

life insurance matters

Focusing on mortality and morbidity

**Pensioner mortality
variation by postcode**

**Intelligent modelling
of mortality**

**Cancer reform strategy
in the UK**

**Costly revolutions
in cancer treatment**

**Vaccinations for
non-infectious diseases**



If you would like to discuss any issues raised in this publication please contact Nick Hall – nick.hall@watsonwyatt.com
Telephone +44 (0)1737 241144



Welcome to life insurance matters

It is difficult to detach ourselves from prevailing fashions and assumptions in search of a perspective that might usefully transcend today's concerns. However, it is a worthwhile challenge; if we try to do so in the actuarial world, seeking a 'time heliview' across the centuries, some things do seem clear.

Any mortality specialist would see one very curious thing from the 'time helicopter': the actuarial profession arose largely as a way to deal with the uncertainty associated with mortality, came to largely forget that issue for much of the 20th century, and then returned in the last 10 years or so to devote a great deal of attention to mortality.

Another trend, although less clear-cut, has been the actuarial profession's gradual move to make more use of the thinking of other professions – in living memory, from statisticians to financial economists, and now increasingly from the medical profession.

A proper understanding of mortality depends on much more than just the ability to manipulate mortality data in a statistically valid way, although that is clearly a vital element. Just as the foundational mortality research of John Graunt in the 17th century considered cause of death (partly as a proxy to age, because of data problems), actuaries too have realised that intelligent mortality modelling must consider how expected medical and environmental developments are likely to affect particular causes of death, and how these may affect overall mortality rates in the future.

In this publication, produced especially for the Joining Forces on Mortality and Longevity Conference, we have compiled several of our recently published mortality articles with particular reference to the interface between actuaries and medical professionals. We have also added more recent material, in particular the fruits of our research into UK postcode mortality effects, a field that many of our clients have expressed great interest in over the last two years.

We hope that you enjoy the conference, and find this publication useful. Visit our stand to find out more!

Contents

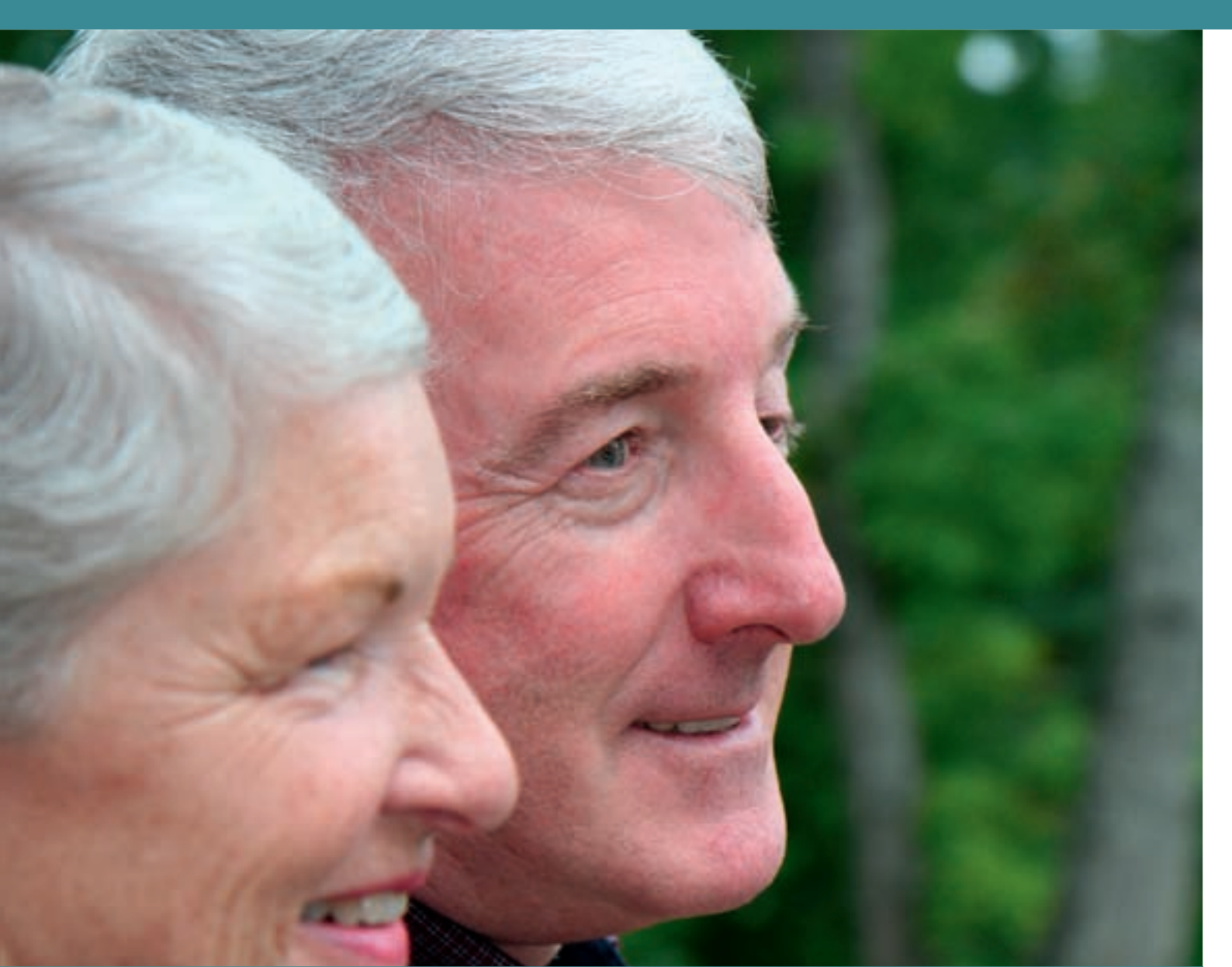
**4 Pensioner mortality variation
by postcode**

8 Intelligent modelling of mortality

12 Cancer reform strategy in the UK

16 Costly revolutions in cancer treatment

20 Vaccinations for non-infectious diseases



Pensioner mortality variation by postcode

Matthew Edwards discusses some of the more important issues that arise when using postcode to model UK pensioner and annuitant mortality.

Much recent work in the field of UK pensioner mortality has focused on the ‘postcode effect’: the extent to which postcode variations seem to explain mortality variations over and beyond age, sex and any available amount of information (pension amount or final pensionable salary).

The postcode effect is now well entrenched in the consciousness of UK pension and annuity practitioners, and postcode has become widely used as a proxy to estimate the underlying mortality characteristics of small pension schemes and annuity portfolios without conducting a traditional mortality investigation.

