existing indicator sets were slightly modified by the research team. Most of these modifications were broadening the age group, changing monitoring frequency according to UK recommendations or restricting the indicator to specific medications within a therapeutic class. The remaining 40/101 (39.6%) indicators were newly identified from the previously stated resources such as the BNF,[39] Maudsley prescribing guidelines [9] and the clinical experience of the research team.

## **Questionnaire design**

Each indicator included in the initial list was presented  in a structured fashion similar to a set of prescribing indicators developed in the UK for hospital settings,[31] as a medication/class, process, and rationale. For example: benzodiazepine [class] prescribed to a patient >65-years-old [process] (risk of fall and fracture [rationale]). The web-based online questionnaire was designed using SelectSurvey.Net (V4.075.003, ClassApps).

The first-round questionnaire of the e-Delphi was piloted with two consultant psychiatrists in order to improve clarity and to identify any ambiguities with the questions and the instructions. Feedback from the pilot was incorporated into the final version of the questionnaire.

## **Expert panel selection and recruitment**

Experts for the e-Delphi were defined as qualified health care professionals with experience and interest in prescribing and/or medicines management and safety for patients with mental disorders, including psychiatrists, mental health pharmacists, mental health nurses and general practitioners (GPs), each

with a minimum of five years post qualification experience. Potential experts were identified through professional and social networks by distributing flyers and introductory emails to gather expressions of interest. Participants were invited via email, and were provided with a participant information leaflet to ensure they were fully informed prior to accepting. A total of 48 experts were invited to participate in the study, of whom 32 agreed. A target of a minimum of 20 experts participating was set prior to the study. Although the optimal size of a Delphi panel is not a subject of consensus in the published literature,[37, 47] previous studies in the UK utilised approximately 20 experts to successfully develop prescribing indicators using the e-Delphi method.[31, 32]

## **Ethics statement**

Consent was obtained by all participants before starting the first survey round. Participants were given four weeks to decide whether or not to take part in the research, and were also informed that they were able to withdraw without giving a reason. The identity of each member was anonymous to other members of the panel, and was known only to the research team. Ethical approval for this study was obtained following proportionate review by the University of Manchester Research Ethics Committee (UREC), Reference 2019-4632-11444.

## **Delphi procedure and analysis**

First stage 

In the first round of stage 1, panellists were asked to rate their level of agreement with the use of each indicator to assess prescribing and drug monitoring safety, using a five-point Likert scale where: 1=strongly disagree; 2=disagree; 3=neutral; 4= agree; 5=strongly agree. Panellists were asked to rate their agreement of including the indicator based on; (a) the indicator described a pattern of prescribing that may put patients at risk of harm; and (b) the indicator described a prescribing practice that was common in the UK. Participants were also given the opportunity to comment on each indicator and to suggest new indicators.

Following completion of the first round of questionnaires, the median agreement value was calculated for each indicator. In addition, the free-text comments provided by the experts were analysed qualitatively in order to modify, remove or introduce new indicators. The results from round 1 were summarised and returned to each expert, with their individual score, the group median agreement rating score and a summary of the free text comments. 

For the second round, the panellists were asked to re-rate their level of agreement for all of the indicators based on the group comments and ratings. The agreement value was recalculated for each statement after this round. The final agreed list of indicators contained indicators that achieved consensus on

acceptance, which was defined as at least 80% of participants rating the indicator as 4= agree or 5=strongly agree.

### Second stage

Panellists were asked to rate the clinical significance of each accepted indicator from stage 1, based on: 1) the severity of the potential harm to patients if the prescribing or monitoring practice occurred and; 2) the likelihood of the prescribing or monitoring practice occurring, based on the UK National Patient Safety Agency Risk Matrix (Table 1).[48] This process is similar to previous publications.[18, 31, 32] The likelihood and severity scores were converted into ‘risk scores’.

The risk score for each indicator was calculated by multiplying the severity and likelihood ratings for each member of the panel, and then by identifying the median risk score between members. Indicators were categorised into four overall risk categories; low, moderate, high or extreme. Consensus was defined as at least 80% of participants rating the indicator in the upper categories (high or extreme), or the lower categories (low and moderate). Therefore, indicators were considered high or extreme risk when the overall median risk category for that item was high or extreme and 80% or more of the panellist rated the indicator as high or extreme risk.

