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Personalised Oncology

(Incorporating Liquid Biopsies and Immunotherapy)

Dr Bill Monday
CMO, Pacific Life Re Australia

Agenda

- The importance of Cancer to the Insurance Industry
- Screening and stage at diagnosis
- What are liquid biopsies and of what benefit are they?
- Potential impact of novel therapies and novel cancer detection on cancer survival
- Conclusion

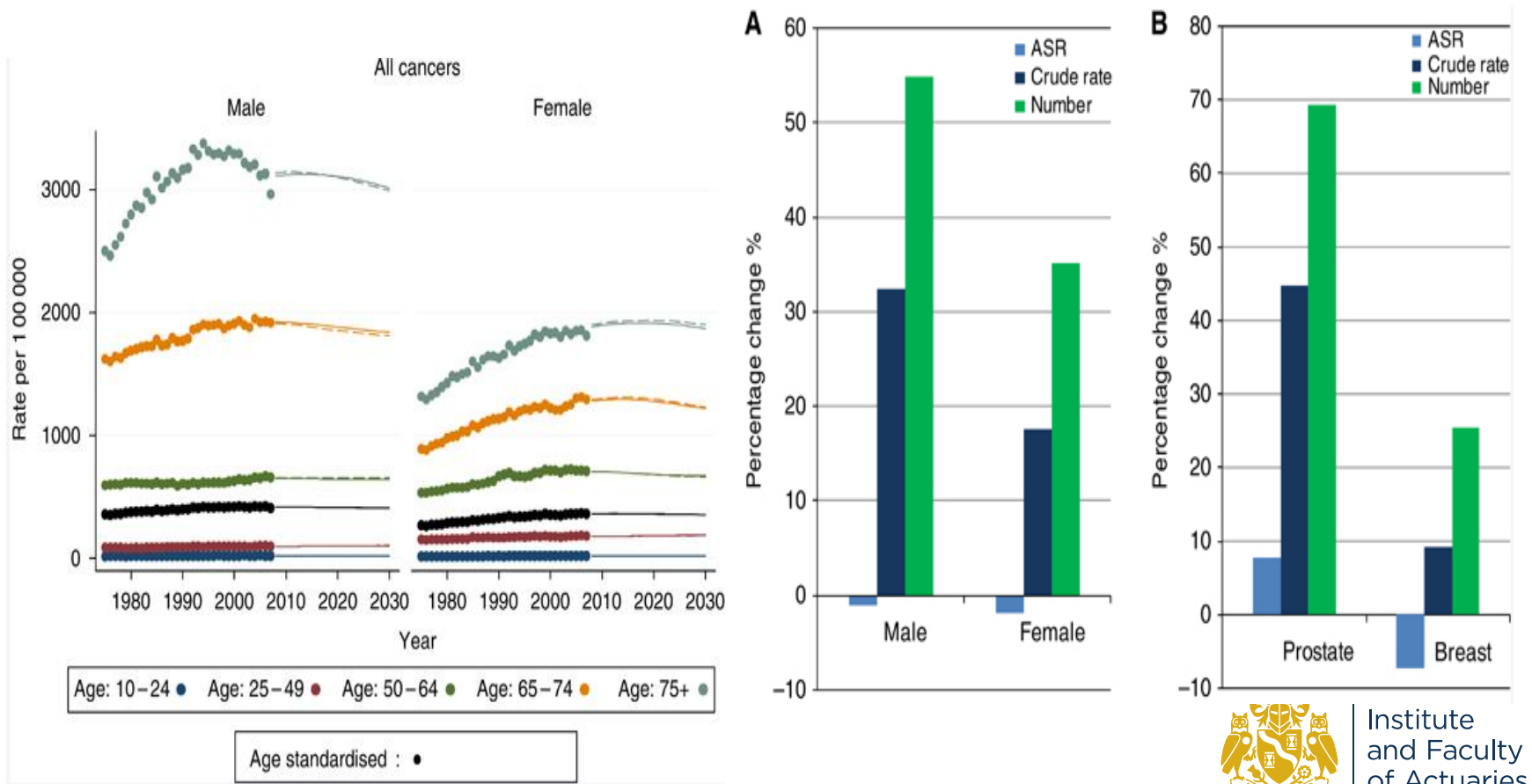


Approx. Cost of Cancer to the UK insurance Industry 2016

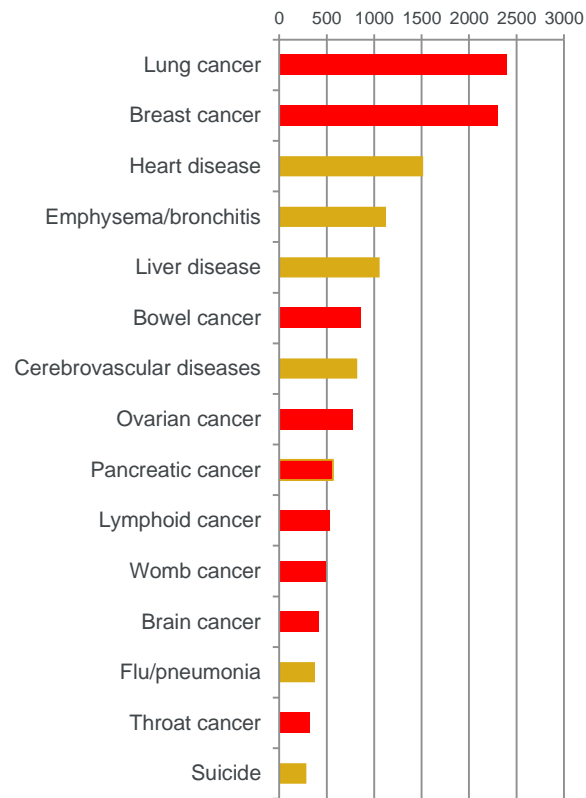
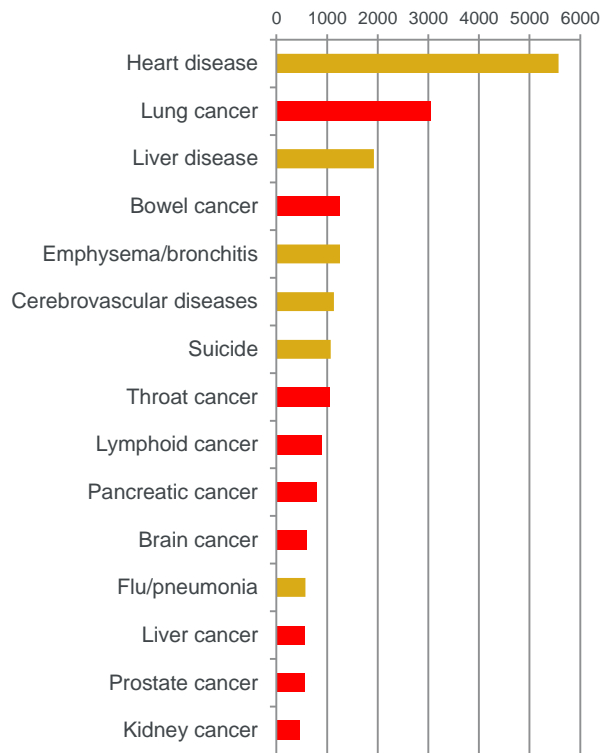
Benefit	Amount paid (£ 000)	% due to Cancer	Amount paid for Cancer (£ 000)
Critical illness	1,047,435	+/- 63%	660,000
Life	2,763,324	+/-28%	774,000
TPD	30,357	+/- 8%	2,430
IP	499,316	+/- 8%	40,000
Approximate cost of Cancer to UK insurance industry			1,476,430



Changes in incidence rate, age standardised rate, crude rate and number of cases of Cancer in the UK 2007-2030