This reliance on observed postcode effect raises various interesting questions. In this article, we consider some of these issues in the light of our recent work developing the Watson Wyatt Postcode Mortality Tool.

Data and methodology

Our work has been conducted on a pool of combined UK pension scheme data, with a total of around 3 million years of exposure and 100,000 deaths across a range of UK industries and sectors. The dataset has been restricted to pensioners in payment only. We have analysed the mortality experience using generalised linear models.

Postcode clustering techniques

However large the starting dataset, it will generally be impossible to analyse the mortality of postcodes in isolation – there will be too little data for most postcodes. Any study of mortality variation by postcode therefore requires some method of combining (or ‘clustering’) postcodes.

A common method is to apply one set of ‘off the shelf’ postcode clusters relating to observed or perceived similarities in wealth and lifestyle. This method can give quick results, and it

is intuitively clear that (if applied correctly) such lifestyle clusters will provide some degree of predictiveness. However, this approach is not ideal since the clustering is based on a proxy to mortality, and not mortality itself: the results may therefore be materially unrepresentative, with such lifestyle clusters hiding material levels of mortality heterogeneity.

We have found that much greater ‘explanatory power’ of observed mortality experience can be achieved by using clustering techniques which have reference to health status and observed mortality, and by using more than one clustering method. **Figure 1** summarises the four techniques we used.

For instance, in our work we found that using only the socio-economic postcode clustering factor gave an explanatory power (by which we mean the relative mortality differential of moving from one extreme of the factor to the other extreme, all other things being equal) of just 137 per cent, while combining various ‘healthstyle’, lifestyle and mortality-based clustering methods provided explanatory power, as shown in **Figure 2** overleaf (for completeness and ease of comparison, we have also included the pension amount factor).

Note that the population mortality cluster and lifestyle cluster effects as shown in **Figure 2** downplay the predictiveness that those factors could achieve in isolation, since in the model underlying these results, their effect is seen ‘after’ the effect of the healthstyle and pension scheme mortality clusters.

Figure 1 | Preferred postcode clustering methods

The approach underlying Watson Wyatt’s Postcode Mortality Tool has been to combine several different methods to cluster postcode, most of which are based on mortality and health rather than simply wealth and lifestyle. By using mortality and health clustering methods, we avoid the problems associated with potentially misleading proxies; by using four conceptually very different clustering methods, we avoid the problem of relying on any one ‘vision’ of how mortality should behave. The clustering methods we have used are:

- ‘health clusters’ based on health status and ‘healthstyle’ information, as provided by the data analysis company CACI (‘HealthAcorn’)
- ‘lifestyle clusters’ based on financial, socio-economic and general lifestyle information, as provided by CACI (‘Acorn’)
- ‘pensioner mortality clusters’ based on a micro-regional analysis of observed UK pensioner mortality in our dataset, using a credibility-based spatial smoothing algorithm
- ‘population mortality clusters’ using high-age mortality data analysed at the micro-regional level from Office of National Statistics sources.

Variations by age

One of the most interesting aspects of this sort of investigation is the ability to quantify the degree to which the postcode effect varies by age. Intuitively, we would expect the relative variation between 'good lives' and 'bad lives' to reduce as age increases, as the inherent vulnerability and finitude of the human frame outweighs the extent to which pensioners may have invested their savings in extra-virgin olive oil rather than high-tar cigarettes.

Our investigation showed that the explanatory power of the main healthstyle factor varied substantially over the typical pensioner age range, as well as by sex, with explanatory power for the three age bandings we used as shown in Figure 3.

Interestingly, the explanatory power of the pension amount factor over and above healthstyle also varied in similar fashion for male pensioners, while for female pensioners there was little variation by age (largely because

Figure 2 | Population mortality cluster and lifestyle cluster effects

Clustering method	Power	Contribution
Healthstyle	157%	33%
Pension amount	148%	29%
Scheme mortality	144%	27%
Population mortality	111%	7%
Lifestyle	105%	4%
Total effect	387%	100%

Figure 3 | Explanatory power of the main healthstyle factor

Clustering method	Male	Female
Young (50-64)	232%	168%
Mid (65-79)	172%	156%
Old (80+)	134%	122%

pension amount for female pensioners has little explanatory power in the first place).

The difference in postcode variations according to age band can also be seen by creating heat maps of the UK, using these maps to show the postcode variations we found in our work on different age subsets.

The map in Figure 4 shows the range in postcode mortality variations for male pensioners with no age subdivision, shown at the postcode sector level for ease of visualisation. Red indicates the highest mortality effect, dark blue the lowest, with red implying an average postcode sector mortality of around 160 per cent of

Figure 4 | Postcode effects: all ages (males)

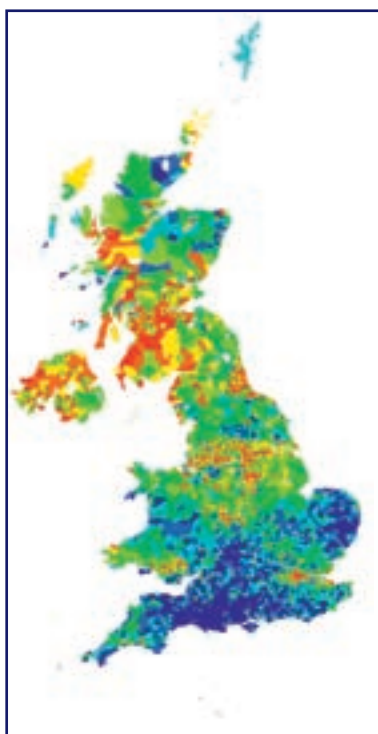


Figure 5 | Postcode effects: young males

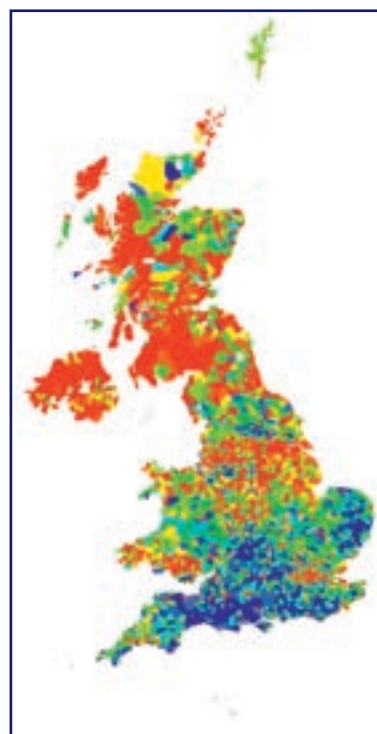
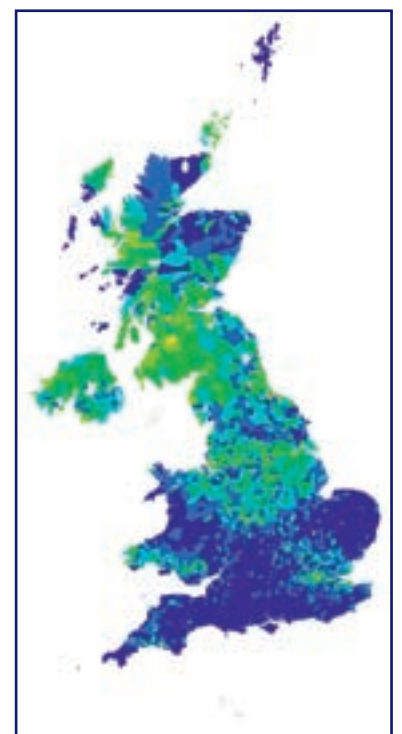


