Cancer Overdiagnosis in the Pursuit of Longevity

by Dr. John Cummins, Gen Re, Sydney

Of retail insurance claims in Australia in 2012, cancer is not only the leading cause of death and critical illness but the third most common cause of TPD and second leading cause of disability under income protection policies.

To be diagnosed with a “cancer” often causes alarm in the patient as cancer historically is defined as “a neoplastic disease the natural course of which is fatal.” This was an accurate definition decades ago when patients presented with symptoms and signs of clinically advanced local disease or metastatic spread. Insurance definitions, to assist claimants with life threatening diseases, were constructed using this paradigm; however, contemporary research challenges this medical definition.

Over the past 30 years, the biology of cancer has been more clearly elucidated. This article explores the movement for re-defining cancer in the context of the research findings, and provokes the question as to whether the insurance industry needs to alter their definitions accordingly.

Screening tests and overdiagnosis

There is a commonly held belief that for an individual to optimize health it is important to “pick up” health conditions at an early stage, and treat or intervene “before it’s too late”. Hence many individuals have health checks and testing in a bid to (understandably) avoid premature death and live a healthier life.

However, as medical technology has advanced and is increasingly able to diagnose organ abnormalities at an early stage, there is a growing body of scientific evidence suggesting many people are being overdiagnosed (and as a corollary, overtreated) across many different conditions – cancers and other disorders. Overdiagnosis (or “pseudo-disease”) is defined as a diagnosis of a “cancer” that would otherwise not go on to cause symptoms or death. Overly aggressive treatments and unnecessary interventions for overdiagnosed conditions not only burden the healthcare system but paradoxically may expose patients to harm without conferring any benefit.
While patient survival is prolonged for many detected cancers, this does not apply to ALL cancers detected with medical technology. Specifically, overdiagnosis of cancers occurs when (1) the cancer detected would fail to grow (or it may even regress spontaneously) without intervention, or (2) grows so slowly that the patient would die from other causes before the cancer ever caused symptoms and was therefore diagnosed. The “overdiagnosed” patient has a tumour that meets the histological criteria for cancer (invasion of cells beyond their anatomic boundaries), but the tumour will not manifest inexorable growth leading to death. The distinction is therefore critical for the patient.

Measuring overdiagnosis
Studies differ in how overdiagnosis is measured and presented. The “excess-incidence” estimation approach uses the difference between incidence (number of new cases diagnosed) in the presence of a screening test as compared to the incidence detected (presumably by presenting with clinical symptoms and signs of disease) in the absence of a screening test. Over time, if the incidence is the same in the screened group versus the unscreened group, there should be no overdiagnosis. For screening to achieve its purpose, mortality for that cancer in the screened group should fall, due to the detection of early stage disease – which left untreated would be fatal.

Redefining cancer
In 2012 a working group of the U.S. National Cancer Institute convened to investigate the phenomena of “the overdiagnosis of cancer”. Among their recommendations in July 2013 was a suggestion that the definition of cancer be changed and that a number of premalignant conditions, including ductal carcinoma in situ and high-grade prostatic intraepithelial neoplasia, should no longer be called cancer or carcinoma. Instead, the conditions should be labeled something more appropriate, such as indolent lesions of epithelial origin (IDLE). An example is a reclassification of grade 1 papilloma to urothelial neoplasia of low malignant potential was “to take the lowest grades of tumor, the most benign-appearing lesions, and remove the word carcinoma.”

There have been precedents for downgrading cancerous conditions. For example, cervical intraepithelial neoplasia (CIN) is a common Pap smear finding. CIN grade 1 is the most common and most benign form and was reclassified in 1988 as low grade squamous intraepithelial lesion under the Bethesda system.

A global concern
In addition to the U.S. researchers’ attention to it, overdiagnosis has also become a global concern. Over 320 international scientists, clinicians, policy makers and consumer advocates attended the first “Preventing Overdiagnosis” conference on 10 - 12 September 2013 in the United States. The event was hosted by The Dartmouth Institute for Health Policy & Clinical Practice, in partnership with one of the world’s most respected medical journals, the BMJ, the leading New York-based consumer organisation Consumer Reports, and Australia’s Bond University. The 2014 conference will be held at a similar time in Oxford, United Kingdom. Over 100 of the conference presentations may be viewed online at http://www.preventingoverdiagnosis.net.

Evidence for overdiagnosis
Data suggest the existence of overdiagnosis across a range of common conditions. Strong evidence is mounting from randomised trials and other studies comparing screened and unscreened populations that a significant proportion of the cancer detected through screening programmes is pseudo-disease.