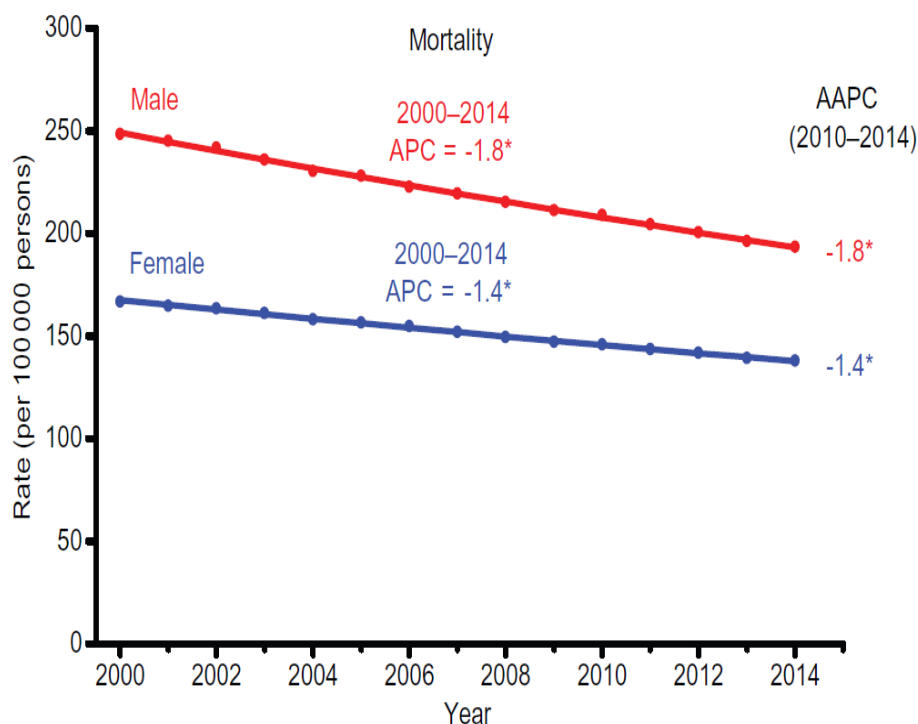


Leading Causes of Deaths registered in England and Wales 2013 Ages 50-64



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Significant Mortality improvements in Cancer USA¹



In the UK between 2003 -2013 the Annual Percentage Change (APC) in death rates fell by 1.2% for men and 0.8% for women²

In Australia between 2001-2010 Annual Percentage Change in death rates fell by 1.1% in Urban areas but by 0.6% in Rural areas.



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1. Annual Report to the Nation on the status of Cancer 1975-2014, featuring survival. Ahmedin Jemal et al JNCI J Natl Cancer Inst (2017) 109(9) : djx0302. 2. Cancer Research UK

3. Australia is continuing to make progress against Cancer, but regional and remote disadvantage remain Michael D Coorey et al MJA 2013; 199(9) 605- 608

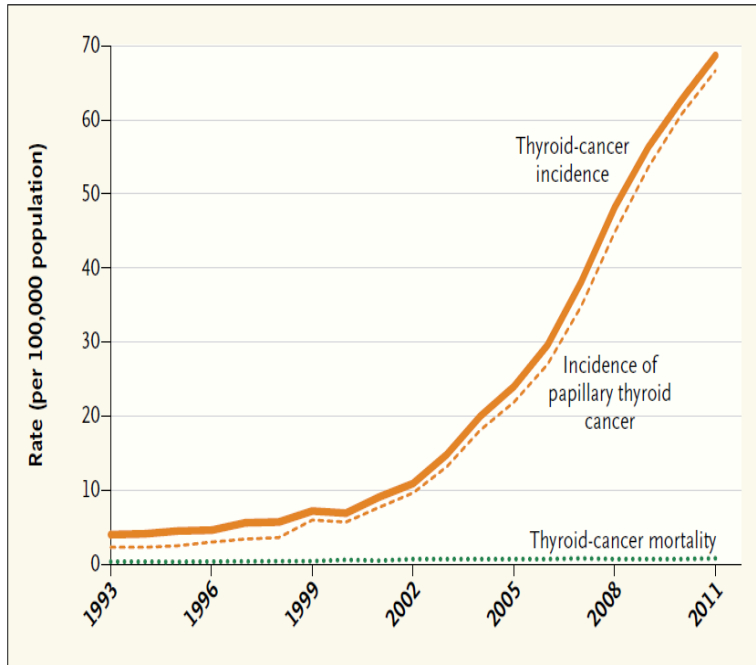
Screening

- Bowel Cancer
- Breast Cancer
- Cervical Cancer
- Lung Cancer (Aged 55-74 ,30 yr pack history (20 Million people in the USA)
- Prostate Cancer (Informed discussion with men with > 10 years of life expectancy)
- Thyroid Cancer (Screening not recommended)



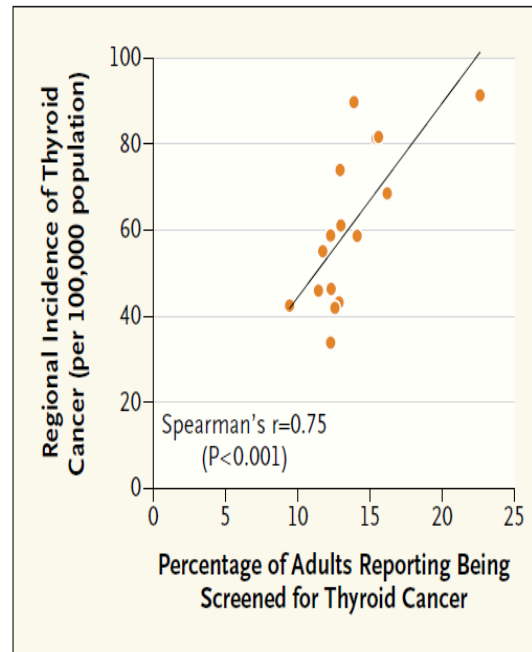
Overdiagnosis

The Diagnosis of “Disease” that will never cause symptoms of death during a patient’s ordinary expected lifetime



Thyroid-Cancer Incidence and Related Mortality in South Korea, 1993–2011.

Data on incidence are from the Cancer Incidence Database, Korean Central Cancer Registry; data on mortality are from the Cause of Death Database, Statistics Korea. All data are age-adjusted to the South Korean standard population.