Figure 6 | Postcode effects: old males



blue (as noted previously, mortality variations between high and low mortality postcodes are much greater than between the postcode sectors used for these maps, where variations are dampened somewhat by the sector-level aggregation).

Figures 5 and 6 show the corresponding maps obtained if we use exactly the same 'colour scale' to plot maps in respect of the age 50-64 postcode effects (Figure 5) and the age 80+ postcode effects (Figure 6). We see far more variation in the young age band than on the all-ages basis, which itself exhibits more variation than on the 'seniors' basis.

Pension amount effects according to postcode band

If our mortality modelling is predicated on some form of postcode clustering and a strong pension amount effect, it is necessary to investigate the extent to which this pension amount effect varies according to which broad postcode healthstyle/lifestyle band lives are in. Intuitively, we might expect variation by pension amount to be lower in the 'good' (low mortality effect) postcode groups than in the 'bad' postcode groups.

Surprisingly, however, our investigation showed that there was no statistically significant effect of that sort, and that the pension amount effect was relatively constant irrespective of postcode groups. Figure 7 shows how the amount effect for males is very similar whether we look at the lightest mortality postcode group (group A in this analysis), the middle group (B) or the heaviest mortality postcode group (C). The lighter confidence interval lines in the graph help with this interpretation. An equivalent investigation for female pensioners led to identical results.

Clearly, it may be possible to observe some alteration in the apparent pension amount effect if we split the population down into a larger number of postcode groups than the three broad groups used for this particular investigation, but we then have the problem that the total amount of data in any particular 'cell' (combination of postcode group and pension amount) will mitigate against our being able to rely on the results seen.

Conclusion

The points discussed in this article show the degree of complexity needed for robust postcode modelling.

Many practitioners now use postcode as a proxy in pension scheme or annuity portfolio mortality investigations. If postcode is simply being used as a factor in a bespoke investigation for any particular large scheme, then the blurring of 'mortality reality' that comes about from insufficiently sensitive postcode clustering may not be financially dangerous (although clearly, if a job is worth doing it is worth doing well...).

However, if postcode mortality results are being used directly to estimate the mortality of one small scheme or portfolio, any heterogeneity in the underlying tool may lead to financially material errors in the resulting mortality assumptions.

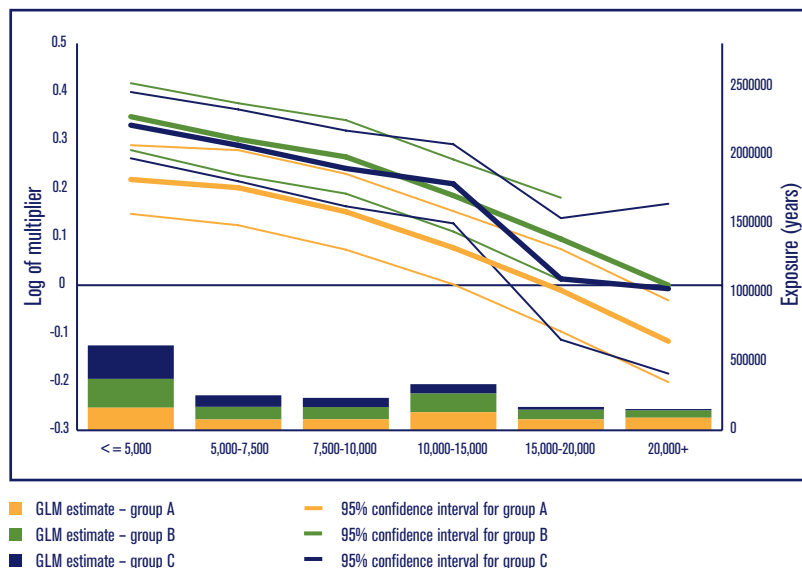
For further information contact:

Matthew Edwards

+44 (0) 1737 274300

matthew.edwards@watsonwyatt.com

Figure 7 | Interaction between amount effect and postcode band





Mortality has long held a professional fascination for actuaries, and mathematicians before them, with Gompertz first drawing attention in 1825 to the exponential increase in rates of mortality that occurs over much of adult life. In the 21st century we have seen an explosion of interest in new and updated modelling techniques for projecting future mortality rates, taking advantage of rapid improvements in computer processing power.

Intelligent modelling of mortality

Daniel Ryan explains how predictive mortality models involve more than just historical extrapolation.

However, it is only recently that there has been a sustained effort to shift the focus from models of all-cause mortality to those that either consider trends in different causes of death across generations or the diagnosis and progression of diseases that conspire towards death in the individual. This takes mortality modelling substantially forward from the simplistic 'extrapolation of past trends' approach that had hitherto dominated.

Cause and effect

The UK Actuarial Profession's 'Mortality Projections by Cause' Research Group has highlighted how longstanding series of cause-specific mortality studies in the general