Randomised trials of screening
Breast cancer
Of the nine randomised trials of mammographic screening, only one has reported long-term follow-up data. After 15 years of extended follow-up of the Malmo mammographic screening trial, it was estimated that 115 of the 741 cases of mammographically detected breast cancers were overdiagnosed.
Even though breast cancer mortality has fallen by approximately 30%, estimates of overdiagnosis of breast cancers are often of the same order of magnitude and can vary from 10% to 50%.4

Lung cancer
With respect to lung cancer, the Mayo Lung Project trial suggested an overdiagnosis of lung cancer by 51% based on chest x-ray and sputum cytology screening.5

Long-term follow-up over 16 years of these cases suggested a persistence of overdiagnosis with 85 excess cases diagnosed out of 500 cases in the control group.6

More recently, using low dose CT comparing conventional radiography in current or recent smokers, a publication demonstrated a relative reduction in mortality from lung cancer with low-dose CT screening of 20.0%. It is too soon to estimate the rate of overdiagnosis with this trial. The Mayo study indicates that 10 to 15 additional years of follow-up will be necessary to test the hypothesis that low-dose CT screening led to overdiagnosis.7

Prostate cancer
There have been no long-term follow-up studies in the PSA screening trials for prostate cancer; however, there are some insights worth commenting upon with regards to overdiagnosis.8

The PLCO trial found a 22% increase in prostate cancer incidence as a result of screening; the ERSCP trial showed a 70% increase in cancer in the screening group.9 While these findings are highly suggestive of overdiagnosis, due to differences within the design of the two trials and lack of long-term follow-up to date, these figures are indicative only.

Neuroblastoma
Large-scale screening programs in Germany and Quebec found that screening doubled the number of cases detected with no subsequent fall in mortality.10,11

Autopsy studies
Autopsy studies can estimate the true prevalence rates of various cancers. The existence of a substantial number of subclinical cancers (“reservoir”) in individuals who died from causes other than cancer is best assessed in prostate and thyroid cancer, as these tissues are small enough for precise evaluation. Autopsy studies for prostate cancers show a 25% prevalence rate in men age 50-59.12

In an autopsy study of Mediterranean men, the prevalence of prostate cancer is plotted by age in Figure 1.13

Similarly, the prevalence of thyroid cancer was 35.6%, in 101 sequential autopsies. The authors of the study suggested that small papillary carcinomas (<0.5 mm) would be better called occult papillary tumour rather than carcinoma.14

Population data
For Australians under the age of 75, the overall cancer burden between 1987 and 2007 showed a 21% increase in new diagnosis (13,012 more diagnosed cases in 2007 than in 1987) and a 28% fall in mortality (7827 fewer deaths in 2007 vs. 1987). Cancer types that showed the greatest increase in incident cases were cancers of the prostate (10,245 new cases), breast (2736), melanoma (1138) and thyroid (1107), and other cancers (1353).15 The rise in incidence is partly due to diagnoses being brought forward by technological improvements and increased coverage of screening and early diagnostic testing.

Figure 1 – Prevalence (%) of prostate cancer at autopsy by age
As an aside, Australia has one of the highest rates of cancer incidence worldwide – which may reflect more the health system and the impact of screening than a higher true reservoir of disease.

In the U.S. the most credible evidence for overdiagnosis comes from 30-year mortality data. For three cancers, the trends showed an increase in diagnosis, but not deaths: thyroid cancer (diagnosis has doubled), melanoma (diagnosis has tripled), renal cancer (almost doubled). For two of those cancers, breast and prostate, the diagnosis rate has increased while the death rate has fallen for the latter two).16

Thyroid cancer is likely detected either on physical examination or, similar to renal cancers, is likely an incidental finding on radiological testing performed for other reasons. Melanomas are generally melanoma in situ and mirror the rise of skin biopsy rates, suggesting overdiagnosis.

With regard to prostate and breast cancer, there is almost certainly a combination of overdiagnosis and a mortality benefit from early detection and/or improved therapy.

In Australia the study above17 shows a prostate cancer increase of a staggering 276% in the past two decades, whereas mortality has fallen by a lesser 27%. Internationally, the estimated risk of prostate cancer overdiagnosis is approximately 60%18 and the lifetime risk of being diagnosed with prostate cancer has increased from 1-in-11 to 1-in-6.

Population studies comparing screening for neuroblastoma versus control groups showed a doubling of the incidence rates with screening and no reduction in mortality. It appeared the screening test primarily detected tumors with a favorable prognosis, many of which would have regressed if left undetected.19

**Summary of cancer screening findings**

Three patterns appear to have emerged over the past three decades or so.

One pattern shows a clear reduction in some cancer-specific mortality as a result of screening, while overdiagnosis appears to be minimal. Examples of such cancers are bowel cancer and cervical cancer. This screening is beneficial.

A second pattern shows an increase in incidence of new cancer diagnoses and no impact on mortality from these cancers. This is highly suggestive of overdiagnosis. Thyroid, renal and melanomas are examples.

