Improving earlier diagnosis: reflections and projections from primary care

Willie Hamilton
GP and professor of primary care diagnostics
University of Exeter

Early Diagnosis Conference, Birmingham, February 2019
Back in the good old days...

- GPs taught in secondary care, both as students and post-graduates.
- We didn’t experience the complexity of some cancer diagnoses.
- Once qualified we learned on the job – and in the later years of our career were probably jolly good at spotting possible cancer.
- There were tests: bloods (but how much use are they?); CXR, Barium enema, ultrasound, but most patients had to be referred.
- And referrals were either routine, or urgent (or private) with little feedback other than routine letters, or the rare solicitor’s letter.
Overall...

- Cancer was a non-subject for GPs, other than end-of-life
- We simply didn’t know that our cancer outcomes were poor
- And we had hundreds of other clinical subjects to compete for our attention
And this manifested as...

- Poor survival
- A high percentage of emergency diagnoses (but not recognised)
- Adverse stage at diagnosis (but as staging was ill-reported, this was largely invisible)
- Nobody trying to improve cancer diagnosis: not the DH, not the politicians, not the charities, not even Big Pharma
...but we were part of the problem...

Table 1. Countries (n = 19) with a survival score or total relative 1-year survival above median in relation to gatekeeper system, list system, and primary care being first point of contact

<table>
<thead>
<tr>
<th>Gatekeeper</th>
<th>Survival score</th>
<th>1-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>78.0</td>
<td>0.006</td>
</tr>
<tr>
<td>No</td>
<td>73.4</td>
<td>0.004</td>
</tr>
<tr>
<td>List system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>85.5</td>
<td>0.006</td>
</tr>
<tr>
<td>No</td>
<td>73.4</td>
<td>0.004</td>
</tr>
<tr>
<td>Primary care as first point of contact</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>119.25</td>
<td>0.007</td>
</tr>
<tr>
<td>No</td>
<td>73.4</td>
<td>0.004</td>
</tr>
</tbody>
</table>

*High survival score indicated more cancer types with fivest quartile of 1-year survival. #Non-parametric
median/rank sum test. Fisher's exact test when cells with count less than five.
...and it was (partly) because we were investigating less than our sister countries.
From a GP perspective, the Big Bang was...

- The Two Week Wait clinics: cancer was *different/special*
- They were modelled on a prototype of the breast clinics, which may not have been the best model
- They came in over a 2-year period, alongside *weak* guidance about who should be referred
- This had some counter productive aspects, particularly atypical presentations

*BMJ* 2001;322:1555-1556
doi:10.1136/bmj.322.7302.1555

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A ‘Slower Bang’ was … a mushrooming of GP research

This was mostly into WHO to test, and was enshrined in the NICE NG12 guidance, BUT now...

It’s HOW to test:
• FITs – what is the optimum threshold for a positive?
• In possible ovarian, TVUS or Ca125; or both?
• In possible lung, is CT a better first choice than CXR?
Multi-parametric magnetic resonance imaging

In possible prostate, trans-rectal biopsy generates under- and overdiagnosis

Is mpMRI more accurate?
Could it be done in primary care?

Sam Merriel

#CRUK10YearsOfEarlyDiagnosi5
These tables illustrate the tensions between primary and secondary care.
...but it is saving lives...