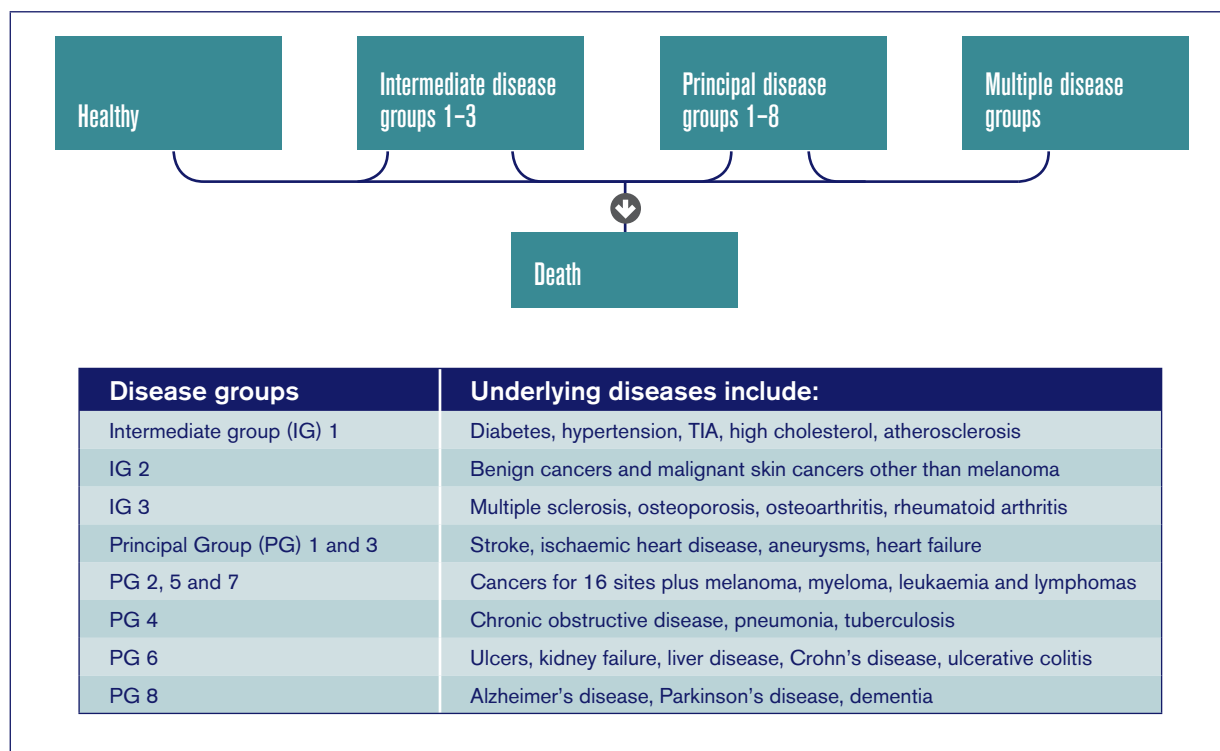
population can provide a basis for the forward projection of mortality through consideration of relatively simple boundary scenarios on a cause-by-cause basis. A Continuous Mortality Investigation (CMI) Working Party set up at the end of last year has developed a generic and modifiable model of mortality improvements that allows for the effect of year of birth, and that model will include comparisons against plausible scenarios for selected causes of death.

Watson Wyatt has long had a leading interest in research into mortality and longevity and the Watson Wyatt Mortality Morbidity Service was established in 2003. Member life offices and reinsurers have collectively directed, funded and

benefited from multi-disciplinary investigations on a wide range of topics, based on models specifically developed for the service or jointly funded with Watson Wyatt.

Over the last two years a particular strand of research resulting from this joint funding has been the application of disease-based mortality models (DBMMs). These are multi-state transition models that track diagnoses of initial and subsequent selected diseases from the healthy population, as well as deaths from all states (see Figure 1). The significant data requirements of such models can only be met by large longitudinal databases that contain event-based clinical data on millions of patients, and we have developed

Figure 1 | Disease-based mortality model structure





a bespoke tool with the leading commercial database in the UK, the General Practice Research Database, to extract the necessary information on disease diagnoses and deaths.

Advantages and applications

A key driver behind the increased attention given to cause-specific mortality models has been the need to develop suitable Individual Capital Assessment stress tests. A common initial approach was to consider the eradication of a particular cause of death, such as the elusive but often mooted concept of a 'cure for cancer'. Certain cancers have been strongly associated with prior infection, such as cervical cancer and human papilloma virus, and liver cancer and hepatitis. Vaccination against such viruses, if acceptable to the public, could prevent

many cases of cancer that would otherwise occur. For other cancers, 'cure' is really a shorthand expression for diagnosis at an early stage through better screening and awareness and access to individually tailored treatment.

The difficulty that cause-specific mortality models need to address is that the original data sources do not provide information as to what other diseases the individual may have had prior to death, and hence the likely new cause of death after the 'cure'. In contrast, DBMMs have already identified the mosaic of different combinations of diseases in the population, and continuing transitions to other diseases will temper the immortality implied by a 'cure' scenario.

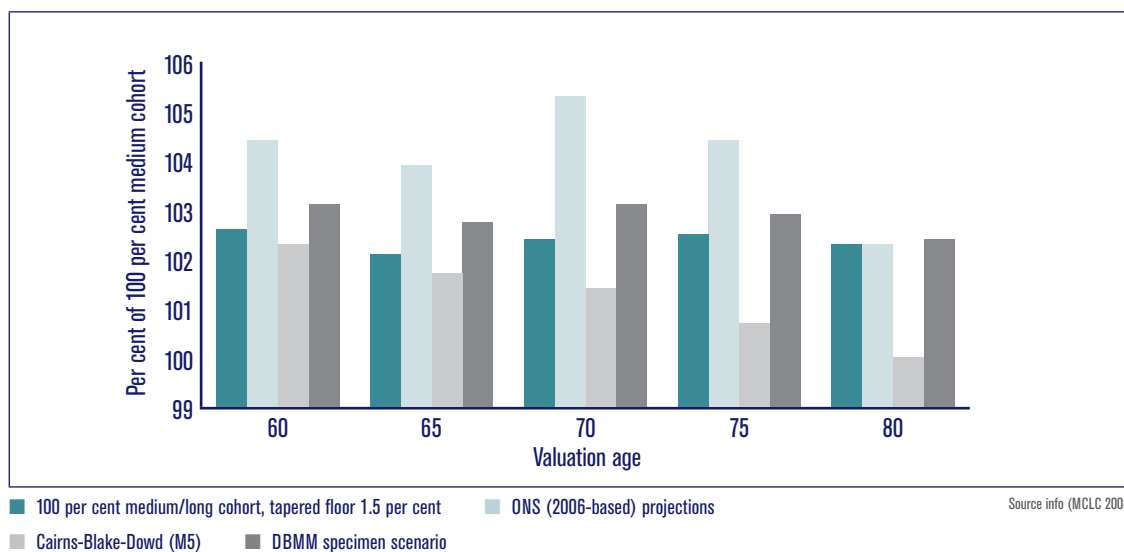
The modular structure of a DBMM readily lends itself to forward

predictive modelling. An all-cause mortality model might use a floor to the long-term rate of mortality improvements as a heavy-handed reflection of expert views over the impact of future medical advances. However, a DBMM could combine forward predictions for those diseases where there was greater understanding of the natural history of the disease and greater transparency over likely benefits from new treatments with a projection approach for other diseases.