## RESULTS

### First stage

The first stage of the e-Delphi was completed by 31 of the 32 experts who had originally agreed to take part. The expert panel comprised psychiatrists (n=6), mental health pharmacists (n=17), mental health nurses (n=7) and a general practitioner (n=1). Participants were from geographically diverse areas in the UK, with a range of professional grades. Table 2 summarises the characteristics of the expert panel.

A total of 101 potential prescribing safety indicators were included in the first round. After analysing the participants’ free text comments received in this round, 20 indicators were modified and four were merged to form two indicators. In addition, five new indicators were included based on panel members’ suggestions following review by the research team. Thus, the final number of potential indicators that were included in the second round was 104.

After two rounds of scoring, the final number of indicators that achieved consensus on acceptance (rated as ‘agree’ or ‘strongly agree’ by 80% of panellists) was 75 indicators. This list contained prescribing safety indicators from the following drug classes: antipsychotics (n=19), antidepressants (n=14), sedative, hypnotics and anxiolytics (n=8), mood stabilisers (n=22), antidementia (n=4), anticholinergic (n=6) and non-specific psychotropics (n=2). The indicators also covered a wide range of prescribing problems, including drug-disease-interactions (n=19), drug-drug interactions (DDIs) (n=18),

inappropriate dose (n=12), potentially inappropriate medications (PIMs) (n=7), inappropriate duration (n=4), omissions (n=4), polypharmacy (n=1), and inadequate monitoring (n=10). The full list of 75 indicators achieving agreement in stage 1 are provided in Appendix 1, and the 29 indicators that did not achieve consensus are provided in Appendix 2.

## **Second stage**

The second stage of the e-Delphi was completed by 29 of the 31 participants who completed the first stage. Table 2 summarises the characteristics of the panel. From this stage, a total of 42 of the 75 indicators identified in stage 1 were considered high or extreme risk by consensus of the expert panel (39 indicators were considered as high-risk and 3 were extreme risk, with 80% of the panellists rating these indicators as high or extreme). These indicators are listed in Table 3. Figure 1 shows the steps taken in arriving at the final set of indicators.

The list of high and extreme risk prescribing safety indicators included different mental health-related medication classes; antipsychotics (n=14), antidepressants (n=6), sedative, hypnotics and anxiolytics (n=6), mood stabilisers (n=8), anticholinergic (n=6) and non-specific psychotropics (n=2). These indicators also reflected different types of potentially hazardous prescribing; including drug-disease-interactions (n=12), drug-drug interactions (DDIs) (n=9), potentially inappropriate medications (PIMs) (n=3), inappropriate duration (n=4), inappropriate dose (n=4), omissions (n=4), polypharmacy (n=1), and inadequate monitoring (n=5).

## DISCUSSION

To our knowledge, this is the first suite of prescribing safety indicators to be developed specifically for patients with mental disorders. A total of 75 prescribing safety indicators were identified that can be considered suitable to assess the safety of prescribing for this unique population. A subset of 42 prescribing safety indicators were considered a high or extreme risk to patient safety and could therefore be prioritised for development of improvement interventions. These indicators cover a broad range of prescribing and medication monitoring problems as well as different mental health related drug classes.

The topics covered in the developed suite of prescribing safety indicators contextualise contemporary safety concerns affecting the care of those with mental disorders. Examples include the risk of dementia with the use of anticholinergics,[49, 50] the risk of cerebrovascular adverse events and mortality with the use of antipsychotics for behavioural and psychological symptoms of dementia (BPSD),[51] the risk of fetal congenital malformations due to exposing pregnant mothers to valproate,[33, 52] and the risk of fatal intestinal obstruction, faecal impaction, and paralytic ileus with use of clozapine.[53]

The most frequently named therapeutic class in the high/extreme list was antipsychotics followed by mood stabilisers. These findings were foreseeable given the enduring risks posed with medication within these classes, such as the high risk medicines clozapine and lithium.[9] Accordingly, all the chosen inadequate medication monitoring indicators fell within these two classes. The presence and absence of indicators within classes was also affected by the frequency of how common medications were prescribed. For example, none of the indicators specified monoamine oxidase inhibitors (MAOi). When examining data concerning antidepressants dispensed in the UK in 2016, MAOi represented only 0.07% of all antidepressants. In comparison, selective serotonin reuptake inhibitors represented more than 50%, and were named in four out of six of the antidepressant indicators.[5]

When comparing mental health-related indicators in previously published broader suites of prescribing safety indicators in the UK with the indicators in this study, there are noticeable differences.[18, 27, 28, 31] These might be partially explained by involving experts more focused on managing mental disorders in developing the current suite. Furthermore, previous studies concerning the development of prescribing safety indicators in the UK targeted specific settings, such as primary [18, 27] [28, 29] and secondary care.[31, 32] However, this research was not restricted in this way to avoid excluding indicators that would not be applicable to a specific setting such as those related to aspects of prescribing or monitoring of clozapine that may not always be applicable to primary care settings. In addition, the aim of this research was to develop prescribing safety indicators that are relevant to populations with mental disorders across organisations that could provide mental health care, including primary care, hospitals, specialised inpatient and community mental health services, care homes and prisons.