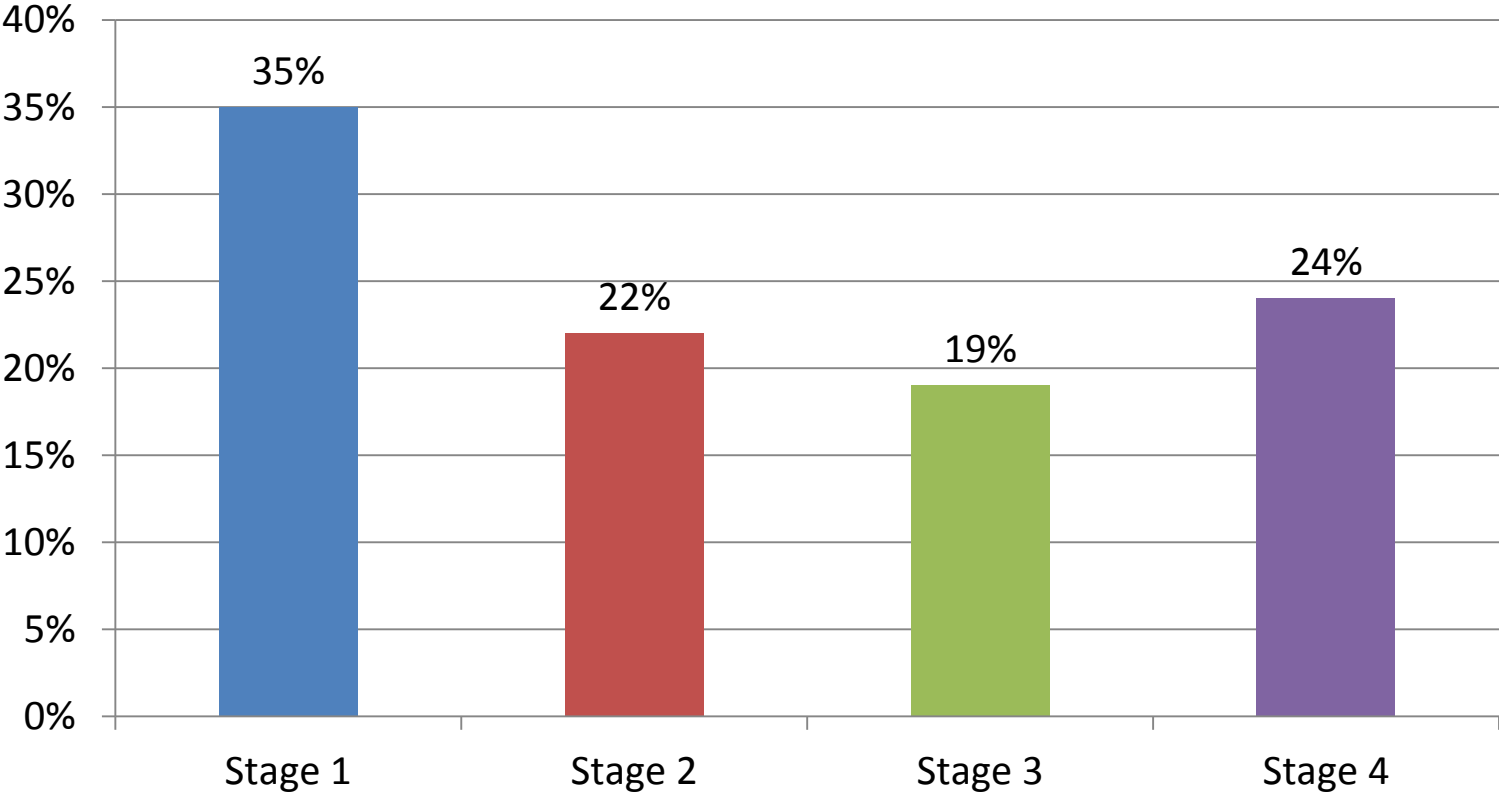
Penetration of Thyroid-Cancer Screening (2008–2009) and Incidence of Thyroid Cancer (2009) in the 16 Administrative Regions of South Korea.

- In Korea- Cost of Thyroid screening \$30.
- 40 000 diagnosed with Thyroid cancer in 2011
- Tumour size < 1 cm rose from 14% to 56%
- 11% going to surgery developed Hypoparathyroidism and 2% vocal cord paralysis

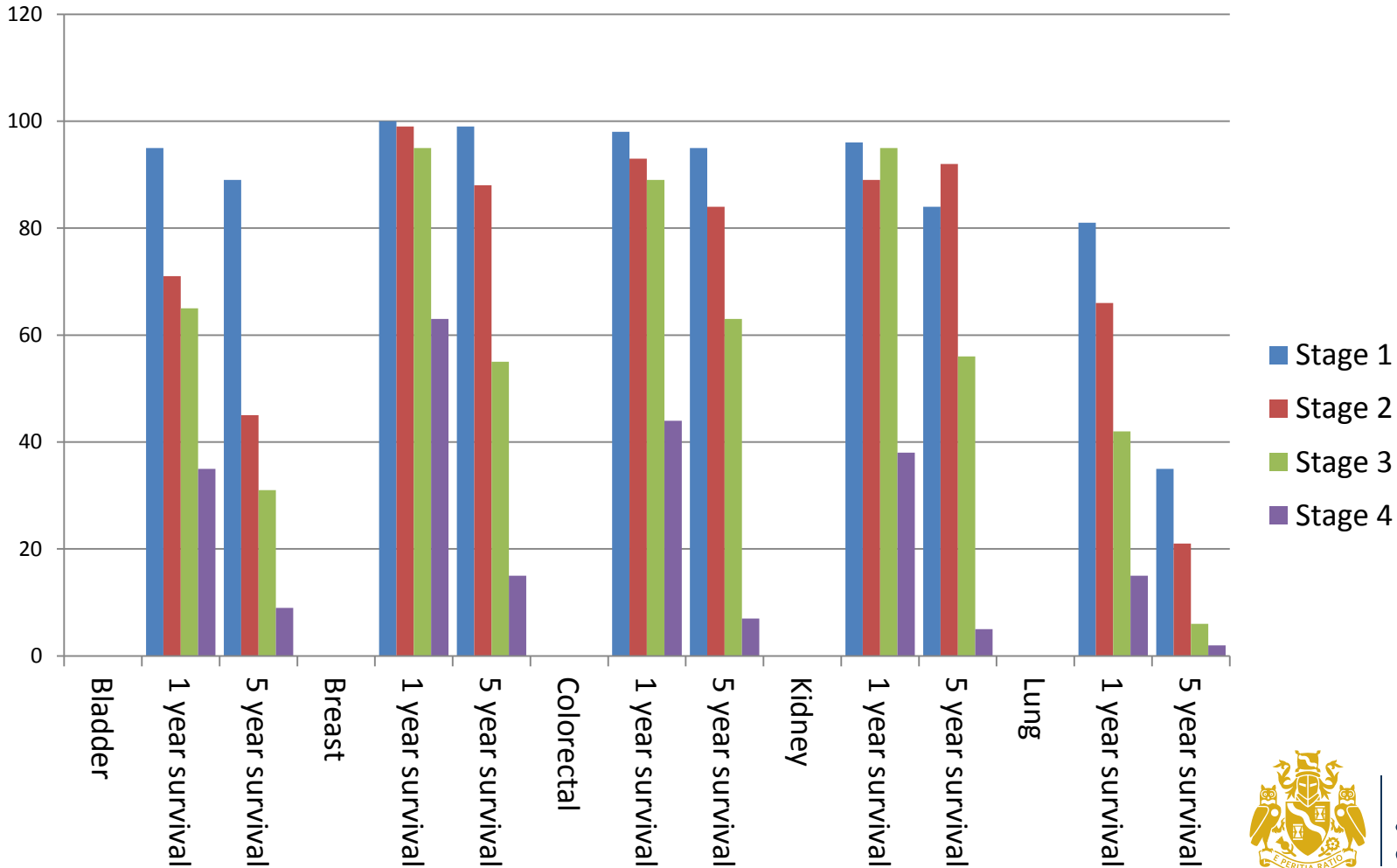


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480,897 cancers by stage at diagnosis UK 2012-2014.



