Quality in healthcare

Dear Editor

It is true that quality in healthcare means different things to different people, and that different countries have tried different ways to improve it (*AFP* March 2012).[1]

I have concerns about the premise of this discussion (that a 'comprehensive' definition is desirable), and with the conclusion (that a 'useful quality framework must support confidence in services and structures, rather than regulating or sanctioning them … the general practice team must own the quality agenda').

'Comprehensiveness' in a definition of quality is not an obvious virtue. Any scientific descriptive system ought to be precise and parsimonious. In healthcare, if quality is held to mean outcomes, a set of secondary qualities can be defined (and measured). Safety: meaning the low probability that an act or system will produce negative quality (harms). Effectiveness: the high probability that an act or system will produce quality. Accessibility: the ability of a system to deliver quality to many people. Efficiency: quality divided by resource inputs. Value: quality divided by costs.[2] Preserving quality as outcomes (and the associated idea of QALYs, the healthcare equivalent of economic utility) allows this descriptive system to exist and connects the clinical world to the broader one of economics and politics. To diverge too greatly from this vocabulary is to risk confusion and exclusion from broader debates about the fundamental issues: cost containment and the just distribution of scarce healthcare resources.

The authors recommend 'ownership', but what is this? Donnebian has carefully described various procedures for formulating criteria and standards and argues that 'when agreed upon and shared the normative consensus imparts purpose and coherence … to the collective enterprise'.[3] But it is unclear if this is what Gardner and Mazza are talking about. They may mean simply that clinicians ought to like the rules or believe there are no rules (only guidelines). They say a 'useful framework must not employ sanctions' – why not? If they have a normative conviction that externally imposed coercive systems are in principle bad (and self governing systems are good), they ought to declare it and argue for it. Only the claimed 'success' of the German model, and 'failure' of the United Kingdom's, seems to support this. It is in any case implausible that the characteristics of a policy framework could be accurately reduced to a single variable (top-down/bottom-up-ness), or results directly generalised from one country to another.

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Melanoma: A management guide for GPs

Dear Editor

In their recent article, Thompson et al[1] outline current therapeutic strategies for the management of cutaneous malignant melanoma (CM) (*AFP* July 2012). However, in such a heterogeneous patient population where the management should be multidisciplinary, we wish to remind readers about the evolving and established roles of radiotherapy (RT) in this disease.

CM has traditionally been considered a radioresistant tumour. However, a plethora of preclinical and clinical data indicate that CM exhibits heterogeneous radiosensitivity on a case-by-case basis, with some CM even being highly radiosensitive.[2,3] Preclinical data suggest that the range of sensitivities of CM to irradiation is similar to other solid tumours, but that their mean radiosensitivity is higher.[4] In the clinic, the broad range of responses of individual CM in the locoregional or metastatic settings is well documented.[2–4]

RT has substantial roles to play for CM in both the curative and palliative settings. The contribution of RT to the management of localised primary CM, although limited, may be considered with certain histological subtypes (eg. desmoplastic melanoma) and where wide excision may be difficult to achieve or cosmetically unacceptable (eg. lentigo maligna melanoma of the face). Very recently, a randomised trial reported that after therapeutic regional lymphadenectomy for stage III CM, RT improved regional nodal basin control compared to observation (further proof-in-principle that CM is not the radio-resistant disease it was once thought to be).[5]

RT also has a valuable role to play in the palliative setting where it may be used to secure loco-regional control in patients with oligometastatic disease, or in palliating symptoms of metastatic disease.[6]

RT should be considered as a therapeutic option in many CM cases, especially in patients with metastatic disease.

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Dear Editor

The recent article by Tompson, Scolyer and Kefford[1] (*AFP* July 2012) strongly advertises sentinel lymph node biopsy (SLNB) to your readers and states that SLNB provides 'a probable survival benefit for patients with intermediate thickness melanoma' and that there is 'a substantial survival benefit for SLNB-positive patients if they have an early complete lymph node dissection' (CLND). We believe that these statements are misleading and are not supported by current evidence and would like to offer your readers an alternative and more balanced interpretation of current evidence.