Similarly, an exclusion criterion that was mentioned in some of the previous studies that developed prescribing safety indicators was the feasibility of extracting the required data from the targeted

setting.[18, 27] In this study, the feasibility of data extraction was not taken into consideration as the practicality of measuring each indicator should be reviewed in the context of the setting and the likely data source. For instance, if the developed indicators were planned to be incorporated into the medication safety dashboard developed for use in the NHS, all the indicators that contain information on clinical conditions or medication monitoring would not currently be feasible for implementation as the dashboard is restricted to using prescription processing data.[21] In contrast, diagnostic information would be available from other sources such as the Clinical Practice Research Datalink (CPRD).[54] Another reason for not considering the feasibility of data extraction at this stage is that advances in databases and clinical information systems may create further opportunities for implementation of indicators,[28] such as development of linked electronic medical records between primary, secondary and social care to create a comprehensive record of prescribed medications.[55]

It was recognised in the first stage of the e-Delphi process that attention deficit hyperactivity disorder (ADHD) related indicators as a group did not reach a consensus, due to a large proportion of expert panel ratings falling in the neutral category. When examining first round free-text comments, it was evident that several participants felt that they did not have sufficient experience with this patient and medication group to rate this category. Therefore, to address this issue, future research could attempt to develop mental health related prescribing safety indicators specific for younger populations exclusively with experts specialising in child and adolescent mental health.

While there are some indicators that could be better suited to a particular setting, others could be applicable to multiple settings that provide care to patients with mental disorders. Accordingly, the prescribing safety indicators we present may require further work to be operationalised and validated to specific health contexts and to provide evidence of their reliability and validity.[56, 57] Although our suite of prescribing safety indicators has been developed for application in the UK, the clinical scenarios addressed in the suite could be relevant in other countries. However, as we did with published indicators for the Delphi, they might need to be adapted to allow for variations in clinical guidelines, medication availability and prescribing behaviours before testing and validation.[28, 58] Once they are tested and ascertained to be valid and reliable they could be used to monitor the overall safety of prescribing on a national, regional and local general practice/hospital level in order to identify areas for improvement. In the future, these indicators could be considered for incorporation into information technology (IT) platform-based interventions to improve medication safety, as observed across primary and secondary care utilising more general suites of prescribing safety indicators. Examples include The Salford Medication Safety (SMASH) dashboard,[59] PINCER tool,[60] the Data-driven Quality Improvement in Primary Care (DQIP) [61] as well as in computerised clinical decision support (CDS) systems.[62] Our indicators could also be considered for implementation in quality improvement reports, such as the reports produced by Royal College of General Practitioners' (RCGP) and CPRD to support general practices to identify patients that require medication review because they triggered

either of two selected prescribing safety indicators.[63] Indicators could also be applied to assess safety and measure improvement after an intervention on a local level in psychiatric units in hospitals, mental health hospitals, care homes, mental health community services and prisons using electronic prescribing systems or following manual search of medical records and medication charts,[64-66] Indicators could also feature as a part of a broader suite of indicators such as The Quality and Outcomes Framework (QOF) to support appraising the overall health care quality.[67]

The strengths of this study include using a robust method, based on information from the existing literature [33] and other professional resources to identify new potential indicators. In addition, this study considered including indicators of all three aspects of prescribing safety, including prescribing safety incidents of commission, omission as well as inadequate medication monitoring. This would allow a more comprehensive evaluation of prescribing safety. Another advantage of this study was that it included broader indicators related to mental health medication and conditions and was not solely limited to psychotropic prescribing. Lastly, the expert panel involved specialised healthcare practitioners with a diversity of professions and of considerable experience, which allowed inputs from different perspectives.