1 and 5 year survival by stage for 5 cancers



10 transformative recommendations

1. Establish a national network allowing patients direct access to trials
2. Create a network devoted exclusively to immunotherapy
3. Develop ways to overcome resistance to therapy
4. Build a national cancer data ecosystem
5. Intensify research on the major drivers of childhood cancer
6. Minimize cancer treatment's debilitating side effects
7. Expand use of proven prevention and early detection strategies
8. Mine past patient data to predict future patient outcomes
9. Develop a 3-D cancer atlas
10. Develop new cancer technologies



Cancer Moonshot Initiatives-10 Transformative initiatives

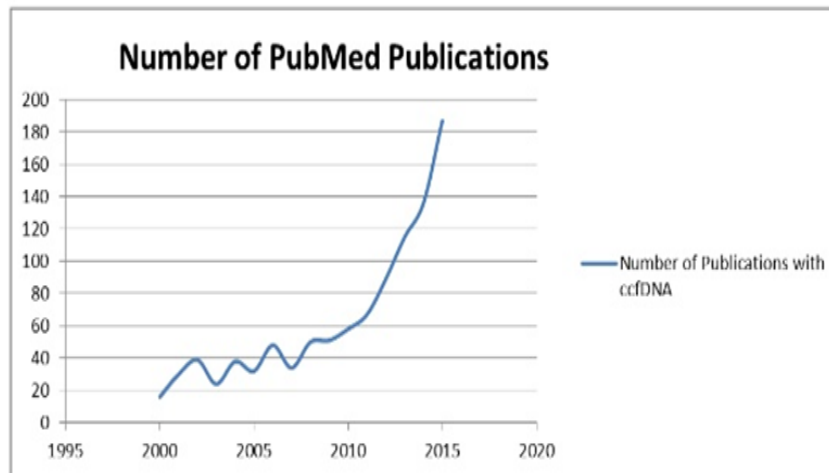


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Liquid Biopsies- Circulating free DNA

- “A liquid Biopsy is a liquid Biomarker that can be isolated from body fluids such as blood, saliva, urine, ascites or pleural effusion. Like a tissue biopsy, a liquid biopsy is representative of the tissue from which it has spread”



The FDA and EMA have approved ctDNA for specific indications in the absence of evaluable tumour tissue.



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Driven by a Need

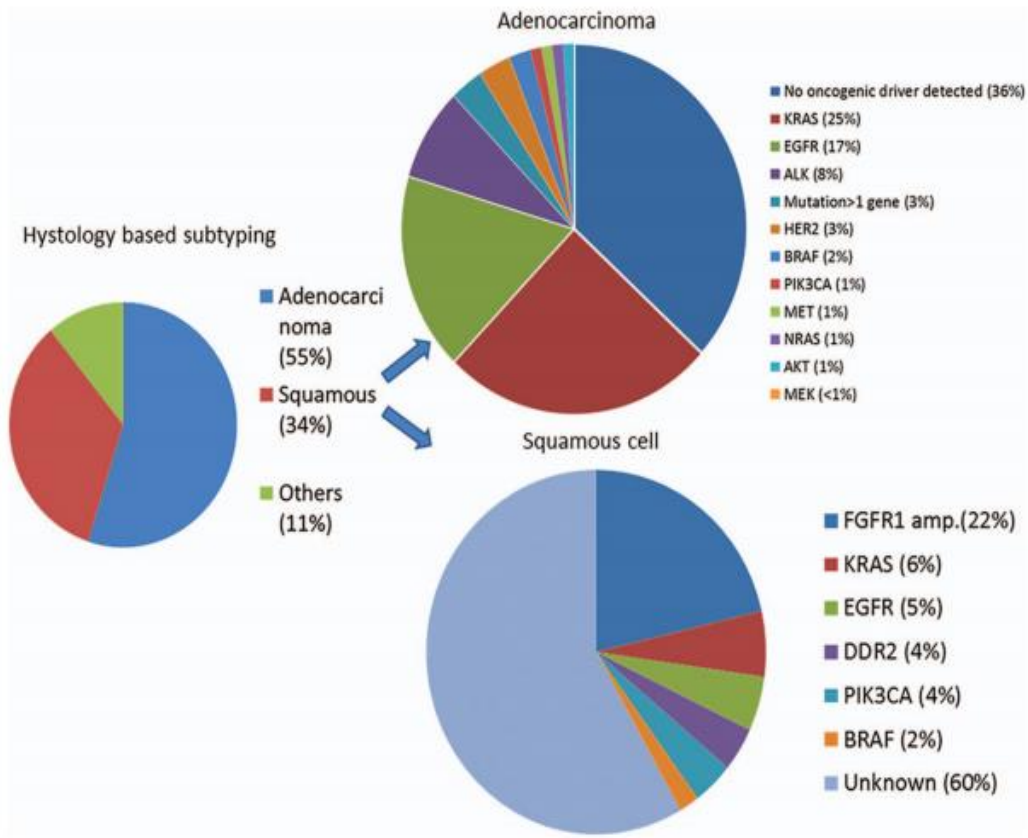


- Prevalence of cancer increasing
- Each patient's cancer is different
- Patient's cancer changes over time
- Effective treatment requires personalised care
- Reducing healthcare costs (\$2 Billion in unnecessary biopsies)
- Major Pharma developing more selective drugs



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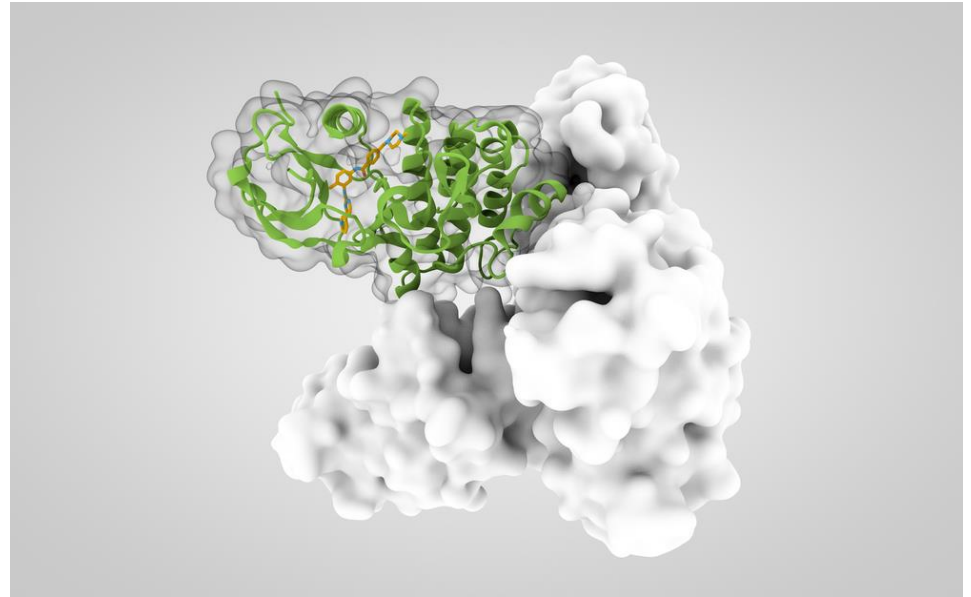
Molecular Subsets of Cancer



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Targeted Therapy – Lock and Key.

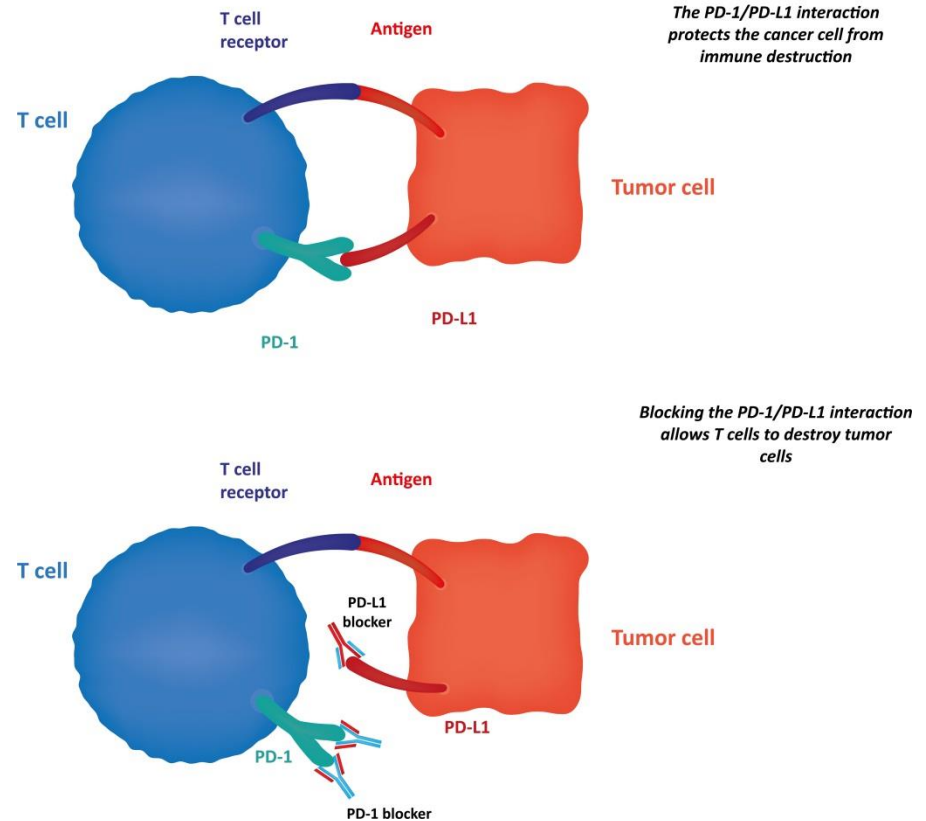
- Targeted cancer treatment molecules lock and communicate with the cancer cell and either:
 - Block or turn off signals that tell cancer cells to grow and divide
 - Prevent cells from living longer than normal
 - Kill the cancer cells
 - Stop the growth of new blood vessels feeding the cancer
- Examples are monoclonal antibodies and small molecule drugs



