Screening and Overdiagnosis

by Dr Ian Cox, Gen Re, London, UK

What is overdiagnosis?

Medicine has undergone rapid advances over recent years with new technologies and therapies available for earlier diagnosis and improved treatment of conditions than was previously possible. However, these advances have come with a cost; a significant number of people are now thought to be overdiagnosed with illnesses or conditions.

Overdiagnosis is when an otherwise healthy person is told they have a condition, yet it is unlikely to cause them symptoms or illness in their lifetime. They will actually die from another primary cause and would perhaps not have even been aware of the presence of an unlinked medical condition had screening not been performed. In a very real sense, detection by screening can also be said to cause an overmedicalisation of benign conditions. The subsequent investigation and therapy experienced by a person with positive screening outcome is clearly more significant than that experienced by an unscreened person whose condition remained undetected.

Screening may increase a person’s belief that they are actually unwell, raising unnecessary fears about their health and longevity. Their life expectancy is unlikely to be improved as they would not have been diagnosed, under usual circumstances, in their lifetime.

Healthy people are reclassified as unhealthy and must disclose this “label”, meaning they may have to pay more for insurance and medicines.

Early diagnosis allows a doctor to begin treatment before major health damage occurs. For example, why leave raised cholesterol for years when early treatment will “normalise” the level, slowing or stopping the development of harmful atheroma? In cancers, why wait for spread to occur as that would make it incurable? Early diagnosis means a person is likely to require less treatment; for example in cancer where early diagnosis suggests a lesion is small so needing small-scale surgery. Early diagnosis is likely to lead to better cure rates but caution is needed when interpreting statistics. Simply by identifying a lesion earlier in life, survival is numerically longer because the time following diagnosis is added to the period of survival. Even in those where the treatment makes no difference this “lead” time increases apparent survival.

The effect of screening is especially keenly felt in cancer diagnosis but can also occur in cardiovascular disease, chronic kidney disease, asthma, attention deficit hyperactivity disorder, pulmonary embolism, hypertension, gestational diabetes and others. All these conditions have a significant number of people with the label of the condition but may have been overdiagnosed.

In the complete issue:

Have Psychiatrists Learnt to Think Yet?
DSM-5 and Medicalising of Everyday Life
Changing diagnostic criteria
Absence trends
Increased prevalence
Increased recognition
Increased treatment
Increased openness
Impact on insurance
Conclusion
Cancer overdiagnosis
The wider availability of and advances in technology have been identified as one of the main drivers of overdiagnosis of cancer. Increasingly sensitive technology and tests allow ever-smaller lesions and early-stage conditions of less severity to be identified. While this is a good thing for patients with cancer that will progress without intervention, it leads to overtreatment if it will cause them no problems. Once cancer is identified and labelled it would take a brave, foolhardy or even negligent doctor to ignore its presence.

It is believed that earlier diagnosis is a good thing in every case but this has been challenged in recent years. For example, it was assumed all cancer cells would continue to divide at a more or less constant rate leading to exponential tumour growth. However, it is now understood that tumour growth and spread is modified by factors like blood supply, patient immune response and the genetic fingerprint of the specific cancer. Not all cancers continue to grow to produce symptoms or illness:

- Cancer may grow at such a slow rate that the individual may die from other causes before the cancer causes symptoms.
- Cancer growth may stop completely.
- Cancer cells may be killed by the immune system.
- Cancer may grow fast initially before slowing.

If a cancer grows only slowly over time other causes of premature death may gain a foothold and a person may die before any cancer symptoms arise.1 If the person is screened they may have a diagnosis of cancer that would not have ever come apparent without that test. This is obviously more likely in those with slow growing, indolent cancers than with rapidly growing aggressive lesions.

It is now accepted that overdiagnosis is a real outcome in breast cancer screening although the extent remains disputed. Between 15 and 30% of women diagnosed with breast cancer, including ductal carcinoma in situ (DCIS), are thought to be overdiagnosed and screening programmes now provide advice to patients explaining this risk. However, it is claimed that screening proffers significant overall mortality benefit to those who undergo it. Critics point to increased unnecessary surgery – including mastectomy – with long-term medical treatment and monitoring as well as anxiety in return for a small or insignificant change in mortality.