One of the limitations of our approach to indicators selection and refinement is the possibility of not including potentially relevant indicators in the first round of ratings that could have been considered important by the panel. However, members of the expert panel were encouraged to suggest new potential indicators in the first round of the e-Delphi which minimised this risk. In addition, the composition of the expert panel might have had an impact on the findings of this study. There were more mental health pharmacists than any other profession, and primary care was under-represented with only one general practitioner. Therefore, our indicators may not fully reflect specific prescribing challenges in primary care for those with mental illness. We attempted to compile a panel with different stakeholders with the same interest in managing mental health medications. A further limitation is that the number of rounds for each stage were selected before starting the study, and the views of the panel were only sought once in regards to the risk of harm associated with each indicator in phase 2. This was due to the time constraint and the burden on the members of the expert panel to take part. However, this approach had been successfully used previously for the development of prescribing safety indicators for primary care.[18] Another important limitation was that members of the panel were not provided with the evidence base for the indicators and they were asked to rate the potential indicators solely based on their knowledge and experience. Nevertheless, the supporting evidence for each indicator was reviewed by the research team. In addition, as previous research has observed, the evidence base for some of the indicators was weak,[27] and this is principally the reason why consensus approaches are warranted.[68] Although in some areas more robust evidence is emerging, such as recent pharmaco-epidemiological studies which provide a stronger evidence base to support indicators related to the use of anticholinergics and the risk of dementia.[49, 50]

## **CONCLUSION**

This study is the first to present a suite of 75 prescribing safety indicators related to mental health disorders and medications that were agreed among an expert panel using the modified e-Delphi technique. Of these, 42 were identified as having high or extreme risk of patient harm and could therefore be prioritised for development of improvement interventions. These indicators incorporate different types of potentially hazardous prescribing and inadequate medication monitoring, and reflect current challenges associated with the pharmacological management of mental health disorders. The indicators have the potential to form the foundation of assessment of prescribing safety for patients with mental disorders in different settings, and be a catalyst for future quality improvement initiatives for this vulnerable population.

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Author contributions: WK, DS, and RNK were involved in planning and preparation of the study. WK, SP, JN, and RNK identified and reviewed the initial list of potential indicators. RNK and JN refined the list of potential indicators. WK, DS, SP, and RNK were involved in statistical design. WK managed and led on data collection and analysis. DS and RNK supervised all research activities. WK drafted the initial version of the manuscript. DS, SP and RNK critically revised the manuscript. All authors approved the final version of the paper.

## **Conflict of interest statement**

WK, DS, SP and JN have nothing to disclose. RNK reports personal fees from MORPh Consultancy Ltd and from Centre for Pharmacy Postgraduate Education, outside the submitted work.

## **Data availability statement**

Additional data are available by request from the corresponding author.

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## Tables (each table complete with title and footnotes and in an editable format)

### Box 1: Inclusion and exclusion criteria

#### Inclusion criterion:

- The indicator describes a pattern of prescribing that is potentially hazardous and may put patients at risk of harm.

#### Exclusion criterion:

- The indicator describes a pattern of prescribing that is unusual in the UK

**Table 1: Risk scoring = consequence x likelihood [48]**

Consequence	Likelihood				
	1 Rare	2 Unlikely	3 Possible	4 Likely	5 Almost certain
5 Catastrophic	5	10	15	20	25
4 Major	4	8	12	16	20
3 Moderate	3	6	9	12	15
2 Minor	2	4	6	8	10
1 Negligible	1	2	3	4	5

  

Low Risk 1-3	Moderate risk 4-6	High risk 8-12	Extreme risk 15-25
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**Table 2: Characteristics of the expert panel**

Characteristics	First stage	Second stage
Participants: n	31 members	29 members
Years of Experience: Median (IQR)	18 years (10.25-27)	17 years (10-25)
Region of practice: n (%)		
England: North	14 (45.2)	14 (48.3)
England: Midlands and East	10 (32.3)	8 (27.6)
England: South	3 (9.7)	3 (10.3)
England: London	2 (6.5)	2 (6.9)
Wales	1 (3.2)	1 (3.4)
Scotland	1 (3.2)	1 (3.4)
Profession: n (%)		
Psychiatrists	6 (19.4)	6 (20.7)
Mental Health Pharmacists	17 (54.5)	16 (55.2)
Mental Health Nurses	7 (22.6)	6 (20.7)
General Practitioners	1 (3.2)	1 (3.4)

IQR, The interquartile range.