There is no overall survival benefit from SLNB

The statement 'a substantial survival benefit for SLNB-positive patients if they have an early complete lymph node dissection' is not true and is not at all supported by the data of the MSLT-1 trial.[2] This false conclusion is based on an inappropriate post-hoc subgroup analysis of MSLT-1 trial data and has been highly criticised in the literature.[3,4] In fact, the unambiguous finding of MSLT-1 is that there was absolutely no survival benefit of SLNB over observation but the MSLT-1 authors failed to mention this crucial finding in the abstract. Instead, the authors highlighted the inappropriate conclusion related to the above subgroup analysis. Gonzalez has stated that MSLT-1 'is a good example of how the investigators' current perception of the superiority of one intervention over another has clearly biased the reporting of results by overstating an inappropriate subgroup analysis'.[3] Of particular interest, an international expert panel of sentinel node surgeons recently concurred 'that it is not necessary to demonstrate a survival advantage for SLNB before recommending this procedure,'[5] suggesting that even this group does not believe that SLNB improves survival.

Since 1977, there have been five randomised prospective trials performed (of which MSLT-1 is the latest) to determine if elective lymphadenectomy can prolong the survival of melanoma patients. All five trials have failed to show any overall survival benefit from the procedure yet melanoma surgeons still advertise SLNB and CLND.

There are deficiencies in the concepts underpinning SLNB

SLNB proponents assume that nodal micrometastases invariably proceed to macrometastases and that nodal basin clearance of these micrometastases improves prognosis, but both of these assumptions are unproven. There is simply insufficient evidence that SLNB/CLND changes the natural history of melanoma. SLNB advocates ignore the significant issue of haematogenous spread that occurs in melanoma.

Further, the examination of cells within an SLN is potentially unreliable because benign naevus cells are found in up to 22% of normal nodes and in 14% of melanoma-positive SLNs. Even experienced pathologists find analysis of melanocytic cells in the SLN difficult and immunoperoxidase or polymerase chain reaction (PCR) cannot reliably distinguish between benign and malignant melanocytic cells.[6] In one study, up to 60% of tested nodes in patients with thin melanomas were positive with PCR, yet clinical disease and distant metastases were rare, and prognosis excellent.[7]

SLNB and CLND are invasive procedures with significant risk of complications

SLNB is an invasive procedure with complications even in expert hands. CLND results in complications in about a third of patients with a rate of clinically significant lymphoedema following axillary or groin dissection of up to 10%.[8] This is a high price to pay given there is no proven survival benefit.

SLNB is not the ideal prognostic test

SLNB proponents advertise the prognostic value of SLNB but rarely acknowledge the significant number of false negative and false positive test results. Nodal or distant metastatic disease will later develop in as many as 11% of SLNB-negative patients and up to 24% of SLNB-positive patients will not progress to higher-stage disease.[9–12] So patients with negative SLNB may still die of melanoma whilst those with positive SLNB may have no further problems. Thus, the information provided by SLNB may not be particularly useful to an individual patient (and it certainly does not alter their actual prognosis) but it may result in significant morbidity. The prognostic information provided by clinical assessment and factors such as Breslow thickness and tumour infiltrating lymphocytes is adequate for patient guidance. An invasive procedure such as SLNB adds nothing to help the individual patient.

Prevention of local lymph node disease

SLN surgeons justify performing SLNB and CLND on the grounds that it achieves local disease control (of the lymph glands). However, this can be adequately obtained by ultrasound monitoring of the lymph node basin (which can detect 4 mm sized metastases), after which patients can progress to have lymphadenectomy if needed.

What should a patient do if they have a positive SLN?

Patients should be counselled about this possibility before undergoing SLNB. Currently SLN surgeons advocate CLND if there is a positive SLNB even though we know that there is no difference in survival for melanoma patients whether CLND is performed immediately after SLNB, or is delayed until clinically palpable nodes develop.[13] Patients should understand that if they have positive sentinel nodes they will need to decide whether to undergo completion lymphadenectomy, enter a trial, or undergo observation.

Current guidelines state that 'Patients with a melanoma greater than 1.0 mm in thickness be given the opportunity to discuss sentinel lymph node biopsy'.[8] GPs are pivotal in advising patients about current clinical evidence and referring patients to appropriate specialists. We know that most SLN surgeons believe that SLNB is standard of care for melanoma (contrary to guidelines) so melanoma patients referred to SLN surgeons are probably more likely to undergo SLNB than patients referred to, for example, dermatologists.[14]

Patients diagnosed with melanoma or any form of potentially lethal cancer are at their most vulnerable. As physicians we must be truthful with our patients and advise them that SLNB/CLND will not prolong their lives and may well cause significant morbidity. Despite the controversy of SLNB/CLND, early clinical diagnosis of melanoma and appropriate wide local excision still remain the cornerstone of melanoma management in Australia.