Immunotherapy

- Immunotherapy helps your own immune system to locate and destroy cancer cells which try every trick in the book to evade detection and death
- The example on the right is a “Programmed Death Ligand 1 inhibitor and it switches off inhibitory signals and allows the immune cell to kill the cancer cell

The PD-1/PD-L1 Blockade



Chronic Myelogenous Leukaemia – The Star of targeted therapy

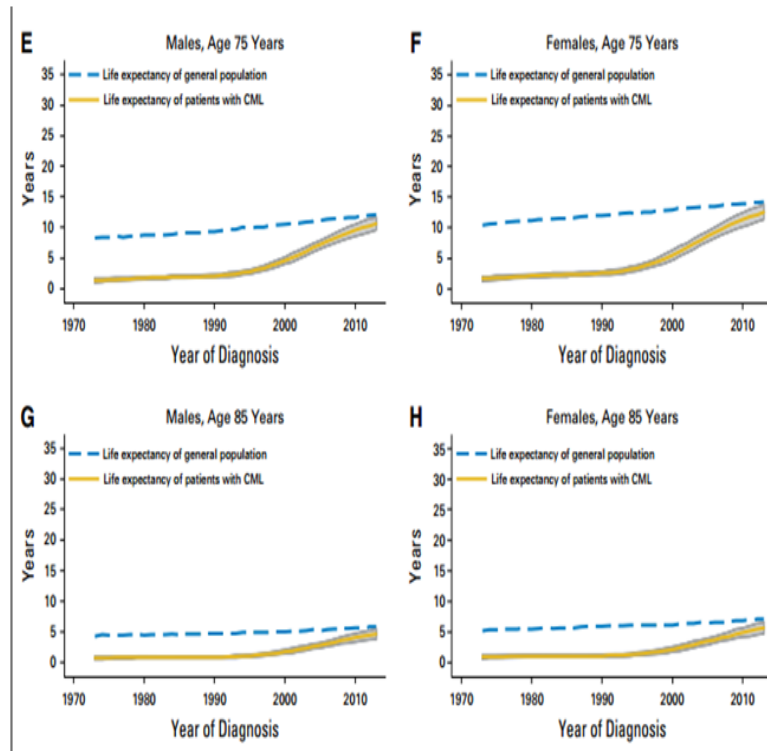


Fig 1. Life expectancy of the general population and of patients with chronic myeloid leukemia in Sweden, over year of diagnosis, by age at diagnosis and sex. Shaded area around the yellow line represents 95% CI. Abbreviation: CML, chronic myeloid leukemia.



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Life Expectancy of Patients With Chronic Myeloid Leukemia Approaches the Life Expectancy of the General Population

Hannah Bower, Magnus Björkholm, Paul W. Dickman, Martin Höglund, Paul C. Lambert, and Therese M.-L. Andersson
Journal of Clinical Oncology 2016 34:24, 2851-2857

