Role of primary care in the prevention of malignant melanoma

NEIL JOHNSON
DAVID MANT
JULIA NEWTON
PATRICIA L YUDKIN

SUMMARY. One of the targets for health in the United Kingdom is the reduction in the year-on-year increase in the incidence of skin cancer. Most of the mortality associated with skin cancer is attributable to malignant melanoma. One possible way to reduce the incidence of malignant melanoma is to develop a strategy for prevention based in primary care. This paper considers the arguments for and against three possible strategies: giving general advice; identifying patients at high risk; and undertaking early diagnosis. It is concluded that elements of all three strategies are likely to prove useful, but that major studies need to be undertaken before any strategy is adopted on a national basis.

Keywords: skin cancer; melanoma; morbidity risk factors; early diagnosis; general practitioner role.

Introduction

The incidence of malignant melanoma is on the increase all over the world.1 In the United Kingdom in 1977 there were 1673 cases registered;2 by 1987 the number had risen to 3139 with 36.5% of new cases in patients aged under 50 years.3 Five-year survival rates are poor — 75% for women and 50% for men in England and Wales.3 Can general practitioners do anything to reverse this trend? There are three possibilities: they can advise all their patients, systematically or opportunistically, about the risks of sun exposure and the characteristics of melanomas; they can try to identify those at high risk of developing malignant melanoma, and selectively advise and perhaps screen these patients; or, because prognosis is highly dependent on the thickness of the melanoma at the time of excision,4 they can attempt to improve their ability to make an early diagnosis of melanoma. How effective and feasible are these strategies in general practice, and should we now be making an attempt to implement them?

Giving general advice

There is strong evidence linking malignant melanoma with sun exposure.5-8 If the population as a whole could be encouraged to reduce the amount of time (and skin) exposed to the sun it is likely that the incidence of malignant melanoma would fall.

Although opportunities frequently arise in primary care for giving advice about sun exposure (for example when treating sunburn or when giving travel advice and vaccinations) there is currently no evidence that one-to-one advice about sun exposure given in general practice consultations alters behaviour. The path between a doctor or nurse knowing about the causes of melanoma and patients changing their behaviour based on advice given is complex and remains ill-understood; blocks can occur among both patients and doctors because of insufficient knowledge or skills, or because of attitudes that militate against giving or accepting advice. Until these blocks are better understood and appropriate means by which they can be overcome have been identified a preventive campaign based solely on encouraging doctors and nurses to give general advice is unlikely to succeed.

There is evidence that some forms of education can make some difference. An educational campaign designed to improve knowledge about the characteristics of melanomas directed at both the general public (through a mass media campaign) and general practitioners (through postgraduate education) was associated with an increase in the proportion of patients with melanoma presenting early.9 Unfortunately, because there was no control group it is uncertain whether this improvement was entirely due to the publicity campaign; indeed there is some evidence from similar trials that some of this improvement may have happened without any intervention.10 Even if the improvement was caused by the publicity campaign, it is not clear which component (the lay education or the professional education) was the more important. Although no formal assessment was made of the increased workload for general practitioners, similar campaigns undertaken elsewhere resulted in increases in the number of general practice consultations for pigmented lesions from one every two to three weeks before the campaign to one every three to five days in the month after the campaign.11,12

The future

If a large-scale educational campaign to give general advice were to be adopted the current evidence supports a mass publicity campaign directed both at the public and at professionals working within primary care. If such a campaign were to be initiated its effect on patient outcomes would need to be assessed. Although much has been done by charitable organizations to encourage awareness of sun damage it would be essential for any mass campaign to be supported by the government. Such a campaign and its assessment is likely to be expensive but is totally consistent with the declared aims of the Department of Health.13

Identifying patients at high risk

Risk factors

Evidence suggests that there are three major risk factors which independently affect the development of malignant melanoma: namely the total number of naevi present, the presence of freckles and the reaction of the skin to the sun.14,15

If general practitioners and their teams are to target advice to a high-risk group it is vital to know which of the risk factors are the most important. One measure of the importance of a risk factor is the population attributable risk percentage which estimates the proportion of disease in the population that is associated with...
exposure to the risk factor; it is based on a combination of the prevalence of the risk factor and the relative risk associated with it. Using the method described by Cole and MacMahon for case-control studies, estimates of the population attributable risk percentage for the three major risk factors are shown in Table 1. The estimates vary widely, and it is clear that different studies have produced markedly different estimates of both the prevalence and relative risk attached to each risk factor, partly depending on the exact definition used.

