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The Cost-Effectiveness of a Novel SIAscopic Diagnostic Aid for the Management of Pigmented Skin Lesions in Primary Care: A Decision-Analytic Model

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ABSTRACT

Objectives: Pigmented skin lesions are commonly presented in primary care. Appropriate diagnosis and management is challenging because the vast majority are benign. The MoleMate system is a handheld SIAscopy scanner integrated with a primary care diagnostic algorithm aimed at improving the management of pigmented skin lesions in primary care. **Methods:** This decision-model–based economic evaluation draws on the results of a randomized controlled trial of the MoleMate system versus best practice (ISRCTN79932379) to estimate the expected long-term cost and health gain of diagnosis with the MoleMate system versus best practice in an English primary care setting. The model combines trial results with data from the wider literature to inform long-term prognosis, health state utilities, and cost. **Results:** Results are reported as mean and incremental cost and quality-adjusted life-years (QALYs) gained, incremental cost-effectiveness ratio with probabilistic sensitivity analysis, and value of information analysis. Over a lifetime horizon, the MoleMate system is expected to cost an extra £18 over best practice alone, and yield an extra 0.01 QALYs per patient examined. The incremental cost-effectiveness ratio is £1,896 per QALY gained, with a 66.1% probability of being below £30,000 per QALY gained. The expected value of perfect information is £43.1 million. **Conclusions:** Given typical thresholds in the United Kingdom (£20,000–£30,000 per QALY), the MoleMate system may be cost-effective compared with best practice diagnosis alone in a primary care setting. However, there is considerable decision uncertainty, driven particularly by the sensitivity and specificity of MoleMate versus best practice, and the risk of disease progression in undiagnosed melanoma; future research should focus on reducing uncertainty in these parameters.

Keywords: cost-effectiveness, diagnosis, malignant melanoma, primary care, value of information.

Introduction

Pigmented skin lesions (moles) are a common reason for patients presenting in primary care. The vast majority of moles are benign, and, in the United Kingdom, only 5% to 12% of those referred via the urgent referral route to specialist care are diagnosed as malignant melanoma [1,2]. The incidence of malignant melanoma worldwide continues to rise, doubling every 10 to 20 years [3]. In the United Kingdom, in 2008, there were 11,770 incident cases diagnosed and 2070 deaths from melanoma [4]. Prognosis is predicted by tumor thickness at diagnosis [5], making early detection and treatment critical in improving survival rates.

There is conflicting evidence concerning general practitioner (GP) diagnosis of melanoma. While GPs appear to be as sensitive as dermatologists at diagnosing melanoma, they may be less specific, thus accounting for the high false-positive rate observed in referred patients [6]. Because of the severe consequences for

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the patient, GPs are naturally concerned not to overlook any potentially malignant lesions. Overreferral, however, has implications not only for the patients themselves in terms of anxiety but also for other patients as the opportunity cost of the referral is unnecessary delays to other patients.

The MoleMate system is a novel diagnostic aid comprising a handheld SIAscopy scanner incorporating an algorithm developed for use in primary care [7]. SIAscopy is a noninvasive scanning technique that produces images of hemoglobin, melanin, and collagen in the epidermis and papillary dermis: it has been shown to improve diagnostic accuracy in secondary care settings [8,9].

The MoleMate UK Trial (ISRCTN79932379) [10,11], set in English general practice, aimed to determine whether the use of the MoleMate system in primary care would result in more appropriate referrals of suspicious pigmented lesions to specialist care compared with current best practice alone (as recommended by the National Institute for Health and Clinical Excellence [NICE] [12]: clinical history, naked eye examination, and seven-point checklist). This economic evaluation, comprising a decision model drawing on key data collected in the randomized controlled trial (RCT) as well as other relevant literature, aims to establish the cost-effectiveness of the system plus best practice compared with best practice alone in a primary care setting in England from the perspective of the National Health Service.

Methods

We developed a decision model comprising a decision tree with Markov chains at the terminal nodes drawing primarily on the results of an RCT of the MoleMate system. Full details and results of the trial are reported elsewhere [10,11]. Briefly, the trial was a pragmatic RCT enrolling 1293 participants in 15 general practices in the East of England. Participants were aged 18 years or older having at least one suspicious pigmented lesion, defined as any lesion presented by a patient, or opportunistically detected by a GP or practice nurse, that could not immediately be diagnosed as benign. Participants were randomized to comparison (best practice) or intervention (MoleMate) groups. The comparison group had their lesion(s) assessed by a lead clinician according to NICE guidelines [12], including clinical history, naked eye examination, and completion of the seven-point checklist [13,14]. The lead clinician then decided to either refer or reassure the patient. The intervention group followed the same protocol with the addition of the MoleMate system. All patients who were not referred were offered a follow-up with the lead clinician 3 to 6 months later to confirm the benign diagnosis.

