Protocol for a workshop to elicit and quantify expert opinion for the effectiveness of ePrescribing systems and prototype for other health service interventions

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ABSTRACT

Background

Expert opinion may serve as an input to statistical models where there is a paucity of reliable and high quality data. Bayesian statistical methods incorporate ‘prior’ information into analyses in the form of a prior distribution which represents the current state of knowledge. This prior distribution can reflect the quantified opinions of experts with relevant knowledge. However, there is no standardised format for conducting an expert elicitation that aims to minimise bias. In this protocol we identify the issues that may bias the responses from an expert elicitation and explicate a method for an expert elicitation workshop. The aim of the workshop will be to elicit a subjective prior distribution for the effect of an electronic prescribing system on the rate of medication errors and adverse drug events in an acute care setting in hospitals. This prior density will serve as an input to a cost-effectiveness model.

Methods/Design

The parameters of interest that will be elicited from the experts will be the relative risk of experiencing a medication error and the relative risk of experiencing an adverse drug event for a patient treated in a hospital with an electronic prescribing system compared to a patient treated in a hospital using a paper-based prescribing system. The workshop will consist of seven parts: (i) Presentation of key information; (ii) training exercise; (iii) group discussion and presentation of data; (iv) first round belief elicitation; (v) break; (vi) feedback and group discussion; and, (vii) second round belief elicitation. Each section is designed to minimise the potential biases identified in the scientific literature including anchoring bias and base rate neglect. A 67% confidence interval will be elicited on the log relative risk scale. The elicited opinions will be aggregated by using the group median mean estimate and median standard error.
BACKGROUND

Expert opinion can be used as an input to statistical models where there is a paucity of reliable and high quality data; it can also be used to facilitate decision making.[1–3] There are two steps to this process that are described in this protocol: first, the eliciting of expert opinion in a workshop; and second, the aggregation of the expert beliefs.

The workshop described in this protocol aims to elicit a group subjective prior distribution for the effects of an electronic prescribing (ePrescribing) system on the probability of a patient experiencing an adverse drug event (ADE) resulting from a medication error in a hospital acute care environment. The prior probability densities will be used in a cost-effectiveness model of an ePrescribing system, the full details of which have been published elsewhere.[4] Data from this analysis will be used to ‘update’ this prior. This protocol elaborates on the elicitation process described therein.

Various methods have been proposed in the literature to elicit expert opinions; however, in order to mitigate concerns regarding the validity of these methods it is important to use procedures that have demonstrable methodologic rigour. Johnson et al (2010) conducted a systematic review of methods to elicit beliefs for Bayesian priors and provided a list of biases identified by previous studies.[5] Similarly, O’Hagan (2006) discusses the available evidence regarding best practice in expert elicitation.[3] Where possible, this protocol uses the methods recommended in the literature to eliminate potential biases, which may result from the way in which data are presented or the opinion is elicited. The final method aims to increase the validity of the elicited opinion.
METHODS/DESIGN

Parameters of Interest

The model linking ePrescribing to the relevant downstream health outcomes is conceptually relatively simple and is presented in figure 1. ePrescribing systems are assumed to affect the probability of experiencing a medication error in the hospital, which in turn leads to changes in the probability of experiencing an ADE and therefore affects subsequent individual clinical outcomes. The elicited probability distributions will act as informative prior distribution in this model, which aim to estimate the clinical and cost-effectiveness of ePrescribing systems.[4] The two parameters in the model for which we will elicit prior distributions are: the relative risk of experiencing a medication error with an ePrescribing system compared to a paper-based system and the relative risk of experiencing an ADE with an ePrescribing system compared to a paper-based system.

The effect of the intervention, expressed as a relative risk, may vary depending on the base rates of ADEs and medication errors. As an illustration of this, Nuckols et al (2014), who conducted a systematic review and meta-analysis of studies examining the effectiveness of computerised physician order entry (CPOE) at reducing the ADEs and medication errors. CPOE is a key component of many ePrescribing systems along with clinical decision support. The review authors noted in their discussion that,

As the baseline percentage of hospitalizations associated with medication errors increased from 3.6% to 99.9% (data available from 12 studies), the predicted RR of medication errors with CPOE decreased from 1.90 to 0.08 (p<0.001).[6]

However, it is unclear how this was calculated and we assume that the participants do not possess enough knowledge of a large enough number of hospitals to be able to formulate a belief about treatment effect heterogeneity in terms of a treatment effect as a function of the base rate, or any other variable.
Many decision support systems also include a clinical decision support component, which may further increase the effectiveness of the system. Indeed, there is a lack of reliable evidence regarding the potential factors that may influence the effectiveness of ePrescribing systems; the specific effect in this model is therefore the effectiveness of an ePrescribing system on reducing both medication errors and ADEs averaged over possible conditioning factors.