Lung Cancer

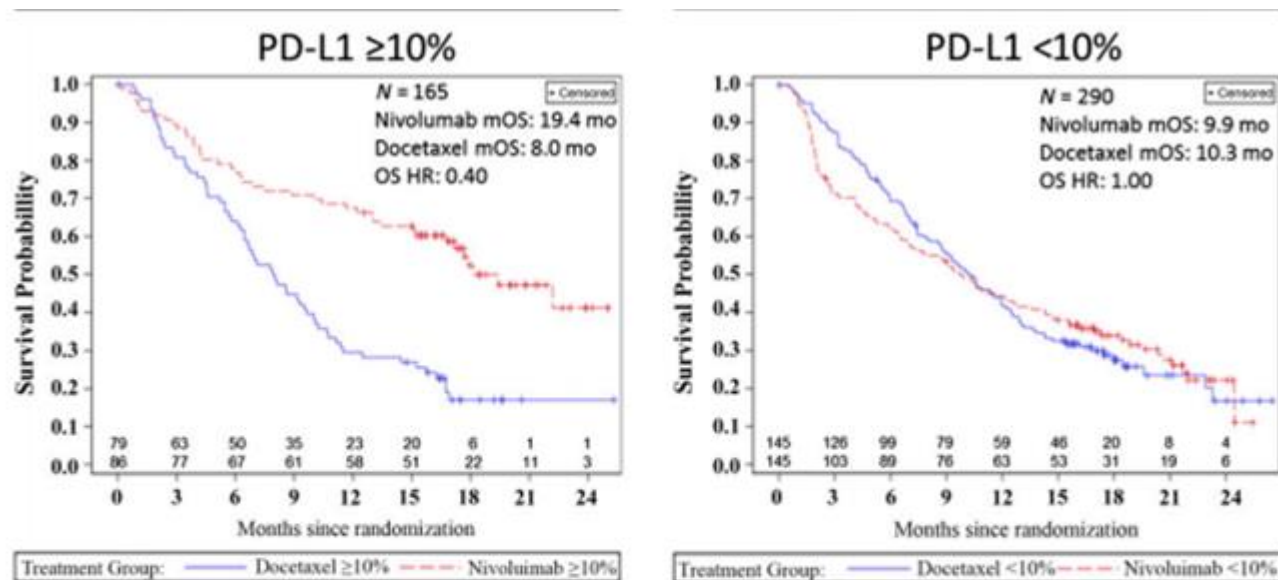


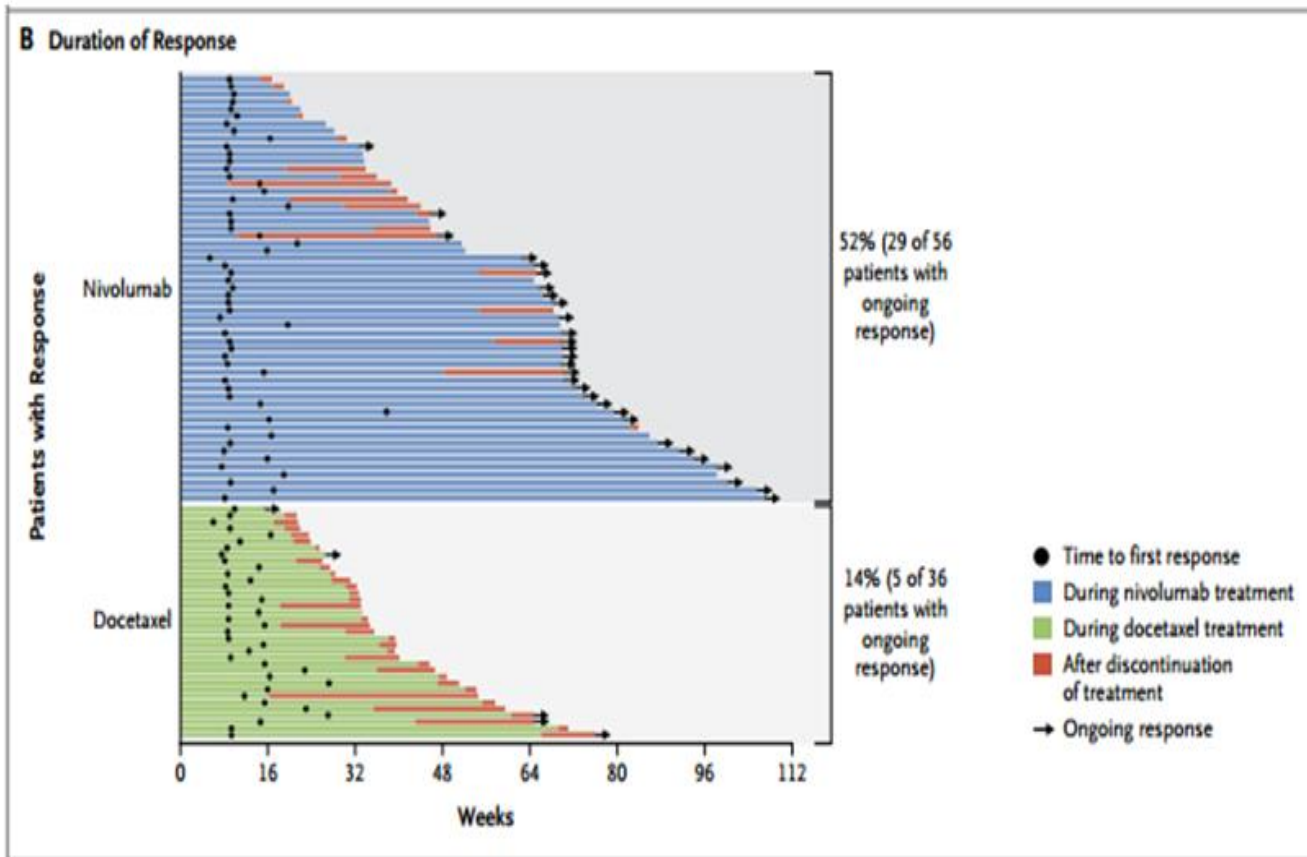
Figure 3. Prespecified retrospective analysis of overall survival represented by Kaplan-Meier survival curves in months based on the PD-L1 cut-points of 1%, 5%, and 10%. Note that the two lines above each x-axis reflect the number of patients at risk.

Abbreviations: HR, hazard ratio; mo, month; mOS, median overall survival; OS, overall survival; PD-L1, programmed cell death ligand 1.



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Immunotherapy in Lung Cancer



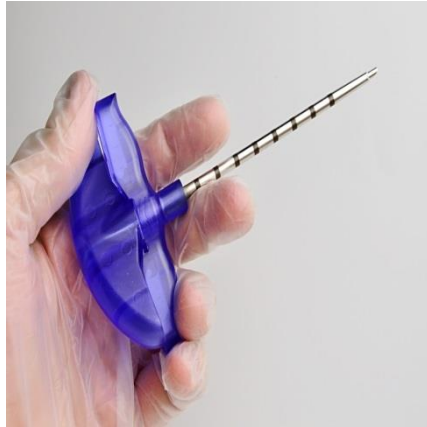
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Non Invasive Prenatal testing started to find Cancer

- “ Sequenom Laboratories revealed today that it’s prenatal genetic test have uncovered cancer in at least 26 pregnant women”



Which one would you prefer?



Prognosis

**Diagnosis
\$15 B (1)**

**Companion
Diagnostics
\$6.7B**

**Recurrence
\$6.9B**



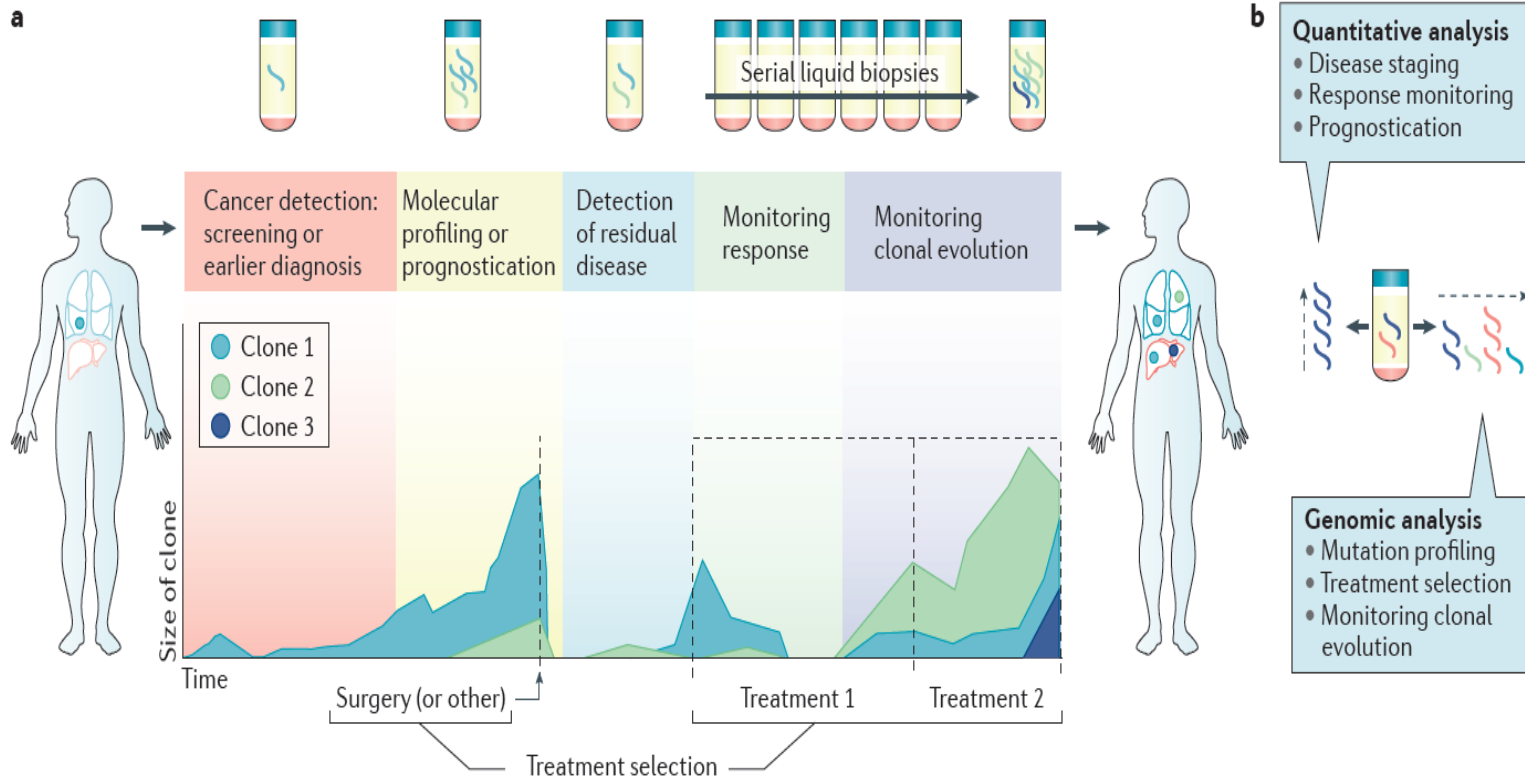
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Advantages of Liquid Biopsies

