Implications of the changing cancer landscape for insurers

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Changing Cancer Landscape
How do Insurers interact with Cancer Patients?

Source: Diagram adapted from Cancer Care Ontario and other Canadian Cancer Care Organisations
How is the Cancer Landscape changing?

- **PREVENTION**
  - Cancer Vaccines
  - Genetic Predisposition

- **SCREENING**
  - Liquid Biopsy
  - Medical Imaging

- **DIAGNOSIS**
  - Tumour DNA Sequencing
  - Artificial Intelligence

- **TREATMENT**
  - Targeted Therapy
  - Immuno-therapy

- **RECOVERY or SURVIVORSHIP**
  - Relapse Monitoring

- **END-OF-LIFE CARE**
Genetic Testing
Many genes have been identified which indicate elevated risk of cancer

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Relative Risk ≥5.0 Family studies</th>
<th>Relative Risk ≥1.5 and &gt;5.0 Resequencing</th>
<th>Relative Risk ≥1.01 and &gt;1.5 Genome-wide association studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>RB1, <strong>TP53</strong></td>
<td></td>
<td>rs1051730, rs8034191 (CHRNA3, CHRN B4, CHRNA5)</td>
</tr>
<tr>
<td>Breast</td>
<td><strong>BRCA1</strong>, <strong>BRCA2</strong>, <strong>TP53</strong>, PTEN, SK11, CDH1</td>
<td>CHEK2, ATM, PALB2, BRIP1</td>
<td>CASP8, FGFR2, MAP3K1, 8q24, 5p, TOX3, 2q, 6q22, LSP1</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>APC, <strong>MLH1</strong>, <strong>MSH2</strong>, MSH6, PMS2</td>
<td>APC (I1307K), BLM</td>
<td>MUTYH, CASP8, 8q24, 8q23 (EIF3H), 10p14, 11q23, CRAC1, SMAD7</td>
</tr>
<tr>
<td>Prostate</td>
<td><strong>BRCA2</strong></td>
<td>8q24</td>
<td>rs6501455, rs721048, NBS1, EHBP1, TCF2, CTBP2, JAZF1, MSMB, LMTK2, KLK3, SLC22A3</td>
</tr>
<tr>
<td>Pancreas</td>
<td><strong>BRCA2</strong>, CDKN2A, STK11, <strong>TP53</strong>, PRSS1, SPINK1</td>
<td><strong>BRCA1</strong>, <strong>MSH2</strong>, <strong>MLH1</strong></td>
<td></td>
</tr>
</tbody>
</table>

Example: BRCA mutations increase the risk of multiple cancers

**BRCA1/2 LIFETIME CANCER RISKS (%)**

- **Breast**: 12% (45-87% increased)
- **Ovarian**: 2% (11-40% increased)
- **Male Breast**: 0.1% (5-10% increased)
- **Prostate**: 14% (15-20% increased)
- **Pancreatic**: 1.5% (increased)

Source: [http://www.amrygen.com/](http://www.amrygen.com/)
Further changes to the genetic testing landscape

• Direct-to-Consumer Genetic Testing
  
• Polygenic Risk Scores
  
• Regulatory Barriers to use of Genetic Testing in Underwriting
# Responding to cancer predisposition genetic test results

<table>
<thead>
<tr>
<th>Response Type</th>
<th>Higher Predisposition</th>
<th>Lower Predisposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifestyle &amp; Modifiable Risk Factors</td>
<td>Possible lifestyle improvements (e.g., quit smoking, improve diet, exercise more, etc)</td>
<td>No urgent need for change in lifestyle</td>
</tr>
<tr>
<td>Cancer Screening</td>
<td>More frequent / most extensive cancer screening</td>
<td>Less frequent / less extensive cancer screening</td>
</tr>
<tr>
<td>Insurance behaviour</td>
<td>Purchase more insurance (if not prevented by underwriting); Lower propensity to lapse</td>
<td>Purchase less insurance, higher propensity to lapse</td>
</tr>
<tr>
<td>Impact on Cancer / CI Incidence</td>
<td>Higher than average due to high predisposition and more screening</td>
<td>Lower than average due to lower predisposition and lower screening</td>
</tr>
<tr>
<td>Impact on Mortality</td>
<td>Higher than average due to higher predisposition offset by lifestyle changes and early diagnosis</td>
<td>Lower than average due to lower predisposition</td>
</tr>
</tbody>
</table>
Swiss Re’s China consumer survey confirms the rapid growth of genetic testing