A number of studies have considered the risk associated with the presence of clinically atypical naevi (that is large naevi, naevi with variable pigmentation and naevi with an irregular edge). Because there is an association between the presence of atypical naevi and the presence of multiple typical naevi, it is unclear whether or not the presence of atypical naevi is an additional independent risk factor. Assuming that it is, it has an estimated attributable risk percentage of 9% to 41%.

An 'atypical mole syndrome' phenotype has also been described. It refers to individuals who have large numbers of moles, clinically atypical moles and a tendency to produce moles in unusual sites (such as the iris, the buttocks, or the dorsum of the foot). The population attributable risk percentage associated with this phenotype is estimated from the results of one study as 11.5%.

Table 1 considers risk factors in isolation. What happens to the risk if an individual has a number of risk factors? From a case-control study MacKie and colleagues derived a personal risk factor score based on the presence or absence of certain risk factors alone or in combination.

**Assessment**

- **Total number of naevi on body**
- **Tendency to freckle**
- **Presence of atypical naevi**
- **Number of episodes of severe sunburn**

**Low risk (relative risk <3)**

- < 20 naevi in total
- No freckles
- No atypical naevi
- <3 episodes of severe sunburn

**High risk (relative risk > 15)**

- > 20 naevi in total
- Presence of freckles

Although the highest risks were found when all four risk factors were present, high levels of risk occurred in those with more than 20 naevi and a tendency to freckle, irrespective of whether or not the other risk factors were present. Because no estimate of the prevalence of these combinations of risk factors in the population is given no estimates can be made either for the population attributable risk percentage of various combinations of risk factors or for the likely workload for a primary care team undertaking targeted primary prevention based on the risk factors listed.

**Potential screening strategy**

Using a cut off for relative risk of 5.0 Table 1 demonstrates that at least 4% of a general practitioner’s list will have a risk factor for malignant melanoma with a relative risk of 5.0 or more — thus a list of 2000 patients will contain at least 80 patients with a risk of developing malignant melanoma of at least five-fold. If it were possible to identify these patients they could be offered advice about sun exposure and early presentation for any changes in their naevi; targeted advice may well be more effective than advice given to all. They could also be offered systematic screening aimed at early diagnosis. Such a strategy based on the separation of a group at substantial risk (by use of some form of simple assessment) followed by periodic review has already been proposed for use in Australasia and Denmark.

The Danish proposal is that those at high risk of melanoma could be identified by an assessment of the total number of naevi on the arms and the tendency to freckle, a conclusion consistent with the high-risk group described by MacKie and colleagues.

**The future**

The current evidence indicates that at least three independent risk factors are important, that others may be important, and that combinations of risk factors are associated with high risk but undetermined prevalence.

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### Table 1. Population attributable risk percentage of various risk factors for malignant melanoma.