A third group shows a fall in mortality accompanied by a disproportionate rise in cancer incidence. Cancers of the prostate and breast follow this pattern; lung cancer may also follow this pattern if high-risk screening is adopted. Disappointingly, Barrett’s oesophagus and surgical excisions of ductal carcinoma in situ have not led to lower incidence of invasive cancer. After years of aggressively treating precancerous lesions and early stage cancers, there has not been a commensurate reduction in invasive cancer. This suggests that overdiagnosis and overtreatment are occurring on a large scale.

**What do we understand about cancer biology?**

Cancers vary tremendously in their behaviour and scientists are just beginning to understand cancer biology. Some grow rapidly and can be fatal; some are slow-growing and will never cause symptoms, and some cancers (including breast cancers, neuroblastoma and melanomas) can regress and spontaneously disappear. The exact causes for these are unknown but causative factors likely include host immune factors that effectively destroy the cancer or, alternatively, a cancer outgrowing its own supportive blood supply and therefore “involuting”.

While numerous predisposing risk factors for cancer exist (such as smoking, genetics, occupational and other environmental toxins and viruses), ultimately, the final outcome is a series of genetic “missteps” and random errors in DNA replication and other changes. At each step, only some lesions progress to the next stage of carcinogenesis. It is likely that overdiagnosis occurs because cancers are being caught at an early stage in progression by screening tests, and they may not have gone on to growth and widespread invasion/dissemination. Histological evidence consistent with cancer does not always progress to growth and spread.
The challenge is to differentiate those early cancers that will go on to cause morbidity and mortality from those that will lie dormant throughout life, even though pathologically they appear the same. Currently, screening technology is not able to do this. The further challenge is recognising which cancers that have been identified should be treated with curative intent and which can be “observed” or even ignored. The intervention option of active surveillance of (low grade and likely indolent) prostate cancer is beginning to address this problem with overdiagnosis and this paradigm may in time extend to other potentially overdiagnosed cancers.

Conclusion

Our understanding of cancer biology has advanced and major strides are anticipated in the near future in diagnosis, imaging, molecular biology and genetic research as well as treatment options. As our knowledge evolves through scientific investigation, we need clarity around a number of issues with cancer detection and screening. Firstly, we should achieve clarity about when (and when not) to screen. Secondly, if a tumour is found, we need clarity around when to intervene early, and when to reassure the patient and do nothing further; confident in the knowledge this tumour will never cause harm. Finally, we need clarity about which specific tumors it is appropriate to not intervene with immediately upon diagnosis but to monitor for rate of growth and aggressiveness of disease (again dictating intervention or not), with the ultimate aim being to “do well and do no harm”.

Dr. John Cummins is Chief Medical Officer, Research & Development. He can be reached at Tel. +61 2 8236 6205 or john.cummins@genre.com

Endnotes

2 Esserman, LJ, Thompson, IM and Reid, B. Overdiagnosis and overtreatment in cancer – an opportunity for improvement. JAMA 2013;310(8):797-798.
17 Ibid Note 15.
18 Ibid Note 16.
19 UpToDate, see http://www.uptodate.com/contents/clinical-presentation-diagnosis-and-staging-evaluation-of-neuroblastoma?source=search_result&search=neuroblastoma&selectedTitle=1%7E138#H20.
The current disability income market in Australia is going through particularly challenging times, with claims costs increasing and lapse rates worsening. There have been many instances of press announcements during this year from major insurers and reinsurers, stating that these issues are hurting their bottom line and announcing various levels of reserve strengthening.

In many respects Australia and New Zealand are unique markets, where we have:

- More generous disability definitions and higher non-medical limits than other global markets
- Yearly Renewable Term (i.e., age-rated) products combined with relatively high upfront sales commission

Selective lapsation means that, on average, unhealthy lives are less likely to lapse than healthy lives. That’s not to say they will never lapse, but just that on a portfolio level, policyholders whose health has deteriorated since taking out a policy are more likely to keep that policy in force. The reasons for this include:

- They are aware their health has deteriorated and so the need for the cover that the policy provides is greater.
- They were going to lapse their current policy to take out a newer, better, cheaper version, but in the process of doing so found that they were no longer eligible for standard rates, and therefore would face a price increase if they did so.
- Lapse and re-enter has become increasingly easy to do as expert underwriting systems are widely used and non-medical limits have been increased. A healthy life can complete underwriting in only a few minutes, whereas a “non-cleanskin life” (meaning an application requires further assessment) has to undergo significant underwriting complexity.

Given that this dynamic must be happening, it is reasonable to assume that people who have had a life insurance policy for a long time are less healthy than people who have had a policy for a short time. If this is true, then we would expect to see deterioration in experience by policy duration.