Many people who undergo ultrasound scanning of their thyroid gland are found to have a lesion that on investigation may prove to be cancer. These thyroid cancers are smaller and less aggressive than those that are diagnosed when people present with symptoms. The mortality of thyroid cancer has not increased although there has been a relentless increase in the incidence of this condition as a result of screening.

Other conditions with overdiagnosis
There is growing evidence and discussion about the degree or presence of overdiagnosis in many conditions. The evidence that it is a real problem has mainly come from cancer screening programmes but there are suspicions that it is a real issue in many other conditions.

Chronic kidney disease
Over the past decade nephrologists have promoted the measurement and calculation of the estimated glomerular filtration rate (eGFR) as a method of identifying people at risk of renal failure and earlier impairment of kidney function. However, eGFR screening has put many people into the diagnostic category of chronic kidney disease (CKD); up to 10% of adults in the U.S. are now classified as having some form of CKD. Most are older people unlikely to suffer any troublesome kidney-related illness but who now have a diagnostic label causing anxiety and requiring repeat monitoring.

Asthma
Many people are labelled with asthma when in fact they do not have the condition. A 2008 study reported that 30% of those diagnosed did not have asthma and two thirds did not require medication over a six month follow-up.

Pulmonary embolism
The diagnosis has always been thought to be that of a major illness as it can be fatal and indeed was severe when diagnosed in previous generations. The increased use and sensitivity of scanning machines has allowed radiologists to diagnose pulmonary embolism in many more people. However, the emboli now being diagnosed are much more minor and many are unlikely to cause death or even serious illness even if untreated.

Hypertension
In previous generations blood pressure elevation due to so-called “white coat hypertension” was a well-recognised problem. Blood pressure rises quite normally in stressful situations and a consultation with a doctor (in a white coat) causes anxiety in some people. The widespread availability of home

---

monitoring and 24-hour monitoring allows such individuals to be identified. However, it is important to recognise the difference between these measurements and those taken in the doctor’s clinic.

**Aortic aneurysm**

Screening for aortic aneurysm has begun in several countries to attempt to reduce the mortality of this devastating condition. The price is that many people are labelled as having small aneurysms that may never expand or rupture. This adds to the overdiagnosis triggering follow-up, medical expenses, radiation exposure and significant anxiety.

**Gestational diabetes**

In 2010, the U.S. Diabetic Association revised the criteria for the diagnosis of gestational diabetes lowering the levels of blood sugar that are diagnostic of this condition. They recognised that this would increase the diagnosis of gestational diabetes with the potential medicalisation of pregnancies previously classified as being normal.

**How big is the potential problem?**

The area where it is easiest to define the potential for overdiagnosis is cancer. How big this problem could be can be examined by looking at the prevalence of certain cancers in post-mortem studies. Studies have been reported on the prevalence of undiagnosed cancers in those who have died of other causes. Obviously this depends on the age range of those studied but there is a large number of people who die with undiagnosed cancers in their body (see table 1).

If all these people had been diagnosed with these cancers would it cause a major problem for critical illness as these have not been factored into the likely claims?

The prostate cancer autopsy prevalence was obtained from a study conducted in the U.S. after screening by means of the PSA blood test became commonplace. The finding that a quarter of men in their 50s had undiagnosed prostate cancer, despite the availability of testing, suggests that a more sensitive test could find many more with the disease.

The underlying prevalence of thyroid cancer – over 35% across all ages – is perhaps even more alarming, especially as all of these would qualify for a payment under the standard UK CI cancer definition. In 2009, over 13% of adults in South Korea reported having been screened for thyroid cancer by means of ultrasound. The high take-up has led to female thyroid cancer incidence increasing at a rate of 25% per year between 1999 and 2008. It is now the most commonly diagnosed female cancer in South Korea with a world age-standardised incidence rate of 80.2 per 100,000 of population, trailed by breast cancer with a 42.1 per 100,000 incidence rate.

Population incidence rate increases in excess of 5% per year have been observed for thyroid cancer between 1998 and 2008 in the UK and between 1998 and 2010 in the U.S. Screening activity – in particular incidental findings during examinations involving imaging – is believed to be a significant contributing factor to these increases.