There exists considerable heterogeneity in the reported rates of medication errors and ADEs which may be due to differences in subjective assessments of an error or an adverse event, or their preventability. Local hospital culture, the presence or absence of mediating factors, and patient case mix are all potential mediating factors that may affect both the data that are observed and the underlying effectiveness of the ePrescribing system.[7] Crucial to error rates, their preventability and the conditional probability of an AE, is the definition of medical error - a point to which we return below. As detailed below, participants will be allotted time to discuss the role these factors may take both on the data and the underlying processes shown in figure 1.

**Preventability**

We distinguish between preventable and non-preventable medication errors and ADEs. The data collected for the project of which this workshop form a part will measure all ADEs and medication errors irrespective of preventability. The relevant parameters in the cost-effectiveness model will therefore be the relative risk reductions in *all* medication errors and *all* ADEs with an ePrescribing system compared to a paper based prescribing system.

As discussed below, participants those medication errors and ADEs that are preventable with ePrescribing and those that are not. Participants should take preventability into account in assessing the potential magnitude of the effect, but provide answers regarding all medication errors and all ADEs. A comprehensive, pre-specified list of medication errors was developed for the project, by means of a Delphi technique, which will be provided to participants.[8] The medication errors are serious errors which portend a real threat to patient health rather than
the myriad small breaches of prescribing rectitude that have no real risk of leading to an adverse event.

**Elicitation Scales**

For each of the sections of the workshop in which participants will have to provide their beliefs, the participant will be given a copy of the elicitation scale (figure 2) and asked to mark a 67% range for the relative risk of experiencing a medication error or adverse drug event such that they feel that the true answer to the question is twice as likely to lie inside the range as outside the range. This method follows that from Turner et al (2009).[9] A 67% interval is used instead of a 95% interval as there is evidence to suggest people tend to be better at assessing intervals at lower levels of uncertainty.[3]

Similarly to Turner et al, we will utilise a log-scale.[9] The upper and lower range limits from expert $i$, $a_i$ and $b_i$ respectively, correspond to range limits $\log(a_i)$ and $\log(b_i)$ on a scale representing the log-relative-risk for ePrescribing versus paper-based prescribing. It is assumed that the 67% range represents approximately $\mu_i \pm \sigma_i$, as it would under normality, so that the elicited values are

$$\mu_i = \frac{\log(a_i) + \log(b_i)}{2}$$

$$\sigma_i = \frac{\log(b_i) - \log(a_i)}{2}$$

**Workshop Protocol**

Here we describe the proposed method for the elicitation of the parameters of interest. The order of the workshop follows that outlined in Lilford et al (2014).[4]
Participants

The elicitation will take place at the level of the individual. A review of previous studies found that the number of participants in belief elicitation workshops was generally small, with a median of 11.[5] However, larger numbers of participants will provide a greater pool of opinion from which to form the group prior. We aim to include 20 participants. The participants in the workshop will be clinical experts with relevant experience in the area of the interventions. The inclusion of clinical experts instead of generalists improves the reliability and validity of elicited priors.[10–13] The workshop will be conducted during a conference on ePrescribing systems in 2016 to maximise the potential number of participants.

The workshop will consist of seven parts as detailed below. The workshop is designed to be as short as possible without sacrificing validity in order to prevent fatigue in the participants. A break is also provided after the first round belief elicitation to prevent fatigue. The form that will be used to elicit beliefs is provided in Appendix A.

(1) Presentation of Key Information

The aim of this section of the workshop is to provide participants with the definitions of the key terms, the base rates as reported in the literature, description of the intervention, and key statistical identities.

Following the US Institute of Medicine’s (now incorporated into the National Academy of Sciences) landmark report, To Err is Human,[14] the following definitions are used and will be provided to participants:

- **Medication Error**: Any error that occurs the medicines management process.[15] An error is defined as the failure of a planned action to be completed as intended (i.e., error of execution), or the use of a wrong plan to achieve an aim (i.e., an error of planning). The specific errors considered here are those identified as potentially serious by the consensus method (see above).
• **Adverse Drug Event**: An adverse event is an injury caused by medical management rather than the underlying condition of the patient. An adverse drug event (ADE) is defined as any injury due to medication. An injury includes physical harm (for example, rash), mental harm (for example, confusion), or loss of function (for example, inability to drive a car).[16]

To clarify the distinction between medication errors and ADEs, and their preventability, figure 3 will be presented. It will be stated that the participants will be asked to provide the beliefs about the reduction in all ADEs and all medication errors, noting that only a proportion are preventable, as stated above.