The segmentation of the population by different prior histories of disease is akin to the classical approach taken by actuaries in considering differences in mortality experience by sex, age and smoking status. We would suggest that DBMMs provide a fertile environment for the

“...DBMMs have already identified the mosaic of different combinations of diseases in the population...”

Figure 2 | Annuity comparisons with retirement at age 65 at 5 per cent with base mortality table of PNMA00



collation and incorporation of expert opinion from doctors and epidemiologists by aligning the model structure with their areas of expertise. Generalists and epidemiologists can comment on likely future diagnosis rates from the general population, whilst specialists can inform as to how changes in risk factors and developments in those treatments that are either in clinical practice or in clinical trials may improve survival rates for those with disease.

Ongoing model development

We have an ongoing process of updating our forward predictive scenarios in collaboration with external experts to reflect changes in clinical guidance, based on collective understanding of the importance of

risk factors and the status of likely medical advances. Such approaches provide a basis for comparative analyses with other widely used mortality improvement assumptions, such as the Interim Cohort Projections with a long-term floor. Figure 2 illustrates some high-level comparisons of life expectancies at different ages for men and women.

Furthermore, in contrast to existing mortality databases, we believe that large longitudinal databases such as GPRD and QRESEARCH offer significant potential for further data mining and justifiable refinement of our mortality models. Expected developments over the next six months include enhanced modelling of different severities of the same disease, whether that relates to stage at diagnosis in the case of cancer or

wider involvement in the case of diabetes and circulatory disease, or the application of generalised linear models to individual patient medical records to quantify better the impact of different risk factors acting in combination.

The morbid but professional fascination that actuaries have for death is unlikely to disappear any time soon.

For further information contact:

Daniel Ryan

+44 (0) 20 7227 2478

daniel.ryan@watsonwyatt.com



Cancer reform strategy in the UK

Daniel Ryan asks, is the UK providing
a world class cancer service?

League tables are everywhere these days, but few lead to as much collective despondency in the UK as cancer comparisons with the rest of Europe and the US.

The EUROCARE project

The EUROCARE project began in 1989 with the aim of measuring and explaining international differences in cancer survival in Europe. The EUROCARE-3 study into cancers diagnosed between 1990 and 1994 suggested that the survival rates were relatively poor in the UK, and in part led to the NHS Cancer Plan being introduced in 2000.

Additional funding on risk awareness, screening and treatment was provided with the intention of closing the gap with our European neighbours by 2010. However, the EUROCARE-4 study into cancers diagnosed between 1995 and 2002 did not show an improvement in the UK's league position, against a backdrop of generally improving survival rates and narrowing differences between Western and Eastern Europe.

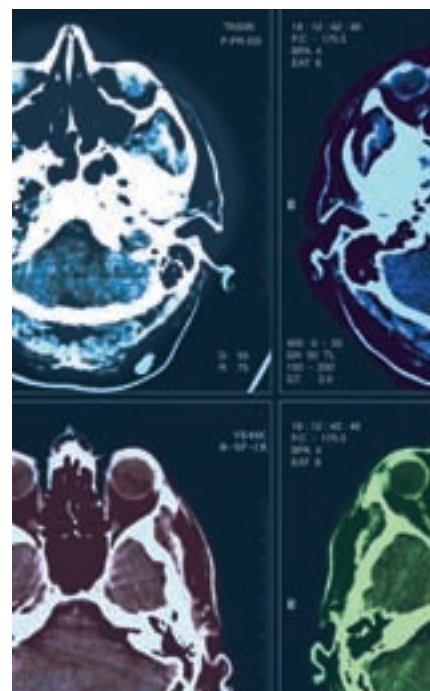
In the UK's defence, it was arguably too early to assess the benefits of the 2000 NHS Cancer Plan. Despite this, and perhaps in response to the impending results, a year-long consultation exercise culminated in the launch of the Cancer Reform Strategy in December 2007, with the stated aim of closing the gap in cancer survival rates with our European neighbours and the rest of the world by 2012.

Detailed studies on particular cancer sites associated with the EUROCARE-3 study indicated the importance of 'cancer stage at diagnosis' in explaining differences in subsequent survival rates, and identified that cancers tended to be diagnosed in the UK at a later and more dangerous stage. It was not clear whether this was because the UK population was less willing to seek medical attention, either generally or in response to symptoms, or if this reflected differences in the approach to routine investigation.

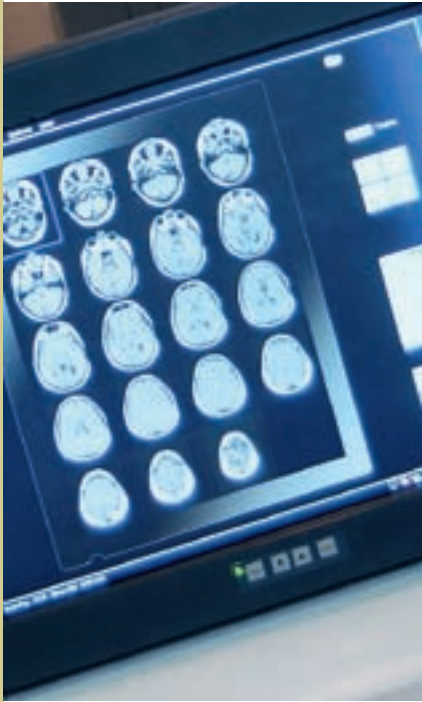
National screening programmes

The 2000 NHS Cancer Plan specifically set out to raise public awareness of risk factors leading to cancer. However, the 'Reduce the Risk' campaign by Cancer Research UK in 2005 indicated that 77 per cent of the population could not name more than two such risk factors. Accordingly, most of the additional funding into early diagnosis over the 10 years of the Cancer Reform Strategy has been on national screening programmes.

It is the role of the UK National Screening Committee to appraise new and existing screening programmes, and make suitable recommendations for implementation. In addition to the long-standing screening programmes for breast and cervical cancer, the NHS Bowel Cancer Screening Programme was approved last year and is being rolled out to all 60–69 year olds by December 2009.



The Cancer Reform Strategy does not introduce any new screening programmes, as explained in the 'Vision' documents for different cancer sites that were prepared by expert working groups. The existing Prostate Cancer Risk Management Programme will be relaunched, and there will be a series of indicative tests, including prostate-specific antigen (PSA) density and velocity, available to men that wish to investigate the presence of significant prostate cancer without a formal screening programme. There is unlikely to be sufficient robust evidence to support a screening programme for lung cancer based on helical computerised tomography (CT) scanning by 2012. Current trials



evaluating cancer markers and ultrasound for ovarian cancer screening will still be ongoing in 2012.