Who’s taking these tests?

- Share of 20-50 year old population with a genetic test
  - USA*: 22.5%
  - China*: 17.4%
  - UK*: 7.7%
  - Hong Kong#*: 8.2%
  - Australia*#: 6.8%
  - Japan#: 2.2%

This # jumped in China by 80% last year

- Of these 85% are medically prescribed
- Of these 40% are predictive!
- If you have a family history of a major disease you are almost 6x more likely to take a predictive genetic test

What do they do with the information?

- 25% who take a predictive medical test reveal elevated risk
- 80% of those who are high risk are 2x more likely to buy insurance!
- CI is similar 90% vs 50%

- Those who bought life insurance:
  - 40% with med/low risk vs. 45%
  - 60% with high disease risk vs. 55%

- * Swiss Re genetic testing consumer survey 2018
- # Swiss Re Asia Health Protection Survey 2018

Diagnostics
Early detection of cancer can save lives

**First come, first saved**
United States, five-year relative survival rate by state at diagnosis, 2016, %

- Localised
- Extended
- Metastasised

- Prostate
- Breast
- Cervical and uterine
- Bowel
- Non-Hodgkin lymphoma
- Bladder
- Stomach
- Lung
- Oesophageal
- Liver

Source: SEER
Economist.com
But is earlier diagnosis sometimes too much of a good thing?

Prognosis of Cancer Patients

- No Symptoms
- With Symptoms
- Life Extension with Treatment

Life Expectancy

Theoretical Start of Cancer

Current Diagnosis of Cancer

Normal Life Expectancy

Over-diagnosis?

Diagnosed by Screening

Diagnosed by Symptoms
But is earlier diagnosis sometimes too much of a good thing?

Prognosis of Cancer Patients

1. Earlier Diagnosis of Cancer
2. Extension of Life Expectancy
3. More over-diagnosis???
The road to over-diagnosis is paved with good intentions

**INCREASING**

- Conventional wisdom dictates that earlier Cancer diagnosis means better survival
- Thyroid ultrasound screening is simple and inexpensive
- Thyroid screening is readily packaged with cervical / breast cancer screening
- Once a tumour is diagnosed, almost all patients opt for surgical removal
- Financial incentives for providers in Korea are skewed towards over-diagnosis and treatment
- Cancer registry statistics chart a more than 10-fold increase in thyroid cancer incidence from 1999 to 2012

**DECREASING**

- Patients require lifelong thyroid hormone replacement
- Korea spent USD 242m treating thyroid cancer in 2012
- Physician Coalition for Prevention of Overdiagnosis of Thyroid Cancer formed by 8 prominent physicians in March 2014 to discourage ultrasound screening
- Korean Guideline for Thyroid Cancer Screening developed by Korean Committee for National Cancer Screening Guidelines in April 2015 concluded that “thyroid ultrasound is not routinely recommended for healthy subjects”
- NHI statistics suggest incidence has been fairly flat since 2015

**Incidence Trends for Major\(^1\) Cancers South Korea – Both Sexes – 1999-2016**

1\(^{1}\)Major sites selected based on 2016 crude rates  
Age-standardized Rate (ASR) was standardized to the Korean standard population (year 2000)  
Source: South Korea National Cancer Center  
https://www.ncc.re.kr/main.ncc?uri=english/sub04_Statistics
Meanwhile in China...