The base rates for hospitals’ medication errors and ADEs are derived from the literature. These rates will be required by the workshop participants for the belief elicitation process. Table 1 in Nuckols et al (2014)[6] is a summary of studies that were identified that estimated the effects of CPOE, a major component of ePrescribing systems (the other being clinical decision support), on both medication errors and ADEs. Included in this table are the baseline error rates where reported. This table will be updated with the baseline ADE rate from the currently ongoing project and presented to workshop participants. Alongside this table, a weighted median and inter-quartile range of baseline rates will be presented.

The following description of the intervention will be provided to participants:

The hospital prescribing module of Cerner Millennium has different components covering pharmacy, inpatient and outpatient prescribing and medicines administration, and includes advanced computerised provider order entry (CPOS) and computerised decision support (CDS) functionality. This CDS can highlight prescribing of contraindicated medications both on account of the clinical history and/or drug-drug interactions, allow dose checking of medication and for any prescribing of duplicate medications, and support the prescribing of order sets. Furthermore, it can facilitate
ordering of drug from pharmacies and issue reminders to promote the timely administration and recording of treatments.

Finally, certain key statistical identities will be presented to workshop participants. In this workshop participants will be asked to provide their beliefs about the relative risk of the intervention. To avoid base rate neglect bias (i.e. where participants fail to take into account the base rate among untreated patients[5,17]) the base rates from previous studies and those identified from primary data collected in this project are provided. As an additional point, the validity of responses has been shown previously to be threatened by insufficient statistical understanding of the questions presented.[18] This section therefore is intended to improve the participants’ understanding of the statistics involved along with the training exercises in the following section. The following relationship will be presented:

\[
\text{Probability of outcome with intervention} = \text{Relative risk} \times \text{probability of outcome without intervention.}
\]

(2) Training Exercise

The purpose of the training exercises is to both instruct the participants on how to report their beliefs and to provide some examples of how the effects of the intervention may operate in practice. The results from these exercises are not an output of interest and no further information regarding each exercise will be provided beyond that in the text given to each participant.

Each participant will be randomly provided with one of two exercises. Randomly presenting the specific exercises will alleviate the bias caused by anchoring participants to specific examples.[2,17] Drug-drug interaction and dosing will be used as examples, which are detailed below. Beliefs will be elicited as previously described.

The following examples will be used as training exercises:
1. **Drug-drug interactions.** Concomitant prescribing of either non-steroidal anti-inflammatory drugs (NSAIDs) or macrolides (e.g. erythromycin) with warfarin leads to an increased risk of internal bleeding greater than the risks of bleeding with each individual drug alone. The interactions work in different ways; NSAIDs act mainly to increase the risk of gastro-intestinal (GI) bleeds, while macrolides increase the risk of any internal bleeding, including intracerebral bleeds. Participants will be presented with base rates and relative risks and asked to estimate the risk of (i) GI bleed with NSAID in combination with warfarin, and (ii) any bleed in patients prescribed NSAIDs and/or macrolides and warfarin concomitantly.

2. **Dosing.** Low molecular weight heparin (LMWH) is an anti-thrombotic agent and has a narrow therapeutic range which makes dosing an important consideration – the patient’s weight should be taken to calculate the appropriate treatment dose. Some LMWH is prescribed without the patient’s weight being used leading to an increased risk of adverse outcomes such as bleeding or recurrent thrombosis and mortality.

For each exercise, participants will be provided with information regarding the probabilities of certain outcomes and be asked to estimate the other probabilities. Participants will not be asked to estimate the effect of ePrescribing on the specific error in order to avoid anchoring bias in the main elicitation exercise. These exercises are presented with the elicitation form in Appendix A. At the end of this section participants will be provided with the answers from the literature in order to improve comprehension of the task, identify any misunderstandings, and allow participants to calibrate their judgements about their certainty.

(3) Discussion and Data Presentation

Data regarding the outcomes of previous studies examining the effect of ePrescribing on the risk of both medication errors and ADEs will be presented to study participants at this stage. Previous elicitation exercises have presented research data such as this,[13,19] however, in order to avoid anchoring bias (i.e. the cognitive bias of focussing on the first piece of
information provided) the following discussion will be directed to address the heterogeneity of the results, identify possible differences between the participants’ clinical experience and the samples in the included studies, and issues with the observed data in the presented studies that may bias the findings. The data are presented at this stage rather than earlier since, as Johnson et al (2010) identify, while the presentation of baseline data may serve to prevent radical opinion and provide data on the relevant base rates, it may result in anchoring bias where the reported beliefs are influenced by the data.[5,20] Potential remedies are either to avoid presenting the data or to scramble the presentation of the sequence of data between participants. In this case, we will not present any data regarding the effectiveness of the intervention for the first round of belief elicitation; in the second round, participants will be presented with the relative risks and combined relative risk for studies included in Nuckols et al (2014) and be permitted to revise their response. This revision may be conceptualised as allowing the participants to update their priors using new data.

