currently recommended cut-off of 1:250, the estimated performance of the two step integrated test is clearly superior, with a detection rate of 91% and false positive rate of only 2.6%. But we know that some women ask for the one stop first trimester package, accepting a slightly inferior screening performance (85% detection rate, 4.2% false positive rate). Also we should not forget that some women access maternity services for the first time in the second trimester and others will request definitive diagnosis by chorionic villus sampling or amniocentesis irrespective of their risk. The integrated test may be the most cost effective, but any "one size fits all" policy sits uncomfortably with pregnant women and clinicians.

The main challenge for pregnant women is to absorb all the relevant information in early pregnancy to allow them to make an informed choice about which, if any, screening option they wish to undergo. The main challenge to health systems will be to ensure that there are enough adequately trained sonographers to deliver an ultrasound based screening programme on a national basis—certainly a major issue.[3]

Other remaining questions are behavioural and contextual. How many women will tolerate the delay between the two gestational stages of the integrated tests? And what is the importance of establishing top quality Down's syndrome screening programmes, relative to other priorities in the maternity services—notably tackling inequalities and ensuring that all women in labour have enough midwives to meet their needs?[4 5]

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Managing metastatic bone pain

Radiotherapy and bisphosphonates are effective for metastases and pain

Patients associate advanced cancer with pain, and for many such patients the source of the pain will be metastatic bone disease. Bone is one of the most frequent sites of spread for many common cancers such as breast, prostate, lung, and kidney and is usually affected in multiple myeloma.[1] Active management of metastatic bone disease can, however, control the symptoms and in many cases prevent further complications such as pathological fracture or compression of the spinal cord.[2]

What can be done? Firstly, patients should be given analgesics and considered for appropriate systemic treatment for the underlying cancer, usually hormonal treatment or chemotherapy. Secondly, patients should be considered for specific treatment for the bone metastases, the principal modalities being radiotherapy and bisphosphonates.

Radiotherapy has long been used. It is most commonly given as external beam to the most painful site or sites. Does it work, and how should it be given? Assessing reduction in pain in patients with advanced cancer is difficult because of changes in their analgesia, changes in the cancer itself, and high dropout rates in patients with advanced cancer. Nevertheless, the data on fractionation trials have been subjected to two overviews (and, for aficionados, an overview of the overviews).[3–5] Both overviews are consistent and show a response rate (pain reduction) in about 60% of patients, which is complete in about 33% (and rises to about 72% and 40%, respectively, if the analysis is of evaluable patients rather than on an intention to treat basis). These response rates are the same whether the radiotherapy is given as a single fraction (usually 8-10 Gy) or as multiple fractions (most commonly 20-30 Gy in 5-10 fractions). The pressure on facilities for radiotherapy in the United Kingdom as well as convenience for the patient in attending only once are strong arguments to use single fractions.[6] The main difference between single and multiple fractions is the higher rate of repeated treatment in the single fraction studies (21.5% *v* 7.4%). The higher re-treatment rate in the single fraction arms may not necessarily lower therapeutic efficacy since time to progression was the same in those studies that examined it. Rather, it may reflect clinicians' greater willingness to repeat treatment after a single rather than after the higher dose of multiple fractions. Whatever the reason, even with single fractions, nearly 80% of patients will not need repeat treatment.

For some patients, especially for those with cancer of the prostate, using a radioisotope such as strontium 89 that localises to bone will relieve pain, albeit with risk of leucopenia and thrombocytopenia.[7]

Given that most patients will have multiple bony metastases, what are the systemic options specifically for treating bone metastases? The most widely used agents are bisphosphonates, for which good evidence indicates that they will reduce the incidence of fractures, the need for palliative radiotherapy, the risk of hypercalcaemia, and the need for orthopaedic surgery (often collectively called skeletal related events), but not the risk of compression of the spinal cord.[8] These benefits are seen mainly after six months of treatment, and the reduction in orthopaedic surgery

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is appreciable only at 24 months. Most of the trials included patients with metastatic breast cancer or multiple myeloma, with more limited data on patients with prostate cancer. Although bisphosphonates presumably work in a similar way in patients with bone metastases from other sites, the benefits may not be apparent since their survival is much shorter. Many studies have concentrated on assessing events related to the skeleton rather than on pain itself, but most clinicians would regard reductions in fractures and need for radiotherapy as good surrogate markers of a reduction in pain. These data are confirmed in a specific overview.[9] Pamidronate has been the bisphosphonate most widely used, but newer third generation bisphosphonates (zelodronate, ibandronate) have been the subject of more recent studies.

Back pain merits a particular mention. If the patient describes a notable increase in the severity of the pain and a new severe nerve root pain (often describing it as "shooting," "sharp," or "like pins and needles") then an epidural component and a risk of spinal cord compression may be present. Traditionally, many patients are left until they develop neurological signs of paraplegia, by which time many will never walk again. The above symptoms in a patient with cancer are an indication for an urgent magnetic resonance scan and treatment (radiotherapy, surgery), to help the patient's pain and preserve his or her mobility.[10]

We can help patients with metastatic bone disease. Pain can dominate the lives of patients and their families; we owe it to them to use all therapeutic options to control the pain. A clear management plan developed between patient, general practitioner, and oncologist will control the pain and often give patients the confidence to cope with their illness.

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Publishing tobacco tar measurements on packets

Figures for tar, nicotine, and carbon monoxide are misleading and should be removed

Admitting mistakes can be difficult, correcting them even harder. Labelling cigarette packets with tar yields (plus nicotine and carbon monoxide) was, and is, a mistake. The mistake was not in the conception of the low tar programme, or even in conducting it as a huge experiment with public health. The error was allowing the tobacco industry to control it.

The tar delivery of cigarettes is routinely measured with a machine and, with the exception of the United States, stated on the packet as a legal requirement in almost every country in the world. It is accompanied by measurement of nicotine and often carbon monoxide.

These measurements are now recognised to be misleading for two reasons, as is the simplistic concept of tar as a substance.[1 2 w1] Firstly, human smoking patterns vary greatly and are not mimicked by the machine. Secondly, modern cigarette design facilitates compensatory smoking (over-inhalation), which may lead to the smoker taking in much greater amounts of tar and nicotine than are measured by the machine.[3] The 1960s' word tar, often called total particulate matter, is a euphemism for what we now know is a chemical cocktail with at least 69 carcinogens and numerous toxins.[4]

This practice has a long history and was originally legitimised by the US Federal Trade Commission,[1] in an attempt to stop a "tar race" that had broken out between manufacturers. It was further supported by the public health establishment, which was swayed by evidence that tar painted on mouse skin gave a tumour dose response analogous to the dose response between cigarettes and lung cancer and implied that "the lower the tar and nicotine content of cigarette smoke, the less harmful would be the effect."[5 6]

This was a reasonable expectation in the context of the times, although the fundamental flaw in the concept was the lack of understanding of the dynamics of cigarette smoking and the extent to which they are driven by nicotine hunger. One did not expect that the tobacco industry would be devious or foolish enough to modify cigarette design in ways that made the modern cigarette at least as dangerous as its predecessor, despite a dramatic lowering of tar delivery.[4] However, this was indeed what happened, and we now find the standard measurement allows the industry to fool both the system and the public.

As well as facilitating compensatory smoking by the use of ventilated filters,[7] other qualitative design changes led to increases in carcinogens,[w2] specifically nitrosamines, which are plausibly involved in the well

Additional references w1-w4 are on bmj.com

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