Instead, the additional funding on early diagnosis is committed to the extension of the target age ranges on existing screening programmes and on the introduction and expansion of enhanced screening techniques. Breast cancer screening is to be extended to cover those aged 47–73, using digital mammography that enables x-ray images to be stored electronically and provides the potential for computer-assisted diagnosis. Liquid based cytology reduces the number of inconclusive films from cervical cancer screening and allows the screening process to be automated. Bowel cancer screening is to be extended to also cover those aged 70–75 in year 2010, switching to more accurate and easier to use immunological faecal occult blood (FOB) tests and wider use of flexible sigmoidoscopy that allows visual examination of the last section of the colon.

Implications for cancer incidence

The impact on malignant cancer incidence rates of these enhanced screening techniques will differ by cancer site. The impact for insured lives might be different, because whilst they would be more likely to take part in any national screening programme, this would be set against existing levels of private healthcare screening.

Cervical cancer screening identifies and removes pre-cancerous cells, and relatively few cervical cancers would be detected in those who were being regularly screened. Positive FOB tests from bowel cancer screening would be further investigated by colonoscopy, leading to an initial surge in malignant cancer incidence rates, but the removal of any polyps in those without cancer provides a long-lasting protective effect against future potential cancer. Use of

digital mammography is associated with increased detection of both malignant cancers and ductal carcinomas-in-situ (DCIS). As some DCIS would go on to become malignant cancers, surgical removal provides a similar protecting effect.

The long-term level of PSA testing in the UK is uncertain. Approximately 50 per cent of the difference in male cancer survival rates across all sites between the US and Europe is explained by diagnoses of prostate cancer where the biopsy was prompted by high PSA concentrations and the cancer is unlikely to become clinically threatening during the lifetime of the individual. It is equivalent to including healthy individuals in the analysis, and misleading as to both the benefits of treatment and comparisons of healthcare systems.

The Cancer Reform Strategy further allows for additional funding for greater provision of radiotherapy and faster access to treatment, and has consulted extensively with medical experts from the US on how in-patient stays can be reduced, with the expectation of benefits to both hospital costs and patient survival.

Conclusion

To some extent, the Cancer Reform Strategy includes and expands on initiatives that were already planned. As the annualised net costs of the Cancer Reform Strategy are less than £3 per capita, it may be optimistic to assume that this additional investment will be sufficient to narrow differences in survival rates between the UK and Europe and the US over the next five years, given the desire for further improvements in all countries.

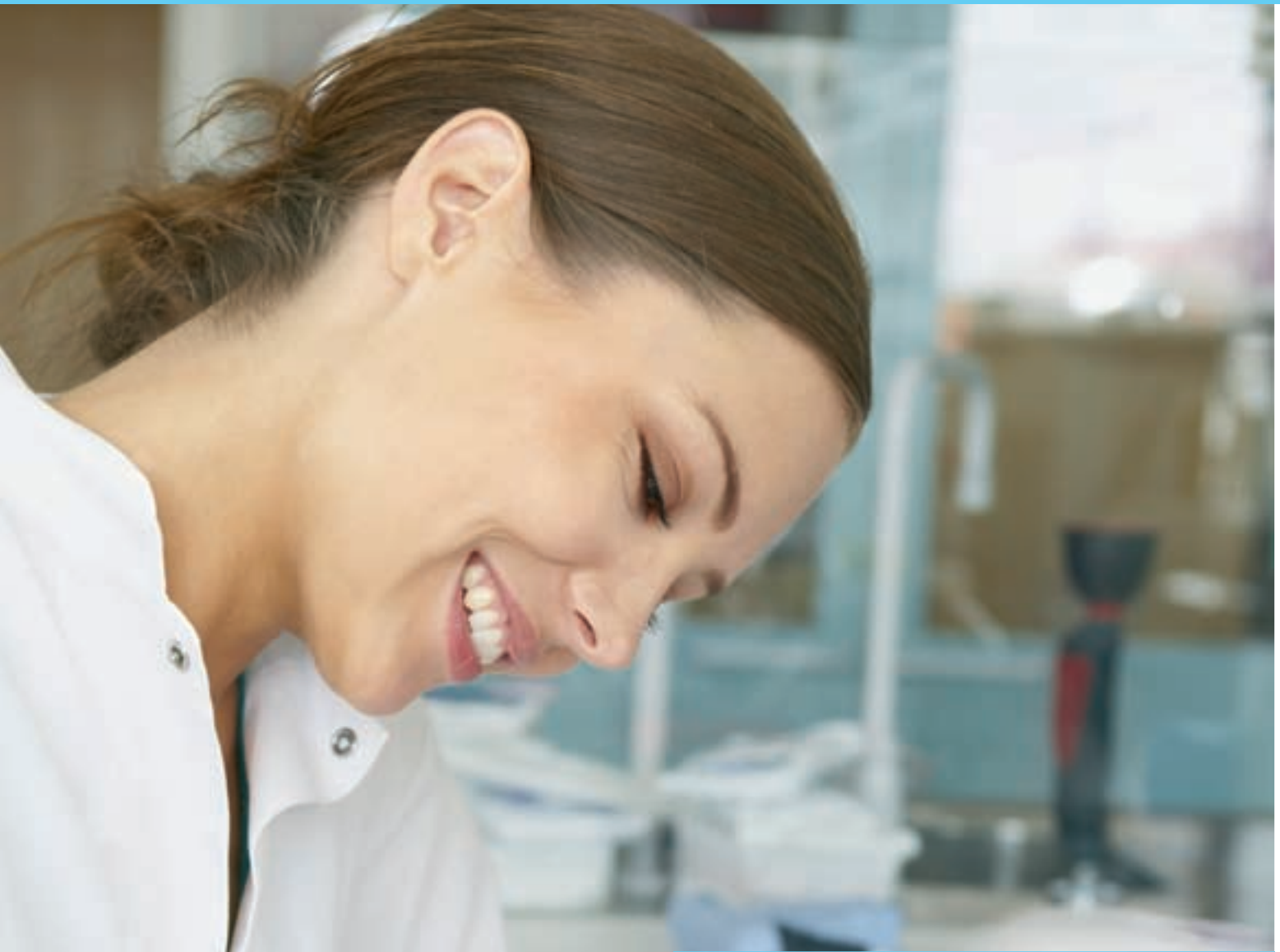
For further information contact:

Daniel Ryan

+44 (0) 20 7227 2478

daniel.ryan@watsonwyatt.com





Costly revolutions in cancer treatment

Daniel Ryan discusses current funding arrangements in the UK.

Herceptin and Avastin are the forerunners of a potential avalanche of monoclonal antibodies (MABs) that have the potential to precipitate dramatic reductions in relative cancer survival rates, as well as improve the management of other diseases such as asthma and rheumatoid arthritis.