**Table 3: Prescribing safety indicators that were considered high or extreme risk to patient safety by at least 80% of the expert panel.**

Prescribing safety indicator	First stage	Second stage	
	Round 2: Agreement <sup>a</sup>	Risk Category	Agreement <sup>b</sup>
<b>Antipsychotic</b>			
1. Antipsychotic prescribed to a patient with dementia or BPSD but not serious mental illness (increased risk of stroke and mortality)	100%	High	93%
2. Prescribing antipsychotic with a QT-prolonging drug (risk of QT-prolongation that can lead to potentially fatal torsade de pointes arrhythmia)	100%	Extreme	93%
3. Antipsychotic prescribed for at least 12 months without monitoring glucose, weight, or lipid profile within the previous year (risk of metabolic adverse effects)	97%	High	90%
4. Clozapine prescribed to a patient with a history of constipation and without a laxative (risk of worsening constipation and potentially fatal risk of intestinal obstruction, faecal impaction, and paralytic ileus)	94%	Extreme	97%
5. Clozapine dose not adjusted in a patient started/stopped smoking/NRT (starting/stopping smoking can change Clozapine blood level, which can lead to sedation, hypotension and increased risk of neurological adverse effects including seizures)	94%	Extreme	97%
6. Prescribing Haloperidol without monitoring ECG at baseline (risk of QTc prolongation and/or ventricular arrhythmias)	94%	High	100%
7. Risperidone prescribed to a patient with dementia and without psychotic illness for more than 6 weeks (increased risk of stroke and mortality)	87%	High	97%
8. Antipsychotic prescribed to a patient with prolonged QTc interval (risk of potentially fatal torsade de pointes arrhythmia)	87%	High	97%
9. Clozapine, Chlorpromazine, Quetiapine or Risperidone prescribed to a patient with postural hypotension, syncope or history of falls (increased risk of falls and fractures)	87%	High	93%
10. Clozapine prescribed with anticholinergic except for hypersalivation (risk constipation and potentially fatal risk of intestinal obstruction, faecal impaction, and paralytic ileus)	87%	High	83%
11. Prescribing more than one regular antipsychotic for more than 2 months excluding clozapine augmentation (increased risk of adverse effects)	87%	High	83%
12. Single/combination antipsychotic(s) prescribed regularly a dose above 100% BNF maximum (increased risk of adverse effects)	87%	High	86%
13. Antipsychotic other than Quetiapine, Aripiprazole or Clozapine prescribed to a patient with Parkinson's disease or with Lewy Body Disease (risk of severe extrapyramidal symptoms)	81%	High	93%
14. Antipsychotic, other than Asenapine, Aripiprazole, Clozapine, Lurasidone, Olanzapine and Quetiapine, newly prescribed for at least 6 months without monitoring prolactin (risk of hyperprolactinaemia)	81%	High	86%
<b>Antidepressant</b>			
15. SSRI or SNRI prescribed with NSAID or antiplatelet to a patient without gastrointestinal protection (increased risk of gastrointestinal bleeding)	97%	High	97%
16. SSRI or SNRI prescribed with NOAC or warfarin (increased risk of bleeding)	90%	High	93%
17. Prescribing a serotonergic psychotropic medication with another serotonergic drug (increased risk of serotonin syndrome)	90%	High	100%
18. Prescribing Citalopram, Escitalopram, TCA or Trazadone with QT-prolonging drugs (risk of QT-prolongation that can lead to potentially fatal torsade de pointes arrhythmia)	84%	High	90%
19. SNRI prescribed to a patient with uncontrolled hypertension (risk of blood pressure destabilisation)	81%	High	83%
20. SSRI or SNRI prescribed to a patient with a history of peptic ulcer or bleeding disorders without gastroprotection (increased risk of gastrointestinal bleeding)	81%	High	86%
<b>Sedative, hypnotic and anxiolytic Indicators</b>			
21. Any sedative-hypnotic prescribed to a patient with a history of falls (increased risk of falling and fracture)	97%	High	97%
22. Benzodiazepine, Z-drug or sedating antihistamine prescribed to a patient with dementia or cognitive impairment (CNS adverse effects)	94%	High	90%