Gen Re has done considerable analysis of our own internal experience, and because Gen Re has been a significant reinsurer of disability income over a long period of time, we are in a position to report experience by duration. (See Figure 1.)

This shape was reasonably consistent across most of our retail disability income business, and was similar for both Agreed Value and Indemnity policies.

What Figure 1 clearly shows is that there is a worsening trend in incidence of approximately 3% per year in force, which appears to level out at around 10 years. Therefore, business that is 10 years or more has incidence experience about 30% worse than policies at early durations – a significant result.
Our internal data did not have credible claims volume after a 13-year duration, so it is hard to tell whether this trend will continue or whether it will stabilise over time.

In order to corroborate this trend, we have available to us the FSC/KPMG 2007 - 2009 Disability Income Experience Investigation.

While long-term selective lapsation was not considered directly in this report, there are two clear references to this issue:

- **Section 7.5 : Claims costs pre-2002 and post-2002**
  The authors provide a table of claims costs showing that for every occupation class, claims costs deteriorate when comparing policies issued pre-2002 with those issued post-2002.

- **Table 1: Incidence rates by duration**
  This table shows that over most age bands and occupation classes, incidence rates increase by duration.

In addition to these analyses, APRA has stated on the record at industry conferences that insurers are reporting their older business performs worse than their newer business. This is consistent with both the above results.

Our opinion on this issue is that selective lapsation is real and should be taken into account when pricing and reserving for these products in order to recognise profits appropriately over time. If not, there is a risk that profits are overstated for many years before losses have to be recognised.

What should be avoided is a pricing model, where we have to increase rates significantly on older duration business relative to younger duration business; increasing those premiums makes the problem of selective lapsation worse.

*James Louw* is Chief Actuary and can be reached at Tel. +61 2 8236 6205 or jlouw@genre.com

---

**2013 CustomerConnect AU/NZ Claimant Satisfaction Survey**

*CustomerConnect* was recently launched in partnership with the Gen Re U.S. Research Centre. It will offer participating companies insights into how to improve the customer focus and claims process. The findings will enable life insurers to leverage new opportunities to provide a more meaningful customer experience at claim time.

Participants also have the opportunity to participate in a Business Improvement and Insights Workshop, following the presentation of their individual Company Results and Industry Report. Gen Re has developed a framework for the workshop that can be tailored to each company’s designated priorities.

The next *CustomerConnect* study will be conducted in 2015 with a wider scope that includes net promoter scores, peer group reviews and a 2013-2014 comparative analysis. Participants will also benefit from further insights and analytics from our U.S. research team and 2014 results.

For inquiries, contact Viviane Murphy on viviane.murphy@genre.com or Tel. +61 2 8236 6204.
The 2013 “Beyond Excellence” COMET program sold out training packages within two months of launching our new offering – delivering over 80 courses and workshops across the Australia and New Zealand life insurance industries.

Following compelling feedback from course participants and training managers plus a thorough review of our roadmap, we have decided to prioritise the delivery of the Gen Re COMET program to our valued clients. In this way, COMET will be tailored to meet the unique needs of organisations. In 2014 we will be making COMET available exclusively to Gen Re new business treaty clients.

COMET Correspondence, “Market Wrap” Webinars

We will no longer be offering the long-running Correspondence course and will be replacing it with new learning opportunities – our “Market Wrap” Webinars. All life risk professionals in Australia and New Zealand, whether or not a Gen Re client, will receive free access to the Webinar series to discuss hot topics and trends in our markets. Webinars will come directly to you on a quarterly basis in a two-hour session format, designed around current topics and trends. You will be able to sit at your desk, or with your team, and engage in discussing emerging insurance issues. The webinars will run in February, May, July and November.

Each session will include a presentation, a facilitator and an opportunity to ask questions along with your industry peers. We want to do more than educate and inform, by stimulating thought and encouraging conversation.

Secure Your 2014 Training Calendars

The package concept and annual training calendars that we introduced this year will remain available to Gen Re new business treaty clients. We look forward to designing 2014 calendars so organisations can meet their development objectives and address the particular challenges they face.

Please contact Viviane Murphy (Tel. +61 2 8236 6204, viviane.murphy@genre.com) with any questions on these changes.

Over the course of 2014, we will announce the exact timing and topics of the Webinars.

Thank you for your continued support and partnership.

Jane Dorter
Head, Client Accounts
Gen Re is delighted to announce the winners of the COMET Correspondence Course 2013.

Jason Lear  
Sovereign, New Zealand  
Underwriting Course

Lisa Igo  
Fidelity, New Zealand  
Claims Course

Both Jason and Lisa are eligible to attend a conference of their choice in Asia, Australia or New Zealand. This sponsorship includes airfare, conference registration and accommodation.
The difference is…the quality of the promise.