MAB therapy uses antibodies produced in the laboratory, rather than by the immune system of the individual. The approach is based on the original work of Kohler, Milstein and Jerne in 1984 which identified that cancerous B-cells produce a single type of antibody. Recombinant DNA technology has been used to produce part-mouse, part-human monoclonal antibodies, otherwise known as chimeric or humanised antibodies, to overcome both rejection of mouse antibodies and difficulties (both technical and ethical) with the production of human antibodies. B-cells that can recognise particular proteins, or antigens, are combined with long-lasting myeloma cells to produce a constant supply of a specific antibody. The use of genetically modified mice reduces still further the possibility of rejection, and is likely to improve the effectiveness of the MAB.

MABs identify and bind to specific abnormal proteins on the surface of cancer cells, and may either initiate an immune attack on the cancer cell, prevent cancer cells from growing, or act as a delivery system. MABs of the first two varieties are described as 'naked'. The last variety, or 'conjugated MABs', could link to radioactive agents, chemotherapy drugs or immunotoxins. The damage to normal cells is lessened because the MAB is uniquely specific to the target antigen, and tracks these down prior to release of the lethal agent.

In the UK, Herceptin is now recommended by the National Institute of Clinical Excellence (NICE) as treatment for both advanced and early-stage breast cancers where the development of the cancer results from overexpression of the growth factor receptor HER2, representing approximately 30 per cent of all breast cancers. Herceptin prolongs overall survival and halves the likelihood of recurrence for early-stage cancers. Avastin blocks the actions of the Vascular Endothelial Growth Factor (VEGF) protein, which is involved in attracting new blood vessels to support cell growth, and Avastin would similarly slow progression of the cancer and prolong overall survival.

The US has pioneered the development of MABs for a range of different diseases since the early 1990s. The Food and Drug Administration (FDA) in the US has so far approved nine MABs for different cancer sites, with the highest percentage of approvals for chimeric MABs (26 per cent). EU approval has generally followed within two years. Over 150 MABs are currently being investigated in various clinical trials, either for treatment or for identification. However MABs are not cheap, as biological agents are more expensive to manufacture than chemotherapy agents, and pharmaceutical companies need to reclaim development costs during the patent period.

The UK trails behind both the US and Europe in recommending MABs for clinical practice. Avastin has been approved by the FDA for the treatment of colo-rectal and lung cancer, whereas NICE produced specific statements that did not recommend the use of Avastin for new patients with colo-rectal cancer in January 2007 or those with lung cancer in June 2008. Their decision





was based primarily on the costs involved, even though Avastin is licensed for use in the UK and can be prescribed. NICE assesses the cost of treatment against quality adjusted years of additional survival (QALYs), and generally regards £30,000 per QALY as a suitable upper limit benchmark for cost-effectiveness. A year's treatment of Herceptin costs about £20,000. More recently, in August 2008 NICE rejected the use of Avastin in combination therapy for renal cell carcinoma after assessing the cost of treatment as £170,000 per QALY.

These funding issues may indeed intensify, as the extensive pipeline of new MABs in ongoing clinical trials does not represent the full potential for further developments over cancer treatment in this area. Existing MABs are large proteins that need to be injected intravenously. Pharmaceutical companies are already investing in the next generation of treatments that involve antibody fragments, and would in theory be cheaper, easier to manufacture and more flexible over use and method of delivery, although it is still too early in the development process to quantify the potential for improvements or cost reductions.

Unlike other treatments, such as statins that have been promoted for their role in primary prevention, none of the MAB cancer treatments reduce the likelihood of the initial cancer. Continued improvements in relative cancer survival rates as a result of such treatments are likely to mean increased demand on resources, and lead to exceptionally difficult choices over appropriate rationing. Some cancer experts have highlighted the potential for insurance to assist in funding access to a wider range of treatments. However, in the UK such developments have been undermined by some hospital trusts proposing to charge patients for all their

treatments, if the patient is prepared to finance for themselves those treatments that are not currently available from the NHS.

MABs and their successors could dramatically improve prospects for cancer patients. Their high specificity significantly reduces the likelihood of adverse effects seen with existing chemotherapy, with resulting reductions in the costs of overall disease management. However, current funding arrangements will severely limit their future usage in the UK, unless the unit costs of the treatment can be reduced and innovative insurance and cost-sharing products, such as payments for treatment only in the event of a successful outcome, increase the overall funding available.

For more information, contact:

Daniel Ryan

+44 (0) 20 7227 2478

daniel.ryan@watsonwyatt.com



A young boy with short brown hair is shown in profile, covering his eyes with his hands. He is wearing a blue t-shirt. In the background, a woman with dark hair, wearing a light blue shirt, is looking towards the boy with a concerned expression. The setting appears to be a clinical or hospital environment.

Vaccinations

for non-infectious diseases

Daniel Ryan describes
the recent developments.

The use of vaccination in medical practice has a long and rich history, with Edward Jenner introducing the term in 1796 to describe the systematic use of cowpox (Latin – vacca) to inoculate individuals against highly virulent small pox. Since then vaccines have been developed for a whole succession of infectious diseases based on the concept of an initial controlled exposure to inactivated infective agents or component fragments, which produce an immune response that would protect the individual against future exposure.

Children in the UK are routinely vaccinated against 12 different infectious diseases. However, the re-emergence of measles in many parts of the UK illustrates how confidence can be shaken in a vaccination process, with public concern over unsubstantiated claims of association between autism and the MMR (measles, mumps and rubella) triple vaccine driving a significant fall in the levels of inoculation.

Expanding roles for vaccination

A number of biotechnology companies have considered the possibility of vaccination being used in the treatment of existing non-infectious disease, rather than just preventing infectious diseases, and more than 20 therapeutic vaccines have been tested over the last 12 years. Some of these vaccines target foreign molecules, such as NicVax from Nabi

Biopharmaceuticals for treating nicotine dependency. These vaccines conjugate virus-like particles that promote a strong immune response with derivatives of the target molecule. Nicotine, for example, is physically prevented from accessing target areas in the brain associated with relaxation and appetite suppression by antibodies binding to the molecule. Phase two clinical trials have indicated comparable smoker cessation rates at one year to the best current treatments, such as bupropion. However, future trials and evaluation are necessary before such a vaccine becomes a commercially available prospect.