Age-Standardized Incidence of Thyroid Cancer in China, 2003 - 2012

- Urban male
- Urban female
- Rural male
- Rural female


Age-Standardized Incidence of Top 10 Female Cancers in Beijing, 2005 - 2014

- Breast
- Lung
- Thyroid
- Colon/rectum
- Uterus
- Kidney
- Ovary
- Stomach
- Liver
- Cervix

Is a simple, cheap, reliable and universal test for cancer just around the corner?

A New $500 Blood Test Could Detect Cancer Before Symptoms Develop

Blood test that can detect eight of the most common cancers could be available in next few years

Cancer blood test ‘enormously exciting’
Liquid biopsy is not fully established yet, but it is coming...

- Things look promising for
  - Relapse or recurrence
  - High risk groups
  - Guidance for treatment of histologically confirmed patients
- The jury is still out for
  - General population screening of asymptomatic individuals

Heitzer, Perakis, Geigl, Speicher, “Precision Oncology Potential of liquid biopsies for the early detection of cancer”, *Nature Partner Journals* 2017 36
Actively monitoring developments in liquid biopsy

**Key Findings**

1. There is not enough evidence, at this time, to know whether use of the majority of ctDNA tests in advanced cancer is justified, outside of screening for participation in, or during, a clinical trial.
2. There is not enough evidence, at this time, to support the routine use of ctDNA tests for early-stage cancer, making treatment decisions, monitoring how well a treatment is working, finding remaining cancer cells, or for cancer screening, except screening for participation in, or during, a clinical trial.
3. There are inconsistent findings when testing with liquid biopsies versus testing with tumor tissue, so negative liquid biopsy results should be confirmed with tumor tissue genotyping.

For the foreseeable future, **histopathology will remain the standard** for cancer diagnosis and staging

Life and health insurance companies should be **actively monitoring** this space for developments

Source: Press release 1 March 2018 on joint paper from ASCO (American Society of Clinical Oncology) and CAP (College of American Pathologists) - Circulating Tumor DNA Analysis in Patients With Cancer.
Insurers need to address over-diagnosis via product design and definitions

• Addressed via exclusions and partial benefits

• Major sites of concern
  – Early-stage Thyroid
  – Early-stage Prostate
  – Carcinoma in Situ and other Pre-Malignant conditions
  – Non-Melanoma Skin

• Do we need an exclusion for diagnosis solely by liquid biopsy?
  – Cancer diagnosed on the basis of finding tumour cells and/or tumour associated molecules in blood, saliva, faeces, urine or any other bodily fluid in the absence of further definitive and clinically verifiable evidence
  – Alternative approach is to strengthen the requirement for histopathological evidence
Treatment
What does the future hold for cancer treatment?

• New & Expensive Treatments
  - More and more expensive cancer treatments being developed (mainly drugs)
  - More treatments excluded from National / Social Health Insurance systems (although in China, the first step will be to increase the coverage of Social Health Insurance)
  - More use of drugs for off-label and experimental purposes
  - More difficult claims adjudication / management for cancer drug reimbursement
  - More challenges to cost vs benefit (survival and Quality of Life) of new cancer treatments
  - Reimbursement with high benefit limits and without insurer control becomes more risky

• Patient Viewpoint
  - More treatment options with large variations in cost
  - More confusion about treatment options
  - More variation in recommendations from treating doctors
So many new cancer drugs in development...