The primary outcome from the trial was the appropriateness of referral defined as the proportion of referred lesions that secondary care experts decided to biopsy or monitor; it was a measure of the diagnostic accuracy of the GP with or without the aid of the MoleMate system, and represented the positive predictive value. The lead clinician's diagnostic performance, namely, the proportion of benign lesions appropriately managed in primary care (negative predictive value), the percentage agreement with the expert decision to biopsy/monitor (sensitivity), and the percentage agreement with the expert assessment that the lesion was benign (specificity), was assessed by using data from all lesions in the trial (histology result or expert clinical diagnosis).

These sensitivity and specificity estimates and prevalence of "suspicious lesions" were used as primary inputs into a decision model to estimate the expected long-term cost and quality-adjusted life-years (QALYs) gained from using the MoleMate system plus best practice compared with best practice alone (see Table 1 and Appendix 2.1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2012.12.008).

Model Structure

A decision tree was developed to estimate the expected cost and outcomes associated with using and not using the MoleMate system in the primary care setting to aid the decision to either refer the patient or reassure (Figure 1). Markov chains (labeled M1, M2, and M3) at each terminal node were used to estimate long-term costs and outcomes following the initial contact with the health service (Fig. 2A–C). The model begins with patients presenting with a mole that is defined to be either "clinically significant" (i.e., needing specialist referral) or "not clinically significant" according to a reference standard diagnosis [10,11] (i.e. D+ or D−, but it is unknown which the patient has at this point; Figure 1). The clinician can choose either to refer (T+) or to not refer (T−). This will either be a true positive or negative (T+|D+ or T−|D−, i.e., a correct decision) or false positive or negative (T+|D− or T−|D+, i.e., an incorrect decision). The probabilities of a true positive or negative are the sensitivity and specificity of the management decision, respectively. The three Markov chains estimate the expected cost and outcomes following detection of a true positive (M1), a false negative (M2), or a true negative or a false positive (M3). The pathways in the comparison group (best practice alone) are identical to those in the intervention (best practice plus MoleMate) group. The transition period for the Markov chains is 1 year.

Histological diagnosis within the MoleMate Trial differentiated between a number of types of benign and malignant skin disease. For the purpose of the decision model, it was important to estimate the (quality-adjusted) life expectancy and lifetime cost of patients. Malignant skin disease comprises basal cell carcinoma following which a normal life expectancy can be assumed, squamous cell carcinoma, and malignant melanoma. As the strongest predictor of prognosis is Breslow thickness and stage at diagnosis [5] and to keep the model as simple and transparent as possible, the model takes account only of disease stage at diagnosis, and does not further differentiate between melanoma or squamous cell carcinoma type.

Patients entering Markov chain M1 (true positives diagnosed and treated; Figure 2A) enter the appropriate state corresponding to disease status at diagnosis. They remain in that state ("Hx.") until death.

Markov chain M2 uses the same basic structure; however, these patients have had a false-negative diagnosis. Therefore, they have undiagnosed disease. Each year they have a probability of remaining in the undiagnosed state, progressing and dying, or of being opportunistically detected and treated. If detected and treated, patients' prognosis and costs are determined in the same manner as for Markov chain M1. Figure 2B presents a stylized summary of the model for clarity. The full structure is given in Appendix 1 in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2012.12.008.

Patients entering Markov chain M3 do not have a clinically significant lesion. Therefore, the Markov chain is trivial: their costs are assumed to be zero and to follow normal life expectancy (Figure 2C).

Model Inputs

The model was populated with data from the MoleMate Trial [10,11] (including the sensitivity and specificity of the comparators and the prevalence of suspicious lesions) and other relevant literature [2,5,15–28] supplemented with expert opinion where necessary (natural history of melanoma, survival, other transition probabilities, health state utilities, and costs).

Costs

Patients enter the model at their MoleMate Trial consultation. Timing a random sample of consultations (n = 32 intervention