Mammography screening has been hailed as one of the great successes of public health services for women. However, it is now recognised that significant overdiagnosis of breast cancers and pre-invasive lesions such as DCIS occur. There is continuing debate on the extent of breast cancer overdiagnosis but estimates of 30% are commonplace. While screening by means of mammography is already done on a national scale for breast cancer in many countries, the autopsy findings suggest that significantly more invasive and in-situ cases could be found, at least in theory.

---

### Table 1: Proportion of autopsy subjects with evidence of cancer (Groyer, Gen Re, 2013)^2

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Age range</th>
<th>Autopsy surprise prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate cancer</td>
<td>All ages</td>
<td>12% approx. 25% approx. 33%</td>
</tr>
<tr>
<td></td>
<td>50 – 59</td>
<td>12% approx. 25% approx. 33%</td>
</tr>
<tr>
<td></td>
<td>60 – 69</td>
<td>12% approx. 25% approx. 33%</td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td>All</td>
<td>35.6%</td>
</tr>
<tr>
<td>Invasive breast cancer</td>
<td>All</td>
<td>0% – 1.8%</td>
</tr>
<tr>
<td></td>
<td>45 – 54</td>
<td>0% – 1.8%</td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>All</td>
<td>0% – 14.7%</td>
</tr>
<tr>
<td></td>
<td>40 – 70</td>
<td>0% – 14.7%</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>All</td>
<td>0.7%</td>
</tr>
<tr>
<td></td>
<td>&lt; 70</td>
<td>0.7%</td>
</tr>
<tr>
<td>Uterine cancer</td>
<td>All</td>
<td>4 x – 6 x diagnosed incidence</td>
</tr>
</tbody>
</table>

Signs that overdiagnosis may be present include a rapidly rising incidence rate of the condition while the mortality rate stays the same. Cancers where this has shown include cancer of the breast, prostate, thyroid, kidney and skin (melanoma).

**How does this affect underwriting?**

More people now have a label of a disease or condition to disclose on applications for insurance. This increases the number of applications where medical evidence is required and increases the overall cost of risk selection.

If an individual has been diagnosed with a cancer it is impossible for anyone to state if that individual has been unnecessarily diagnosed or overdiagnosed. Underwriters can only respond to the medical conditions as described by the applicant and their medical advisors. The survival statistics that underpin ratings have looked at the survival statistics of all those with the label of cancer in the published data. This will include those with an overdiagnosis as statistics pool all the people with certain cancers together. The stage of the cancer is obviously important in long-term survival and that is why we ask for as much detail as possible so that we can accurately assess the stage and outcome of a group of similar people.

Increasingly it is not simply the label of a condition that is assessed but the severity of the underlying condition that has to be weighed by the underwriter. Cancers are underwritten using guidelines that include much of this data. However, in the situation of other conditions such as abdominal aortic aneurysm, blood pressure and asthma for example, the severity and medical interventions put in place to treat and reduce risk must be taken into account.

**About the author**

Dr Ian Cox is Consultant Chief Medical Officer within the Research & Development department of Gen Re. Based in the London office he has been working for Gen Re for 14 years.

---

*Signs that overdiagnosis may be present include a rapidly rising incidence rate of the condition while the mortality rate stays the same. Cancers where this has shown include cancer of the breast, prostate, thyroid, kidney and skin (melanoma).*

More people now have a label of a disease or condition to disclose on applications for insurance. This increases the number of applications where medical evidence is required and increases the overall cost of risk selection.

If an individual has been diagnosed with a cancer it is impossible for anyone to state if that individual has been unnecessarily diagnosed or overdiagnosed. Underwriters can only respond to the medical conditions as described by the applicant and their medical advisors. The survival statistics that underpin ratings have looked at the survival statistics of all those with the label of cancer in the published data. This will include those with an overdiagnosis as statistics pool all the people with certain cancers together. The stage of the cancer is obviously important in long-term survival and that is why we ask for as much detail as possible so that we can accurately assess the stage and outcome of a group of similar people.

Increasingly it is not simply the label of a condition that is assessed but the severity of the underlying condition that has to be weighed by the underwriter. Cancers are underwritten using guidelines that include much of this data. However, in the situation of other conditions such as abdominal aortic aneurysm, blood pressure and asthma for example, the severity and medical interventions put in place to treat and reduce risk must be taken into account.

**About the author**

Dr Ian Cox is Consultant Chief Medical Officer within the Research & Development department of Gen Re. Based in the London office he has been working for Gen Re for 14 years.