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*Methodological Article*

# Expert Elicitation of Multinomial Probabilities for Decision-Analytic Modeling: An Application to Rates of Disease Progression in Undiagnosed and Untreated Melanoma

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ABSTRACT

**Background:** Expert elicitation is required to inform decision making when relevant "better quality" data either do not exist or cannot be collected. An example of this is to inform decisions as to whether to screen for melanoma. A key input is the counterfactual, in this case the natural history of melanoma in patients who are undiagnosed and hence untreated. **Objectives:** To elicit expert opinion on the probability of disease progression in patients with melanoma that is undetected and hence untreated. **Methods:** A bespoke webinar-based expert elicitation protocol was administered to 14 participants in the United Kingdom, Australia, and New Zealand, comprising 12 multinomial questions on the probability of progression from one disease stage to another in the absence of treatment. A modified Connor-Mosimann distribution was fitted to individual responses to each question. Individual responses were pooled using a Monte-Carlo simulation approach. Participants were asked to provide feedback on the process. **Results:** A pooled modified Connor-Mosimann distribution was successfully derived from participants' responses. Feedback from participants was generally positive, with 86% willing to take part in such an exercise again. Nevertheless, only 57% of participants felt that this was a valid approach to determine the risk of disease progression. Qualitative feedback reflected some understanding of the need to rely on expert elicitation in the absence of "hard" data. **Conclusions:** We successfully elicited and pooled the beliefs of experts in melanoma regarding the probability of disease progression in a format suitable for inclusion in a decision-analytic model.

*Keywords:* decision modeling, expert elicitation, melanoma.



## Introduction

*Evidence-based medicine* is defined as the "conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients … [which] means integrating individual clinical expertise with the best available external clinical evidence from systematic research" [1]. These principles apply equally to population-level decision making, such as whether a health care payer should provide reimbursement for a new drug, treatment pathway, or screening program.

Decision-analytic models are frequently used by agencies such as the National Institute for Health and Care Excellence in England as a framework to structure all current best (i.e., relevant, quality-assessed) evidence to estimate the overall costs and consequences of alternative treatment strategies over an appropriate time horizon [2,3]. A judgment is then made to decide whether the added benefit of a treatment exceeds its opportunity cost. Evidence to populate a model is ideally obtained exclusively from good-quality systematic reviews and meta-analyses of randomized controlled trials (RCTs) or other relevant study designs as appropriate. Nevertheless, because of data limitations, evidence is typically obtained from various sources including routine databases and observational studies. When no suitable previous data exist, decision makers are required to rely on expert opinion to bridge the evidence gaps.

Such an evidence gap is the natural history of undetected and hence untreated melanoma.

The MelaTools program (www.melatools.org) is a National Institute for Health Research–funded program based in the

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United Kingdom to improve the early diagnosis of melanoma to reduce associated mortality and morbidity. This includes investigation of the feasibility and cost-effectiveness of introducing a risk-based surveillance program using a self-completed assessment tool [4].

To address this, we developed a decision model to estimate the most cost-effective cutoffs for various intervention policies [5]. Nevertheless, a key component of this is the counterfactual, in other words, the natural history of untreated melanoma in the absence of medical intervention. Good-quality data exist on prognosis after diagnosis and subsequent treatment [6], but there are no data on untreated individuals. Obtaining such data from a prospective study by withholding treatment from newly diagnosed patients would clearly be deeply unethical. Therefore, the only way to estimate the probability of an undiagnosed and hence untreated patient progressing from one disease stage to another is to garner expert opinion.

In this article, we apply a method to elicit multinomial probabilities from experts regarding their beliefs about the rate of progression from different melanoma disease stages (in situ disease to stage IV) to any other stage or death. The primary purpose of the analysis was to use the resulting multinomial distributions in our decision model to predict the cost-effectiveness of a self-completed risk assessment tool and subsequent surveillance program. Nevertheless, the distributions themselves are of interest because they represent a summary of expert opinion and belief.

## Methods

### Research Problem

There are four main types of cutaneous melanoma (superficial spreading, lentigo maligna, acral lentiginous, and nodular) [7], which current guidelines categorize into nine stages of invasion [6]. All but one are also described with a pre-invasive (in situ) phase; nodular melanoma is by definition invasive. We wished to elicit expert opinion on the rate of progression from each stage to any other. We simplified a possible set of 39 questions into 12 by assuming that invasive disease would progress at the same rate irrespective of primary melanoma subtype but we allowed the rate of progression from in situ disease to vary by subtype (Table 1). Each question is a multinomial problem: the quantities to be elicited are probabilities, but there are more than two outcomes. For example, after a defined time period, a patient with stage Ia disease may remain in stage Ia or progress to stage Ib, IIa and so forth. The sum of the probabilities must equal to 1.

**Table 1 – Starting stages for elicitation questions.**

| |
|---|
| In situ superficial spreading melanoma |
| In situ lentigo maligna melanoma |
| In situ acral lentiginous melanoma |
| Stage Ia |
| Stage Ib |
| Stage IIa |
| Stage IIb |
| Stage IIc |
| Stage IIIa |
| Stage IIIb |
| Stage IIIc |
| Stage 4 |

*Note*. Participants were asked for their beliefs about the probability of progression from each of the 12 stages stated to any other stage and death.

### Elicitation Protocol

The protocol and associated materials are given in Appendix 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2017.10.009. The protocol was designed with the following constraints in mind:

1. We wished to elicit opinion from experts of more than one country. We chose the United Kingdom as well as Australia and New Zealand (hereafter ANZ) as areas of relatively high melanoma prevalence. Arranging a single workshop event in the same place at the same time would have been prohibitively expensive and extremely difficult to schedule. Therefore, an online webinar approach that could be repeated to suit availability of participants was desired.
2. Because of demands on experts' time, the webinar could not exceed 2 hours in length.

### Ethics

Ethical approval was not required for this study [8]. Invitation letters explained to participants that their responses would be anonymized, with the only details being their broad job title and country (United Kingdom or ANZ).

### Identification and Recruitment of Experts

Inclusion criteria were that participants had to be located in the United Kingdom, Australia, or New Zealand with an academic or clinical background in dermatology, oncology, plastic surgery, or epidemiology, with a particular interest and expertise in melanoma. A list of potential participants was identified by two of the investigators on the basis of known expertise and relevant publications in the field. Participants were invited to take part via email, and several sessions were scheduled to allow flexibility to maximize recruitment. Participants were paid an honorarium of £200 (A$400) for their time.

### Background Materials

We circulated background materials to participants before the webinars, including confirmation of date and time, an explanation of the overall purpose of the exercise, a user guide explaining how responses would be recorded (on a specifically designed Microsoft Excel spreadsheet), and relevant background literature. The only relevant literature identified was the current American Joint Committee on Cancer staging recommendations for melanoma, which include survival curves by disease stage at diagnosis [6].

### Pre-Elicitation Training

Each webinar began with a 30-minute presentation introducing the concept of elicitation and example questions, followed by a live demonstration of how to use the Excel spreadsheet.

### Elicitation Method

Questions were asked in the format of "Imagine a cohort of 100 patients with stage X undiagnosed and hence untreated disease. After 6 months, the patients may be in any of the following stages." At this point, participants could select from a drop-down list any stage they think it is possible for patients of the cohort to be in. They then ranked these in order of likelihood, from most likely to least likely (screenshot in Fig. 1A). Once participants were happy with their selections, they clicked "Update chart,"