- Allows for early disease detection
- Faster than classical biopsy testing
- Is cheaper than classical biopsy testing
- Enables the investigation of primary tumours (Molecular profiling)
- You can monitor treatment response
- You can investigate for residual disease, resistance and mutated clones
- Allows for the evaluation of metastases in real time



Application of Liquid Biopsies during the course of Disease Management



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Causes of raised cfDNA other than Cancer



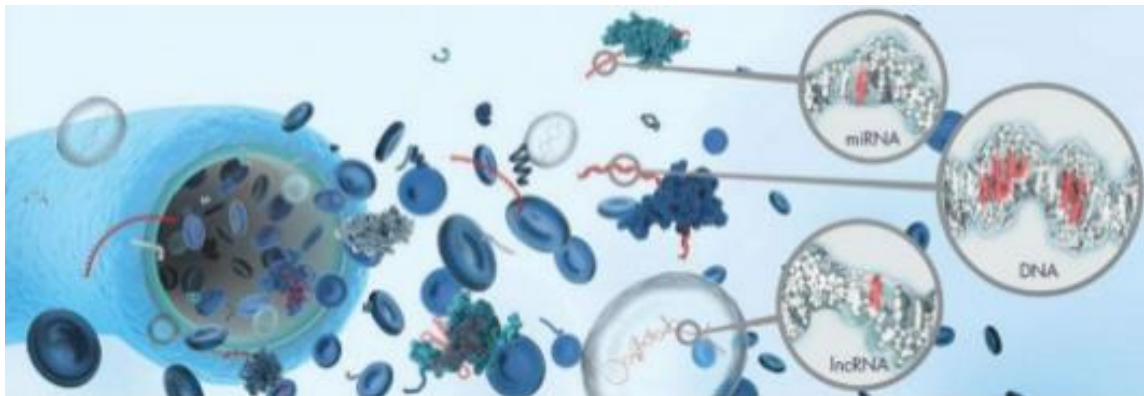
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© Kati1313 | Dreamstime.com - <https://www.dreamstime.com/stock-photo-head-injury-image270810#res18440742>>Head injury

© Hansenn | Dreamstime.com - <https://www.dreamstime.com/stock-photography-wounded-image14754802#res18440742>>Wounded

Refinement and Challenges

- Understand the mechanisms of release
- Understand the mechanisms of degradation
- Understand the factors that affect representation of ctDNA in plasma
- Sometimes extremely low levels of ctDNA are present
- Assay Standardisation



Very Rapid Genome sequencing has become available in 2017

Grail reels in \$900M to bankroll large-scale cancer-screening trials

by Amirah Al Idrus | Mar 1, 2017 9:43am



Grail plans a second close to bring its Series B total beyond \$1 billion.

- Biotech company Illumina can now unravel the human genome in an hour.
- The first purchasers included the Chan Zuckerberg Biohub, MIT and Harvard
- Partnering with IBM Watson linking Artificial Intelligence genomics to Illumina's data to ensure cancer patients receive the specific drugs they need
- Illumina has launched a new company "Grail" to develop a "Pan Cancer" test with lung and Breast being targeted first



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Next Generation of Risk profiling..

- “ In patients with cancer, detection of minimal residual disease by monitoring of peripheral blood after surgery has become the next frontier”
- Successful molecular profiling and matching correct targeted therapy to a cancer and negative liquid biopsies post treatment may be a very useful tool to risk profiling adding to TNM staging and perhaps eventually replacing TNM staging.
- Cancer Type
 - TNM
 - Grade
 - Hormone Receptor
 - **Gene Array profile (Oncotype DX , MammaPrint etc)**
 - **Immunotherapy /Targeted therapy profile**
 - **?Circulating Tumour Cell number**



Breath Test

March 27 2017

- Owlstone Medical announced today that the venture capital arm of Insurance company Aviva has invested \$5 million to support a 3,000 patient study into lung cancer detection using the firms 'breath biopsy'
- The study will focus on lung and bowel cancer and the spectrometry sensors will be portable and suitable for point of care applications
- Aviva Ventures MD investing into entities that look to disrupt the future of insurance. "Going forward preventing medical problems will be just as important as the cure."



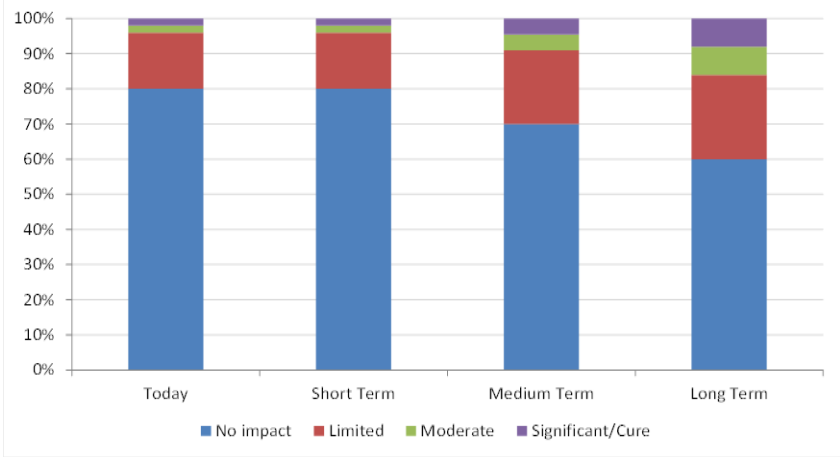
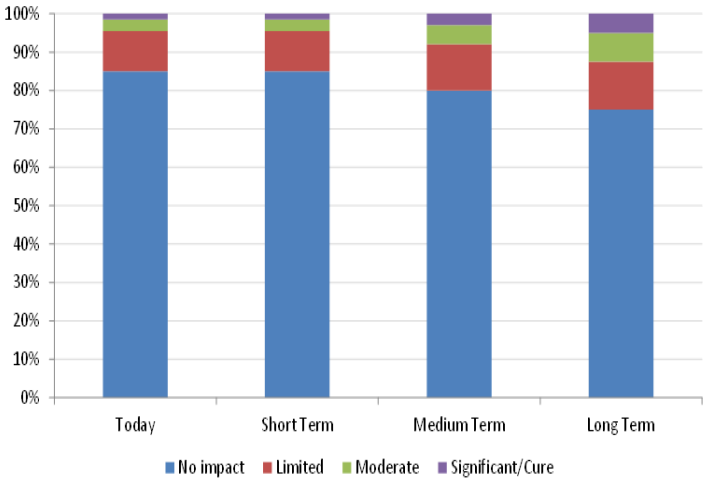
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Are we at a Eureka moment?