<table>
<thead>
<tr>
<th>First author</th>
<th>Risk factor</th>
<th>No. of cases</th>
<th>No. of controls</th>
<th>Adjusted relative risk (cases: controls)</th>
<th>Prevalence of risk factor among controls (%)</th>
<th>Population attributable risk percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Presence of large numbers of typical naevi</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osterlind¹⁵</td>
<td>5+ naevi on arms</td>
<td>474</td>
<td>926</td>
<td>5.1</td>
<td>4.2</td>
<td>14.7</td>
</tr>
<tr>
<td>Elwood¹⁴</td>
<td>3+ raised moles on upper arms</td>
<td>83</td>
<td>83</td>
<td>13.3</td>
<td>4.8</td>
<td>37.2</td>
</tr>
<tr>
<td>Beral¹⁷</td>
<td>Multiple limb naevi</td>
<td>287</td>
<td>574</td>
<td>3.7*</td>
<td>2.4</td>
<td>6.2</td>
</tr>
<tr>
<td>Green¹⁸</td>
<td>Any naevi on arms</td>
<td>183</td>
<td>183</td>
<td>30.1</td>
<td>25.1</td>
<td>88.0</td>
</tr>
<tr>
<td>Nordlund¹⁹</td>
<td>&gt;15 naevi on body</td>
<td>296</td>
<td>143</td>
<td>1.6*</td>
<td>46.2</td>
<td>21.7</td>
</tr>
<tr>
<td>Svardal¹⁰</td>
<td>&gt;50 naevi on body</td>
<td>180</td>
<td>197</td>
<td>53.9</td>
<td>5.0</td>
<td>72.6</td>
</tr>
<tr>
<td><strong>Tendency to freckle</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osterlind¹⁵</td>
<td>Many freckles</td>
<td>474</td>
<td>926</td>
<td>2.9</td>
<td>12.3</td>
<td>17.3</td>
</tr>
<tr>
<td>Elwood¹⁴</td>
<td>Heavy freckling face and arms</td>
<td>83</td>
<td>83</td>
<td>6.0</td>
<td>15.7</td>
<td>43.9</td>
</tr>
<tr>
<td>Elwood²¹</td>
<td>Many freckles</td>
<td>595</td>
<td>595</td>
<td>2.1</td>
<td>1.7</td>
<td>1.8</td>
</tr>
<tr>
<td><strong>Pigmentary factors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osterlind¹⁵</td>
<td>Light hair colour</td>
<td>474</td>
<td>926</td>
<td>1.7</td>
<td>4.0</td>
<td>2.7</td>
</tr>
<tr>
<td>Elwood¹⁴</td>
<td>Burn easily/tan poorly</td>
<td>83</td>
<td>83</td>
<td>1.8</td>
<td>16.9</td>
<td>11.9</td>
</tr>
<tr>
<td>Beral¹⁷</td>
<td>Red hair at age 5 years</td>
<td>287</td>
<td>574</td>
<td>3.0*</td>
<td>8.2</td>
<td>14.1</td>
</tr>
</tbody>
</table>

*Unadjusted relative risk.
If the identification of patients at high risk is to be pursued some of the uncertainties about risk factors need to be resolved. Risk factor identification would need to be feasible and acceptable to patients and to doctors and nurses. The prevalence of single risk factors and combinations of risk factors needs to be sought along with further estimates of the relative risks associated with them. All of this could be done by means of a large prospective community-based study looking at all the currently identified risk factors.

If a system of advice and screening targeted at those identified as being at high risk were to be undertaken the fundamental question remains as to whether such a strategy would affect mortality. An intervention study based on advice and/or screening would be needed to assess changes in the long-term outcome for patients identified as being at increased risk. A sample size calculation for a randomized controlled trial based on a reduction in mortality of 20% demonstrates that it would be necessary to recruit 100,000 adults at increased risk for both intervention and control groups; this would involve all adults living in at least two health regions in the UK. The need for such a large study should not, however, be considered an adequate reason for failing to undertake such a study at all.

**Early diagnosis**

**Presentation of pigmented lesions**

Based on published incidence figures a general practitioner in the UK can expect to see a malignant melanoma once every eight to 10 years. During that same period the evidence suggests that between 140 and 170 pigmented skin lesions will have been presented to that doctor. The ratio seems to be getting even higher with increasing numbers of requests for general practitioners to examine pigmented skin lesions and pronounce whether or not they are malignant (personal observation).

Despite the rarity of malignant melanoma, particularly when compared with the number of benign lesions seen, Doherty and MacKie have demonstrated that general practitioners rarely miss the diagnosis. In a study of 125 patients presenting to one specialist clinic over a period of four years they showed that there were 105 patients in whom the delay between first noticing a new or changing pigmented lesion and undergoing surgical excision was greater than three months; in only three patients could the delay be attributed to the general practitioner (the maximum delay being 16 weeks). In all the other cases the delay could be attributed to the patient. If major improvements are to be made in the early diagnosis of malignant melanoma it is therefore essential that education about the early features of melanoma are directed at patients as well as their general practitioners.

**Screening tests**

The distinction between benign and malignant pigmented skin lesions is often unclear. As the most important prognostic factor for an individual patient is the tumour thickness, which increases with time, it is essential that general practitioners feel confident to separate benign from malignant lesions as soon as possible. If there is any doubt general practitioners need either to refer or to excise the lesion themselves. As a result, for every one malignant melanoma seen in a specialist pigmented lesion clinic there are at least 20 non-melanoma lesions.