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Dear Editor

I commend you on the July 2012 edition of *AFP* with the focus on skin cancer. For my MSc dissertation on melanoma submitted in 2011, I researched sentinel lymph node biopsy (SLNB).

I would be most interested to hear Prof John Thompson's comments on the 2007 article by Gonzalez[1] and the 2009 article by Coldiron et al.[2] Both of these authors reviewed the interim findings of the MSLT-1 and found not only no survival advantage from SLNB but some concerns about data interpretation by special interest groups (SLN surgeons). It was felt that the final MSLT result would be unchanged.

Gonzalez[1] determined that the apparent survival improvement was attributable to inappropriate highlighting of subgroup analysis and lead-time bias.

Coldiron et al[2] were a little more bold and posed this hypothetical: 'Would you have a major surgical procedure (SLNB plus lymph node clearance) if the oncologist said that it would delay the diagnosis of metastatic disease, and when the metastases were detected you would die faster?'

It is widely accepted that SLNB does provide the most accurate prognostic information.

The challenge, and not only for geographically isolated practitioners, is whether it makes sense for a patient to submit to SLNB purely for an 'accurate' prognosis. For the clinician caring for the patient long term the stated 5 year survival rates of 90.2% (SLNB-) vs 72.3% (SLNB+) are cold comfort, even for a patient versed in statistics, unless we can inform them whether their particular case lies inside or outside the stated limits, for example, are they in the 90.2% or one of the 9.8%?

Exclusion of SLNB-negative patients from clinical trials could be construed as unethical as clearly a patient with a 4 mm Breslow melanoma; but negative SLNB, still has a dreadful prognosis.

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Reply
Dear Editor

Dr Zagarella and A/Prof Sladden suggest that there is widespread uncertainty about the value of SLNB in patients with melanoma, and propose that their interpretation of current evidence is more balanced than the one presented in our recent article.[1] However, their strongly anti-SLNB stance is neither widely supported nor evidence based.

SLNB is recommended by the world's leading oncology organisations

SLNB is a minimally invasive procedure now recommended by most national melanoma management guidelines for staging all patients with intermediate thickness (1–4 mm) melanomas. A new, evidence based guideline on SLNB, published by the American Society of Clinical Oncology (ASCO) and the Society of Surgical Oncology (SSO), the largest and most respected medical and surgical oncology organisations in the world makes the same recommendation.[2]

Clinical trial evidence of the benefits of SLNB

Only one large prospective international randomised trial has compared the outcome of patients with intermediate thickness melanomas who have a SLNB and those who have wide excision only. Final results of this trial, the MSLT-I, are not yet available, but the third interim analysis provided a clear indication of the benefits of SLNB plus CLND in those found to be SLNB-positive, with substantially improved 5 year survival (72.3% vs 52.4%).[3] Dr Zagarella and A/Prof Sladden suggest that the analysis of the SLNB-positive patients in MSLT-I was 'an inappropriate post-hoc subgroup analysis'. This is incorrect. It was not a post-hoc analysis, but a prospectively planned subgroup analysis, clearly defined in the original trial protocol. In MSLT-I, after 8 years of follow up, the percentage of patients who had developed clinically-apparent nodal disease (20.5%) was essentially the same as the percentage of SLNB-positive patients plus the small percentage who had a false-negative result (total 20.8%).[4] The only plausible explanation is that virtually all patients with metastatic melanoma in a SLN will eventually develop clinically apparent disease if that node is not removed.[4] If this is so, then the comparison between the two subgroups is valid.

SLNB/CLND improves local disease control

It is of enormous importance to patients to achieve the best possible local disease control. Dr Zagarella and A/Prof Sladden make the bold statement, based on no clinical trial evidence whatsoever, that local disease control of lymph nodes can be adequately obtained by ultrasound monitoring of the lymph node basin. Whether this approach is safe is currently being addressed prospectively in the randomised MSLT-II, the final results of which will not be available for several years.

CLND in SLNB-positive patients is recommended by melanoma management guidelines

The Australian and New Zealand Melanoma Management Guidelines[5] and virtually all other national guidelines recommend that any patient found to have a positive SLNB should have a CLND. The recently published ASCO/SSO guideline similarly recommends CLND for all patients who are SLNB-positive.