Pipeline of Late Phase Oncology Molecules 2007 - 2017

<table>
<thead>
<tr>
<th>Year</th>
<th>2007 (434)</th>
<th>2017 (710)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiotherapies</td>
<td>0.9% (4)</td>
<td>0.4% (3)</td>
</tr>
<tr>
<td>Hormonals</td>
<td>3% (14)</td>
<td>2% (17)</td>
</tr>
<tr>
<td>Cytotoxics</td>
<td>15% (63)</td>
<td>8% (54)</td>
</tr>
<tr>
<td>Targeted Small Molecule</td>
<td>59% (254)</td>
<td>47% (335)</td>
</tr>
<tr>
<td>Targeted Biologics</td>
<td>23% (99)</td>
<td>42% (301)</td>
</tr>
</tbody>
</table>

Source: IQVIA, ARK R&D Intelligence, Dec 2017; IQVIA Institute, Mar 2018
And so expensive...

### Average Annual Costs For Oncology Products by Launch Year in the United States

- **Source:** ICVIA Institute, Apr 2018
## And many of the new and expensive ones are not very cost effective...

<table>
<thead>
<tr>
<th>QoL Impact</th>
<th>Drug Name</th>
<th>Cancer Type</th>
<th>Comparison</th>
<th>Annual Cost (US)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Better</td>
<td>Crizotinib</td>
<td>Non-small-cell lung</td>
<td>Conventional Chemotherapy</td>
<td>$169,680</td>
</tr>
<tr>
<td>No difference</td>
<td>Pazopanib hydrochloride</td>
<td>Soft-tissue sarcoma</td>
<td>Placebo</td>
<td>$112,572</td>
</tr>
<tr>
<td></td>
<td>Bevacizumab</td>
<td>Breast</td>
<td>Placebo</td>
<td>$134,125</td>
</tr>
<tr>
<td></td>
<td>Bendamustine hydrochloride</td>
<td>Chronic lymphocytic leukaemia</td>
<td>Conventional Chemotherapy</td>
<td>$53,315</td>
</tr>
<tr>
<td></td>
<td>Axitinib</td>
<td>Renal cell carcinoma</td>
<td>Cheaper Targeted Therapy Drug</td>
<td>$143,184</td>
</tr>
<tr>
<td></td>
<td>Rituximab</td>
<td>Follicular lymphoma</td>
<td>Observation</td>
<td>$20,237</td>
</tr>
<tr>
<td></td>
<td>Ofatumab</td>
<td>Chronic lymphocytic leukaemia</td>
<td>Observation</td>
<td>$64,494</td>
</tr>
<tr>
<td>Worse</td>
<td>Peginterferon alpha-2b</td>
<td>Melanoma</td>
<td>Observation</td>
<td>$26,268</td>
</tr>
<tr>
<td></td>
<td>Cabozantinib-S-malate</td>
<td>Medullary thyroid</td>
<td>Placebo</td>
<td>$169,836</td>
</tr>
<tr>
<td>Mixed</td>
<td>Everolimus</td>
<td>Renal cell carcinoma</td>
<td>Placebo + Other</td>
<td>$144,840</td>
</tr>
<tr>
<td></td>
<td>Pazopanib</td>
<td>Renal cell carcinoma</td>
<td>Placebo + Other</td>
<td>$112,572</td>
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<td>Placebo</td>
<td>$144,840</td>
</tr>
<tr>
<td></td>
<td>Bevacizumab</td>
<td>Glioblastoma</td>
<td>Placebo + Other</td>
<td>$134,125</td>
</tr>
<tr>
<td>No evidence</td>
<td>Nilotinib</td>
<td>Ph-positive chronic myeloid leukaemia</td>
<td>N/A</td>
<td>$132,924</td>
</tr>
<tr>
<td></td>
<td>Bevacizumab</td>
<td>Renal cell carcinoma</td>
<td>N/A</td>
<td>$134,125</td>
</tr>
<tr>
<td></td>
<td>Everolimus</td>
<td>Pancreatic neuroendocrine</td>
<td>N/A</td>
<td>$144,840</td>
</tr>
<tr>
<td></td>
<td>Bendamustine</td>
<td>Indolent non-Hogkin lymphoma</td>
<td>N/A</td>
<td>$85,358</td>
</tr>
<tr>
<td></td>
<td>Dasatinib</td>
<td>Ph-positive chronic myeloid leukaemia</td>
<td>N/A</td>
<td>$130,392</td>
</tr>
</tbody>
</table>

Few new drugs are readily available, especially in emerging markets...