(4) First Round Belief Elicitation

Beliefs will be elicited as previously described. The question that will be posed, for both medication errors and ADEs, is:

Please provide a 67% interval for the relative risk of a medication error with an ePrescribing system compared to a paper based system so that you feel that the true answer to the question is twice as likely to lie inside the range as outside the range. Please consider the data that has thus far been presented along with the group discussion.

(5) Break

Participants will be provided with a ten minute break to prevent fatigue and boredom and to allow for calculation of the feedback.
(6) Feedback and Discussion

Provision of feedback to participants has previously been shown to improve both the probability assessment\cite{21} and reliability of elicited beliefs\cite{22}. This feedback also allows for self-correction\cite{12} and as such is provided before the final round of belief elicitation. In particular, the median and range of elicited relative risks from the group will be provided to participants. The implied distribution of the probability of experiencing both a medication error and ADE after the implementation of an ePrescribing system, calculated by multiplying the base rate distribution observed in English hospitals, collected as part of this project, by each participants' relative risk, will also be presented. The causal model under consideration, as shown in figure 1, implies that the relative risk reduction in medication errors should equal the relative risk reduction in ADEs. The responses will be checked for coherence by examining whether the elicited distributions overlap. In cases where there is no overlap, participants will be asked to discuss this. The discussion will also be directed towards the heterogeneity in elicited relative risks with reference to particular types of medication error.

Figures 2 and 3 from Nuckols et al (2014) will be presented which show the reported results, sample sizes, and combined effect from the studies identified by their systematic review\cite{23}. Participants will then be permitted 10 minutes to discuss these findings; they will be instructed to discuss the sources of potential heterogeneity in the results and compare how these relate to their own clinical experience.

Discussion will take place for 10 minutes to allow the participants to reassess their estimates and update their individual priors.

(7) Second Round Belief Elicitation

The final section will mimic the first round belief elicitation and participants will be allowed to revise their beliefs. The results from this section will be the results utilised from the workshop to be aggregated into a combined prior.
Aggregating Responses

There are a number of methods that are used in practice to aggregate individual beliefs, including Bayesian and opinion pools.[1] The former method treats the opinions as data, then seeks to develop appropriate likelihoods to represent the relative confidences in the experts. However, while this method is conceptually strong, there are concerns about calibration and correlation between expert opinions that have yet to be addressed.[1] The latter method is more pragmatic and simply weights together expert opinions. Various methods exist to do this. Logarithmic opinion pooling is often used to pool probability densities and has a number of desirable properties including being externally Bayesian.[24] Being externally Bayesian means that the result of opinion pooling does not depend on whether the experts are provided data and update their individual priors or whether the combined prior is later updated with the data. However, a logarithmic opinion pool is sensitive to over-confident participants so that any participant providing a particularly certain response can dominate the pooled response.

In this study, we will instead opt for a very simple approach, and take the median responses for the mean and standard deviation of the effect of interest.[9]

Weights may be chosen to reflect the degree of confidence, experience, or ability of each expert. Cooke’s method involves the use of a calibration exercise to determine the ability of the experts to approximate already known probabilities to determine the weights with the best performing experts given the highest weight.[25] However, the aforementioned heterogeneous nature of the intervention suggests that there is no one particular ‘true’ value for the effectiveness of the intervention, rather a distribution of effect, suggesting that each expert’s knowledge of their own environment may be indistinguishable from any other expert’s. We opt therefore for equal weights. Furthermore, there is no strong evidence to suggest Cooke’s method outperforms equal weighting in practice.[26,27]
DISCUSSION

In conclusion, we will carry out an elicitation exercise to elicit the parameter of interest which will serve as the prior distribution for this parameter in an evaluation of ePrescribing in hospitals in England. This prior distribution will be used in a Bayesian model to estimate the costs and benefits of ePrescribing platforms. The prior distribution will be elicited in February. The model will be estimated with the data collected from the project with primary output expected by mid-2016.
COMPETING INTERESTS
None declared.

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AUTHOR CONTRIBUTIONS
SIW and RJL initiated the protocol design. SIW, AJG, AS, and RJL contributed to the development of the method. SIW prepared the first draft. This and all subsequent drafts were reviewed and revised by all authors; all authors approved the final version submitted.

REFERENCES


FIGURES

**Figure 1** Qualitative causal model for the effects of ePrescribing on health and cost outcomes. This model allows for changes in ADEs as a result of medication errors, ADEs may occur for other reasons, which are not included in this model as they are not within the scope of the exercise since they do not lie on the causal pathway between ePrescribing and patient outcomes.

**Figure 2** Example belief elicitation scale.

**Figure 3** Diagram representing the probabilistic relationship between medication errors, adverse drug events, preventability, and the potential effects of an ePrescribing (eP) system.