23. Benzodiazepine, Z-drug or sedating antihistamine for more than 1 month (Risk of prolonged sedation, confusion, impaired balance, falls) (risk of tolerance, and dependence with benzodiazepines and Z-drugs)	94%	High	93%
24. Benzodiazepine or Z-drug prescribed to a patient aged $\geq 65$ years (increased risk of falling and fracture)	87%	High	90%
25. Benzodiazepine or Z-drug prescribed to a patient with hepatic impairment or cirrhosis (risk of accumulation and encephalopathy)	87%	High	90%
26. Benzodiazepine or Z-drug prescribed to a patient with asthma, COPD or sleep apnoea (risk of exacerbation of respiratory failure)	84%	High	86%
<b>Mood stabiliser</b>			
27. Valproic acid prescribed to a woman of childbearing potential (risk of congenital malformations to the exposed foetus)	94%	High	83%
28. Prescribing Lamotrigine with combined oral contraceptive (risk of decrease lamotrigine exposure and efficacy. Possible risk of failure of contraception)	94%	High	83%
29. Lamotrigine dose not re-titrated after a treatment break of more than 5 days (risk of sedation, tremor, ataxia, fatigue and serious skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis)	94%	High	86%
30. Lamotrigine initiated at a dose higher than 12.5mg/day or 25mg on alternate days to a patient already on Valproate (risk of sedation, tremor, ataxia, fatigue and serious skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis)	90%	High	83%
31. Prescribing Lithium with ACEi/ARB, NSAID or a diuretic (risk of lithium toxicity which can cause tremor, dysarthria, ataxia and confusion)	90%	High	90%
32. Prescribing Lithium without monitoring lithium plasma level within the last 6 months or within the last 3 months if the patient is aged $\geq 65$ years or have a renal impairment or during the first year of treatment (risk of lithium toxicity which can lead to blurred vision, muscle weakness, coarse tremor, slurred speech, confusion, seizures and renal damage)	90%	High	83%
33. Lithium prescribed for at least 6 months without monitoring U&E or thyroid function within the last 6 months (U&E: risk of lithium toxicity and renal impairment) (thyroid: risk of thyroid disorder)	90%	High	83%
34. Prescribing Carbamazepine with oral or intravaginal contraceptives, patches or pure progestogen pills (risk of failure of contraception and risk of foetal malformation)	81%	High	86%
<b>Anticholinergic</b>			
35. A medication with medium/high anticholinergic activity prescribed to a patient with dementia or cognitive impairment (risk of exacerbation of cognitive impairment)	100%	High	90%
36. Prescribing two anticholinergics with at least one of them with moderate/high anticholinergic activity (increased risk of adverse effect)	100%	High	90%
37. A medication with medium/high anticholinergic activity prescribed to a patient with a history of urinary retention or benign prostatic hyperplasia (risk of urinary retention)	94%	High	90%
38. A medication with medium/high anticholinergic activity prescribed to a patient aged $\geq 65$ years (risk of falling and fracture, acute confusion and urinary retention)	90%	High	97%
39. A medication with medium/high anticholinergic activity prescribed to a patient with constipation and without a laxative (risk of worsening constipation)	87%	High	90%
40. A medication with medium/high anticholinergic activity prescribed to a patient with angle closure glaucoma (Risk of acute exacerbation of glaucoma and risk or permanent loss of vision)	84%	High	86%
<b>Other</b>			
41. Four or more psychotropics prescribed to a patient for more than 3 months (increased risk of adverse effects)	90%	High	90%
42. Three or more psychotropic drugs prescribed to a patient on an as required (PRN) basis (increased risk of adverse effects)	84%	High	86%

<sup>a</sup> Percentage of members rated the indicator as “agree” or “strongly agree”. <sup>b</sup> Percentage of members rated the indicator as high or extreme.

ACEi, Angiotensin-converting-enzyme inhibitor; ARB, Angiotensin receptor blocker; BNF, British National Formulary; BPSD, Behavioural and psychological symptoms of dementia; CNS, Central nervous system; COPD, Chronic Obstructive Pulmonary Disease; ECG, Electrocardiogram; NOAC, New Oral Anticoagulant; NRT, Nicotine replacement therapy; NSAID,

Nonsteroidal anti-inflammatory drug; SNRI, Serotonin–norepinephrine reuptake inhibitor; SSRI, Selective serotonin reuptake inhibitors; TCA, Tricyclic antidepressant; U&E, urea and electrolytes.

## **Figure legends**

Figure 1: The steps taken in arriving at the final set of prescribing safety indicators

## **Appendices**

Appendix 1: Prescribing safety indicators that achieved consensus on acceptance after first stage (round 2)

Appendix 2: Prescribing safety indicators that did not achieve consensus on acceptance after first stage (round 2)