<table>
<thead>
<tr>
<th>Variable and group</th>
<th>Median value</th>
<th>Lowest value</th>
<th>Highest value</th>
<th>No of people</th>
<th>No of deaths</th>
<th>Hazard ratio (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Referral ratio</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>0.68</td>
<td>0.20</td>
<td>0.86</td>
<td>71,773</td>
<td>31,136</td>
<td>1.05 (1.04 to 1.07)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>1.01</td>
<td>0.86</td>
<td>1.16</td>
<td>71,768</td>
<td>30,417</td>
<td>1.00</td>
</tr>
<tr>
<td>High</td>
<td>1.39</td>
<td>1.16</td>
<td>3.44</td>
<td>71,743</td>
<td>30,067</td>
<td>0.97 (0.96 to 0.99)</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Conversion rate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>0.08</td>
<td>0.00</td>
<td>0.10</td>
<td>71,811</td>
<td>30,206</td>
<td>1.00 (0.99 to 1.02)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>0.12</td>
<td>0.10</td>
<td>0.14</td>
<td>72,101</td>
<td>30,672</td>
<td>1.00</td>
</tr>
<tr>
<td>High</td>
<td>0.17</td>
<td>0.14</td>
<td>1.00</td>
<td>71,372</td>
<td>30,762</td>
<td>1.01 (1.00 to 1.03)</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.117</td>
</tr>
<tr>
<td><strong>Detection rate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>0.33</td>
<td>0.00</td>
<td>0.39</td>
<td>71,804</td>
<td>31,072</td>
<td>1.04 (1.02 to 1.06)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>0.43</td>
<td>0.39</td>
<td>0.48</td>
<td>72,065</td>
<td>30,769</td>
<td>1.00</td>
</tr>
<tr>
<td>High</td>
<td>0.54</td>
<td>0.48</td>
<td>1.00</td>
<td>71,415</td>
<td>29,799</td>
<td>0.96 (0.95 to 0.98)</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
...and continues to do so....
But how much of this improvement is early diagnosis?

Certainly some – as the emergency admission percentage shows
But have times to diagnosis fallen?
And stage at diagnosis? Is it better?
The hope is to have 75% of cancers diagnosed at Stage 1 or 2 in 10 years.

This includes:
- Lowering the threshold for investigation
- Rapid diagnosis centres
- More CT and MRI scanners
Lowering the threshold for investigation?

The ERICA trial examines the use of GP software to identify patients with at least a 2% risk of any of: oesophago-gastric, lung, colorectal, ovarian, kidney or bladder.

It’s massive, requiring 710 practices to take part.

It builds on considerable preliminary work by Macmillan and CRUK, and is funded by a philanthropic grant from D & M Gillings.

EOIs to: erica@exeter.ac.uk

#CRUK10YearsOfEarlyDiagnoses
Does it have to be GPs, and GPs alone...?

We have many skilled disciplines available

Alexander Thomson

#CRUK10YearsOfEarlyDiagnoses
How will we lower the threshold?

Is it simply GPs not thinking of cancer?
Or being discouraged from doing so?
Are there areas in the GP consultation which are contributing?
Is the answer cell-free DNA – the ‘liquid biopsy’?

Or volatile organic compounds?
Or biomarkers?
...but let’s have a reality check (sorry)...

Diagnostic Biomarkers: Are We Moving from Discovery to Clinical Application?

Lucy A. Parker, Elisa Chillet-Rosell, Ildefonso Hernández-Aguado, María Pastor-Valero, Sonia Gea, Blanca Lumbierbas

DOI: 10.1372/clinchem.2019.202084 Published October 2019

**RESULTS:** In the 10-year period analyzed, 4257 articles cited the 107 diagnostic studies; 118 (2.8%) were diagnostic studies of the same test, and of these papers, 25 (21.2%) did not constitute progress toward validation of the test for use in clinical practice (potential research waste). Of the 107 molecular- or “omics”-based tests described in 2006, only 28 (26.2%) appeared to have made progress toward clinical application. Only 4 (9.1%) of 44 proteomics-based tests had made progress toward clinical application.
• The ACE programme MDCs largely targeted awkward symptoms
• They could offer a rapid-test service
• This would need good supporting information, as most would test-negative, yet still have symptoms
• Could they be open access?
Can we learn from Denmark?

Can we trust a negative test?
We’ve come a very long way from ignorance and bad cancer figures:
It’s now understanding, and fair cancer figures
There’s a reasonable chance improvements will continue
GPs want to be part of the solution, and can take pride in progress

There are some potholes though:
GPs are overworked, and numbers static
Some hospital specialities are really struggling: notably radiology and scoping
Testing must increase, so must be simpler and slicker
We must do the right test, at the right time, and in the right patient, and for the right cost

Thank you