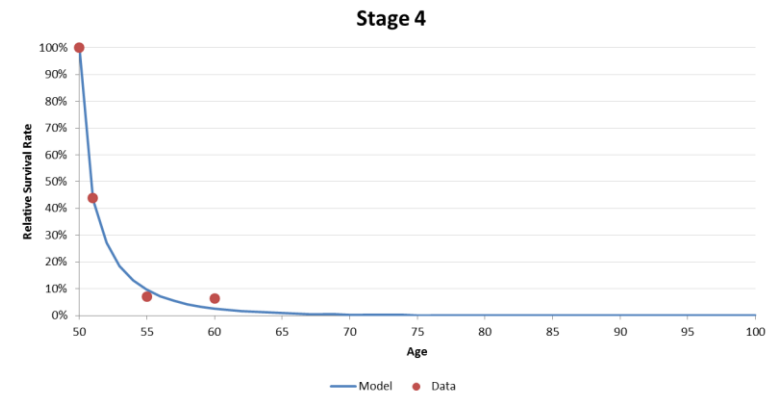
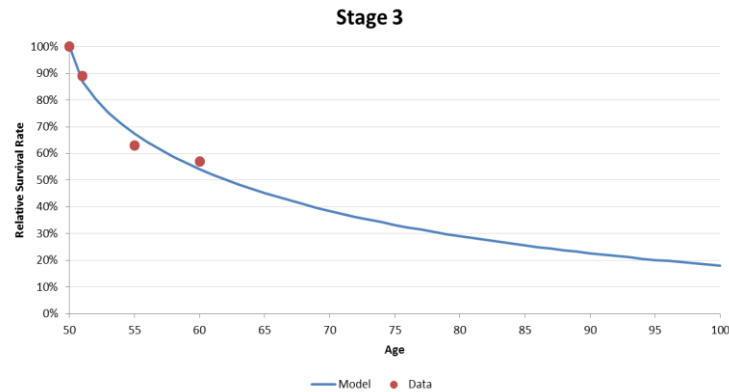
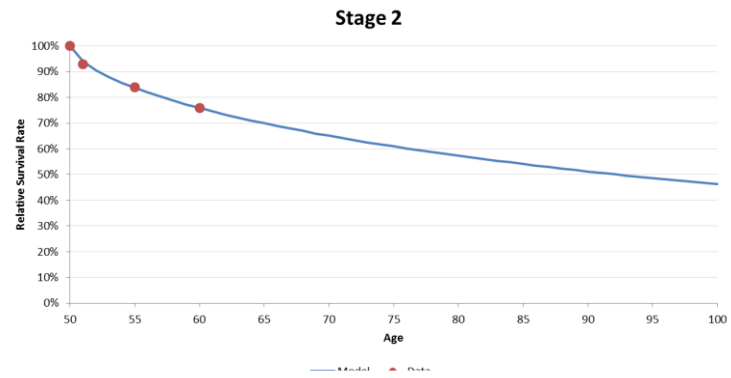
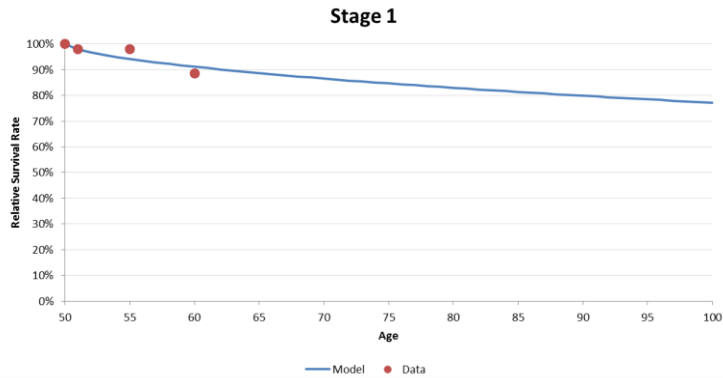
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Projected Impact of Immunotherapy and Targeted therapy on Colon and Lung Cancer survival

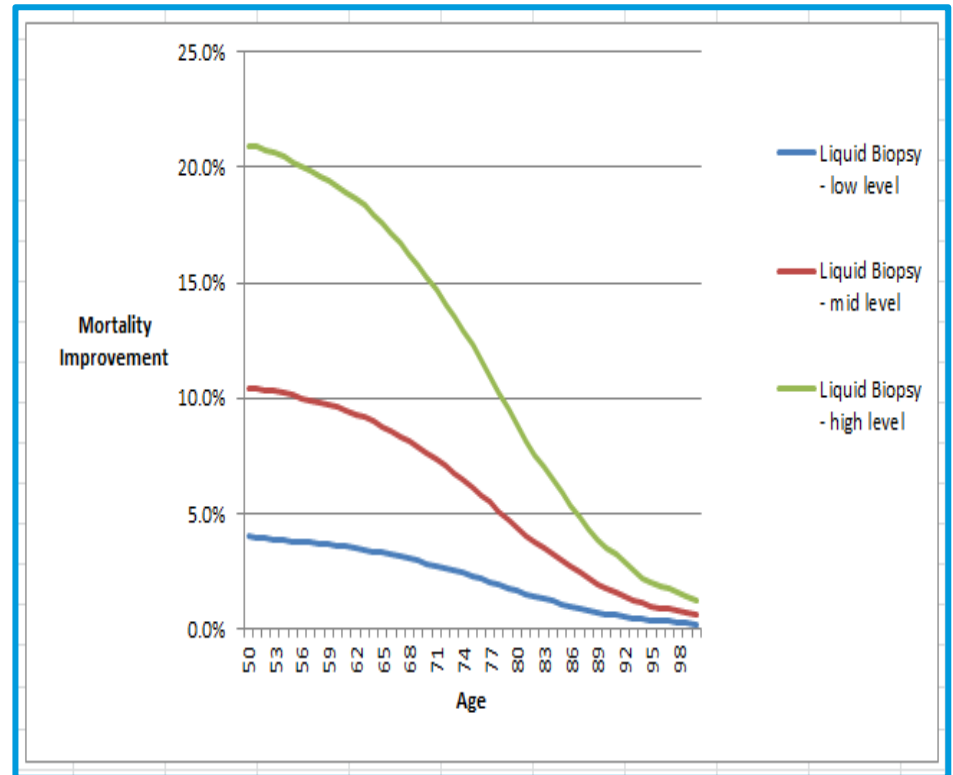
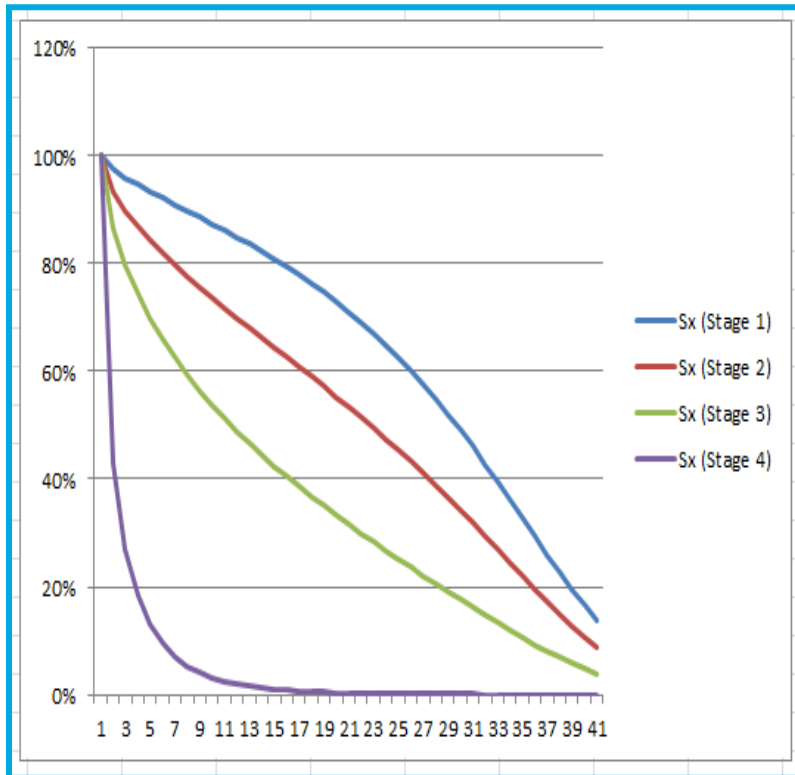


Colon Cancer Survival Rates

Fitted aggregate relative survival rates for colon cancer at age 50



Colon Cancer Survival Rates at potential Mortality improvement if liquid biopsies had to diagnose an additional 5, 10 and 20% of cases in Stage 1 disease rather than Stage 2,3 and 4



Conclusion

- We are at the 'End of the Beginning' of Immunotherapy and targeted therapy in Cancer treatment and it is moving rapidly into mainstream medicine and impacting survival very positively
- Liquid Biopsy is in it's infancy but has the potential to impact survival significantly not only from disease monitoring and aiding treatment choice but potentially also from detecting cancer at an earlier stage.
- Combine the two and you have a major impact on cancer survival.



Thank You.



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