A test that helps general practitioners decide whether a pigmented lesion is benign or malignant might be very useful. For a serious but rare condition it is vital that the general practitioner does not miss the diagnosis on the few occasions that it does arise. Any test must therefore have a very high negative predictive value. If, as a consequence, the positive predictive value is low then it has to be accepted that a number of patients will be referred (or have their lesion excised) needlessly. Any changes to the test that might improve its positive predictive value must not reduce its negative predictive value.

The principal candidate as a screening test is the 'revised seven-point checklist' advocated by MacKie. The recommendation is that a patient with a pigmented lesion with any one of the three major signs (change in size, change in shape, change in colour) should be considered for referral and that the presence of any of the four minor signs (inflammation, crusting or bleeding, sensory change, diameter > 7 mm) should be a further stimulus for referral. The seven-point score was a major component of the educational campaign described by Doherty and MacKie. This study suggested that there was an increase in melanomas presenting at an early stage (the proportion with a depth of less than 1.5 mm rising from 44% to 52%) that may have been at least partly attributable to the use of the score, and a more recent follow-up study suggests that this campaign may also have had a positive effect on mortality. These results suggest that the seven-point score might have been useful in helping patients, their general practitioners, or both to improve the early diagnosis of malignant melanoma.

Although the seven-point scoring system has never been assessed in a primary care setting the original seven-point checklist has been tested in a hospital setting. The negative predictive value of the test when used by either dermatologists or patients was 99%. The positive predictive value of the score when used by dermatologists was 8% and when used by patients 7%. This suggests that the original seven-point score is good at ruling out a benign lesion but is not effective as a tool for diagnosing a malignant melanoma. When the dermatologists used clinical skills alone the negative predictive value remained at 99% but the positive predictive value was 64%.

It may be that using the seven-point score in conjunction with clinical skills in primary care would result in a higher positive predictive value than the seven-point score used alone while retaining the high negative predictive value. To test this a large number of patients would be needed (1600 in each group for a randomized controlled trial based on a reduction in false positives of 30%). The main difficulty, however, would be that while any reduction would be advantageous in public health terms a reduction as great as 30% would still only result in a general practitioner referring one fewer patient every two years; general practitioners might need to be convinced of the benefits of the score before adopting it widely.

**The future**

Based on the evidence available there is no reason why the seven-point score should not be used as part of any educational input to patients to help them to assess at an early stage whether or not they should consult their doctor about a skin lesion. Its use in primary care in conjunction with clinical skills deserves adequate testing in order to help general practitioners make a balanced decision about using it in their everyday practice.

**Conclusion**

Malignant melanoma frequently affects young people, often has a poor prognosis and is on the increase. This suggests that the time is right for attempts to reduce the mortality from this condition.

Education about sun exposure should be aimed at everyone. There is evidence to suggest that general advice about malignant melanoma can be given by means of mass media campaigns.
However, the effect of such campaigns on patient outcomes (both positive and negative) remains substantially untested. Similarly, as yet, there is no evidence about the effectiveness of one-to-one advice. Before national campaigns are undertaken both these areas deserve research.

A targeted strategy based on identifying, advising, and possibly screening those at high risk (those with large numbers of naevi, the tendency to freckle, high risk pigmented traits or a combination of these risk factors) should also be considered seriously. The feasibility, acceptability and reliability of such a strategy would need to be studied before undertaking an appropriate intervention trial to see if such a strategy was effective. The size of the intervention study to achieve sufficient power would be large — in the order of 10% of the adults in the UK within the chosen age range.

Strategies aimed at improving the early diagnosis of malignant melanoma will need to be directed at the general public as well as their doctors. The seven-point score deserves further attention, both as a self-administered tool used by patients and as a test to be used in conjunction with clinical skills by general practitioners; it needs testing in a community setting.

At present we will do no harm and we may do some good, by advising patients about sun exposure on an opportunistic basis.

We should be encouraging research that might help to identify the most effective strategies to reduce the incidence of malignant melanoma. We also need to recognize and plan for the workload that is likely to be generated by campaigns directed at increasing public awareness of suspect naevi.

Rare problems present a major dilemma: because of their rarity research is needed to provide information upon which logical management decisions can be made; their very rarity provides major challenges in undertaking that research.

References

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Address for correspondence
Dr N Johnson, The Medical Centre, Badgers Crescent, Shipston-on-Stour, Warwickshire CV36 4BQ.