Year 2017 Availability of 55 Oncology Medicines First Launched Globally 2012–2016

China developments
- C-FDA in 2018 approved 16 new cancer drugs
- From 1 Dec 19, import and sale of new drugs approved by US, European or other major country FDA will no longer be illegal in China

Source: IQVIA MIDAS, Dec 2017
So what role should insurers play?

Insurance products can provide to customers

- financing for a wider choice of treatments
- access to more expensive treatment options

But how should customers exercise that choice?

- maximise effectiveness of treatment for a given cost
- target level of effectiveness with available resources

Needs-Based Products
Insurers can help navigate the complex landscape of Cancer treatment

- Surgery
- Radiotherapy
- Chemotherapy
- Hormone Therapy
- Targeted Therapy
- Immunotherapy
- Combination Therapy
- Clinical Trials
- Side-Effect & Pain Management
- Alternative Therapies
And address many other unmet support needs for Cancer patients

- Specialist Referral
- Second Opinion
- Own Research
- Lifestyle Changes
- Psychological Support
- Social Support
- Spiritual Support
- Financial Counselling
Cancer Products of the Future – an Ecosystem of Care?

**Prevention**
- Wellness & health monitoring
- Cancer prevention

**Screening**
- Regular screening & check-ups

**Diagnosis**
- Lump sum upon diagnosis (amount varies by severity)
- Navigator services for medical second opinion, overseas treatment

**Treatment & Support**
- Testing for targeted therapy suitability
- Systematic side effect logging
- Liquid biopsy relapse monitoring
- Platform for patient support & counselling

**Recovery**
- Rehab services, Occupational therapy
- Cancer survivor returning to work
Future of Cancer
The Future of Cancer – What do we know? What don’t we know?

*There are known knowns. There are things we know that we know. There are known unknowns. That is to say, there are things that we now know we don’t know. But there are also unknown unknowns. There are things we do not know we don’t know.*

- Donald Rumsfeld

<table>
<thead>
<tr>
<th>Near Certainties</th>
<th>Quite Probable</th>
<th>Unknowns (today)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Continued push for earlier detection of cancer</td>
<td>- A wider variety of diagnostic tests, treatment options and financing models (potentially more confusion among providers and patients)</td>
<td>- Will liquid biopsy overtake histopathology as the “gold standard” for diagnosing some types of cancer?</td>
</tr>
<tr>
<td>- More accurate diagnostic tests available for some cancers</td>
<td>- More expensive personalised treatments for cancer (mostly more effective, some very much more effective)</td>
<td>- Will liquid biopsy / non-invasive tests be used for mass screening?</td>
</tr>
<tr>
<td>- Improved treatments (more effective, fewer side-effects)</td>
<td>- More patients on long-term follow-up for cancer with some on maintenance therapy (to prevent recurrence, with few side-effects)</td>
<td>- Will the medical profession be able to restrain over-diagnosis and over-treatment of low-risk cancers?</td>
</tr>
<tr>
<td>- Continued improvements in survival, lower cancer mortality</td>
<td>- Not much further progress on cancer prevention?</td>
<td>- Will low-risk cancers be reclassified?</td>
</tr>
<tr>
<td>- Improved identification and monitoring of high-risk patients (genetic / environmental)</td>
<td></td>
<td>- Will Cancer / CI products with long-term guarantees turn out to be profitable?</td>
</tr>
<tr>
<td>- Improved monitoring of relapse or recurrence (less invasive, earlier detection, more accurate)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In an increasingly complex cancer landscape, insurers need to anticipate and monitor medical developments very closely – the sustainability of our products and the well-being of our customers depends on it!
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