

# TESTING TREATMENTS

## Chapter 4, 4.2.3 TESTING TREATMENTS

### **Phenylketonuria screening: clearly beneficial**

Newborn babies are routinely screened for an inherited disease called phenylketonuria (PKU). Babies with PKU are unable to process phenylalanine, a substance which is present in everyday foods such as milk, meat, fish, and eggs. If the condition is left untreated, phenylalanine accumulates in the blood and leads to serious, irreversible, brain damage. PKU testing involves taking a few drops of blood from the baby's heel, which are analyzed in a laboratory. If this 'heel prick test' is positive, and the diagnosis is confirmed by further tests, babies are treated with a special diet to help them develop normally.

**Abdominal aortic aneurysm screening: proceed with care** At the other end of the age spectrum, abdominal aortic aneurysm screening can also be beneficial. The aorta is the main blood vessel in the body, running from the heart through the chest and abdomen. In some people the wall of the aorta in the abdomen weakens as they become older and the vessel starts to expand – this is an aneurysm, a condition that seldom gives rise to symptoms and is most common in men aged 65 and over. Large aneurysms can eventually rupture and leak without warning, often causing death.<sup>8</sup>

This evidence concerning the frequency of aneurysms in older men can be used as the basis for introducing a screening programme. In the UK, for example, men (but not women) as they turn 65 are being offered a screening ultrasound scan. The scans can show the large aneurysms so that these men can receive specialist advice and treatment, usually surgery. Men with smaller aneurysms are monitored by further scans, and those whose aorta is not enlarged need not be screened again. The quality of the screening and the surgery is crucially important. Aneurysm surgery is a major procedure and if complication rates are high then more men would be harmed than helped.

### **Breast cancer screening: well established but remains contentious**

Since routine breast screening with mammography is well established in many countries one could well assume that

mammographic screening must be based on sound evidence of benefits outweighing harms. As one US public health expert remarked in 2010: 'No screening test has ever been more carefully studied. In the past 50 years, more than 600,000 women have participated in 10 randomized trials, each involving approximately 10 years of follow-up'. But he went on to say 'Given this extraordinary research effort, it is ironic that screening mammography continues to be one of the most contentious issues within the medical community'.<sup>9</sup>

Why is mammographic screening so contentious? A fundamental reason is that it has been 'sold' to women as a sensible thing to do by those providing screening and by patient groups. The information provided to women who are invited for breast screening emphasizes the benefits while glossing over the harms, limitations, and consequences.<sup>10</sup> Yet mammography not only leads to early diagnosis but also, much as with prostate cancer (see below), to diagnosis of cancers that would never have become apparent in a patient's lifetime. And inevitably there will be false-positive results too.

The most reliable evidence comes from reviewing, systematically, the results of clinical trials in which women have been randomly allocated to screening or no screening. And the results make for interesting reading. They show that if 2,000 women are screened regularly for ten years, one will benefit from screening, as she will avoid dying from breast cancer. But at the same time, ten healthy women will, as a consequence of screening, become 'cancer patients' and will be treated unnecessarily. Mammography in these women has in fact detected lesions that are so slow-growing (or even not growing at all) that they would never have developed into a real cancer. These healthy women will go on to have either part of their breast removed, or even the whole breast, and will often receive radiotherapy and sometimes chemotherapy.<sup>11</sup>

Furthermore, 200 screened women out of 2,000 will experience a false alarm, and the psychological strain until the woman knows whether it was cancer, and even afterwards, can be severe. And mammography is often promoted to women alongside advice on breast self-examination or breast awareness,

when both these methods have also been shown to result in more harm than benefit.<sup>12</sup>

A British public health expert noted that the potential for individual benefit from mammography is very small. He remarked: ‘this is not widely understood. In part this is due to obfuscation from organisers of mammography services assuming that a positive emphasis is needed to ensure reasonable compliance [with screening]’. Assessing the available evidence in 2010, he commented: ‘Mammography does save lives, more effectively among older women, but does cause some harm.’ The harms he is referring to are overdiagnosis and false positives. Critically, he observed that full examination of all the individual results from recent screening studies had yet to be examined dispassionately.<sup>13</sup> While such an impartial evaluation is awaited, women continue to be invited for mammographic screening. At the very least, they need to be given sufficiently balanced information to enable them to decide (together with their family and their doctor if they wish), whether to attend for screening – or not.

### Prostate cancer screening: clear harms with uncertain benefits

Prostate cancer is the second most common cancer in men worldwide,<sup>14</sup> and broadly falls into two types. Some men have an aggressive form of the disease; these dangerous cancers spread rapidly and the death rate is high. But many men have slow-growing cancers that would never progress to cause a danger to health during a man’s lifetime. Ideally, a screening test would detect the dangerous cancers – with the hope that they could be treated – but not the slow-growing ones. The reason is that treatment of any sort of prostate cancer risks distressing side-effects such as incontinence and impotence – a heavy price to pay if the cancer would not have caused problems in the first place.<sup>15</sup>

Blood levels of a substance called prostate-specific antigen (PSA) are raised in most men with prostate cancer. However, there is no clear cut-off level that will distinguish between men who have cancer and those who do not,<sup>16</sup> and as many as one in five men with clinically significant cancers will have normal PSA levels. Moreover, despite its name, PSA is anything but ‘specific’