Other vaccines provoke immune responses that block potentially damaging pathways in the body. Cytos Biotechnology and Protherics have both developed vaccines that target angiotensin, and have demonstrated reductions in blood pressure for those with hypertension. In 2003, Avant announced results from a phase two clinical trial on the cholesterol management vaccine, CETi-1, which boosts the concentration of HDL or 'good' cholesterol in the blood, whilst more recently, Bioinvent and Genentech are developing a vaccine that targets oxidised LDL or 'bad' cholesterol, which is instrumental in plaque formation in arterial walls.

The role of infectious disease in some cancers is also well-established. For example, certain strains of human papilloma virus (HPV) and hepatitis B and C virus have been implicated in cervical and liver cancers respectively. This has led to the implementation of a new vaccination programme against HPV for girls at age 12 in the UK.





However, more recent research has focused on cancer vaccines that restrict the growth of existing tumours or that act synergistically with other treatments to prevent recurrence.

The key difficulty for such cancer vaccines is that the immune system has evolved to identify very different organisms such as bacteria and viruses, whereas the differences between normal and cancerous cells are more subtle. Auto-immune diseases, such as rheumatoid arthritis, are the hallmarks of an immune system that is too active and intolerant. Cancer vaccines need to either identify unique cancer-related molecules that are rarely found on normal cells, improve the visibility of cancerous cells to the immune system or 'educate' key components, such as dendritic (immune) cells.

Patient compliance is a particular concern for the treatment of chronic disease, whether due to forgetfulness or reactions of patients to the diverse effects of the treatment. Vaccination could replace the need for daily or

more frequent tablets with periodic booster injections, as well as providing for significant cost savings in treatment administration. Vaccines would be expected to avoid the 'off-target' effects commonly seen with existing drugs, but may have unforeseen effects where the underlying processes and pathways that are affected by such vaccines are not fully understood.

Implications

Despite the wealth of different strategies being researched for the use of vaccines in the treatment of non-infectious diseases, it should be remembered that as yet, there are no such vaccines available outside of clinical trials.

However, it is clear that the pace of development is increasing and some of these vaccines are likely to enter clinical practice over the next five to ten years. Cytos Biotechnology, for example, announced an agreement with Pfizer in August 2008 involving funding of CHF150 million (US\$140 million) for research and development. In return, Pfizer gained worldwide exclusive rights to any new vaccines that are based on the 'Immunodrug' technology of Cytos.

As insurers attempt to assess the effect of such vaccines, it is unlikely that cost will limit uptake in an insured population, even if national vaccination programmes are not implemented. The retail cost of the

recommended three doses of the recently developed HPV vaccine is £240. In contrast, the total cost of administering herceptin for early or late stage breast cancer over a recommended period of up to one year is £20,000. Potential improvements in morbidity and mortality could be significant given the tightly focused actions of the vaccine, for example, leading to significant improvements in smoking cessation or reductions in blood pressure to more optimal levels.

In practice, it is likely that the overall impact on any population will be much more subdued. If a significant minority of parents are unwilling to allow their children to be vaccinated against measles, is it reasonable to assume that the level of concern will be far greater when the targets of vaccination are only subtly different from normal cells and vital pathways. Individuals, after all, can always stop taking medication.

For more information, contact:

Daniel Ryan

+44 (0) 20 7227 2478
daniel.ryan@watsonwyatt.com

Powerful predictive modelling...

...Pretium 3.1 – new version, new features

Be it data manipulation and deduplication, flexible multivariate modelling of mortality, sophisticated postcode analysis involving mortality clustering as well as geodemographic data, or tailor-made age curves with our powerful splines, this new version of Watson Wyatt's Pretium can help you to understand what's really driving your mortality experience. Making complex analyses beautifully simple.

Pretium

For more information on Pretium, please contact
Matthew Edwards on +44 (0) 1737 274300
or email pretium@watsonwyatt.com

watsonwyatt.com

Watson Wyatt Limited, 21 Tothill Street, Westminster, London SW1H 9LL.
Authorised and regulated by the Financial Services Authority.



locations

ASIA-PACIFIC ▪ Bangkok ▪ Beijing ▪ Bengaluru ▪ Delhi
Guangzhou ▪ Hanoi ▪ Ho Chi Minh City ▪ Hong Kong ▪ Jakarta
Kolkata ▪ Kuala Lumpur ▪ Manila ▪ Melbourne ▪ Mumbai
Seoul ▪ Shanghai ▪ Shenzhen ▪ Singapore ▪ Sydney ▪ Taipei
Tokyo ▪ Wuhan

EUROPE ▪ Amsterdam ▪ Apeldoorn ▪ Birmingham ▪ Bristol
Brussels ▪ Dublin ▪ Düsseldorf ▪ Edinburgh ▪ Eindhoven
Frankfurt ▪ Lausanne ▪ Leeds ▪ Lisbon ▪ London ▪ Madrid
Manchester ▪ Milan ▪ Moscow ▪ Munich ▪ Nieuwegein
Paris ▪ Purmerend ▪ Redhill ▪ Reigate ▪ Rome ▪ Rotterdam
Stockholm ▪ Vienna ▪ Welwyn ▪ Wiesbaden ▪ Zürich

LATIN AMERICA ▪ Bogotá ▪ Buenos Aires ▪ Mexico City
Montevideo ▪ San Juan ▪ Santiago ▪ São Paulo

MIDDLE EAST ▪ Dubai

NORTH AMERICA ▪ Atlanta ▪ Berwyn, PA ▪ Boston
Calgary ▪ Charlotte ▪ Chicago ▪ Cincinnati ▪ Cleveland
Columbus ▪ Dallas ▪ Denver ▪ Detroit ▪ Grand Rapids
Hartford, CT ▪ Herndon, VA ▪ Honolulu ▪ Houston ▪ Irvine
Kitchener-Waterloo ▪ Los Angeles ▪ Madison, WI ▪ Memphis
Miami ▪ Minneapolis ▪ Montréal ▪ New York ▪ Paramus, NJ
Philadelphia ▪ Phoenix ▪ Portland ▪ Rochelle Park, NJ ▪ St Louis
San Diego ▪ San Francisco ▪ Santa Clara ▪ Seattle ▪ Stamford
Tampa ▪ Toronto ▪ Vancouver ▪ Washington, DC

watsonwyatt.com

21 Tothill Street, Westminster, London, SW1H 9LL UK

Telephone +44 (0) 20 7222 8033

Fax +44 (0) 20 7222 9182

Authorised and regulated by the Financial Services Authority.

The information in this publication is for general interest. No action should be taken on the basis of any article without seeking specific advice.

To unsubscribe, email unsubscribe@watsonwyatt.com with the publication name as the subject and include your name, title and company address. You can manage your Watson Wyatt subscription at watsonwyatt.com/mywatsonwyatt

This publication is printed on paper produced using a chlorine-free process and wood pulp originating from managed sustainable plantations.