SLNB is the most accurate predictor of clinical outcome currently available

The suggestion by Dr Zagarella and A/Prof Sladden's that the prognostic information provided by clinical assessment and primary tumour characteristics is 'adequate' for patient guidance, when much more accurate and reliable information is available from a minimally invasive, low risk SLNB procedure, is very difficult to comprehend. Numerous studies have shown, using multivariate analysis, that SLNB provides the most accurate staging and prognostic information currently available for patients with clinically localised primary cutaneous melanoma. This is why the American Joint Committee on Cancer (AJCC) recommends SLNB staging for all patients with melanomas ≥1.0 mm Breslow thickness.[6]

The statement that 'SLNB proponents advertise the prognostic value of SLNB but rarely acknowledge the significant number of false negative and false positive test results' is not true; false positive results are extremely rare, and most major melanoma treatment centres have reported their false negative rate, and are making strenuous efforts to reduce it. Today, most pathologists are able to identify metastatic melanoma deposits in SLNBs with great reliability, assisted by immunohistochemistry. Only very occasionally is differentiation between melanoma cells and benign naevus cells a problem.

Physicians must be truthful with their patients We agree completely with Dr Zagarella and A/Prof Sladden that we must be truthful with our patients, and those of us who are surgeons always discuss the risks as well as the benefits of any procedure as part of the process of obtaining informed consent. To state categorically that SLNB/CLND will not prolong their lives is not appropriate, because there is persuasive evidence that it may do so, if they are found to be SLNB-positive. A SLNB will certainly provide the patient with the most accurate staging currently available, and will of course be essential when effective, nontoxic adjuvant therapies become available, as is likely to occur in the near future.

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Dear Editor

My concerns relate to the section in the article by Prof Thompson, Dr Scolyer and Prof Kefford[1] on 'When is assessment of regional lymph nodes indicated' (*AFP* July 2012). I may have incorrectly sensed from this section that melanomas of an intermediate thickness should be referred to a specialist centre for definitive wider excision and SLNB. SLNB-positive patients subsequently having an CLND.

My reading of the MLST-trial is that patients randomised to the wider resection and SLNB arm had no melanoma specific survival benefit over those patients with the wider resection and a wait-and-see approach. The implication being that patients had early additional surgical procedures (SLNB +/- CLND) with their inherent additional morbidity and cost for no significant gain.

I understand some patients may want to undergo these additional procedures to help stratify them into the 72.3% vs 90.2% 5 year survival, but it would have to be made clear to them that there is additional morbidity and no additional survival benefit.

My interpretation of the difference in 5 year survival between SNB+CLND group (72.3%) vs CLND once regional node metastasis was clinically evident (52.4%) is that a proportion of those with micro-metastases did not progress to aggressive disease at the 5 year mark.

From the evidence to date, the additional travel, costs, morbidity and potential delay in definitive wider resection for no significant survival benefit makes such a management option unfavourable for many patients, especially those in rural areas.

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Reply

Dear Editor

Most of Dr Azzopardi's concerns about the value of SLNB are addressed in our response to Dr Zagarella and A/Prof Sladden. It is important to understand that although an overall survival benefit for the patients who had a SLNB was not demonstrated in the third interim analysis of the MSLT-I it is incorrect to conclude that there is in fact no survival benefit for SLNB with early completion lymph node dissection in those found to be SLNB-positive. The statistical difficulty is that approximately 80% of patients in MSLT-I were SLNB-negative and therefore could not benefit. The trial was not adequately powered to detect a benefit in the total patient cohort (100%) if there was a benefit only in the 20% who were SLNB-positive.

Dr Azzopardi also raises the more general problem of providing specialised medical services to those who live in rural areas. SLNB for melanoma (and breast cancer) requires not only a surgeon with appropriate training and experience but also a nuclear medicine service able to obtain short half-life isotopes and perform lymphoscintigraphy (necessary to identify the site of SLNs preoperatively), as well as a pathology service familiar with the particular challenges of identifying metastatic tumour deposits in SLNs. Thus, it is unrealistic to expect that every nonmetropolitan centre can provide a SLNB service, just as it is unrealistic to expect the provision of services such as radiotherapy or cardiac surgery in every country town. However, SLNB can be performed as a day-only procedure, and our experience at Melanoma Institute Australia is that most country patients are not only willing but indeed eager to travel to a major centre for specialist advice and a SLNB procedure.

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