The epidemiology of cancer diagnosis: Current problems, future directions

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The challenge of early diagnosis
  – And the contributions of epidemiology

Recent / current research examples
  – Measuring early/late diagnosis in patient populations

Future research needs & opportunities
  – Broader alliances across disciplines / disease areas
The challenge of early diagnosis
  – And disciplinary contributions from epidemiology

Recent / current research examples
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The challenge of early diagnosis comprises ‘two problems’

- **The forever problem**
  - 50 common symptoms nested within 8000 diseases (cancer / non-cancer; self-limiting / consequential)

- **The now problem**
  - We don’t know how best to support patients / doctors / systems in the Dx process
  - Limited (screening / diagnostic) tests
  - Services ill-equipped for the challenge (at least in UK)
The diagnostic process is complex and “distributed in space and time”; multiple actors; many “socio-technical” aspects

- US Institute of Medicine, *Improving Diagnosis In Health Care* 2015
- Scott SE, Walter FM et al, *BJHP* 2013
‘Epidemiology of early diagnosis / diagnostic healthcare’

Mission:

Identifying who is at greater / lower risk of untimely Dx

• Critical for elucidating responsible mechanisms and targeting interventions / evaluations – only

• Borrowing of methods from treatment disparities research

• Increasing number of organisations / groups involved
A new discipline (last decade and a bit...)

- **Many more** epidemiology papers currently on whether coffee/tea cause cancer, than early diagnosis

- Many key papers appeared post-2005 (examples all UK)
  - **CPRD PPV**: Hamilton & Kenrick *2007*; Jones et al *2007*
  - **Awareness in populations**: Robb et al *2009*; Waller et al *2009*
  - ‘**Routes**’: Elliss-Brookes et al *2012*; McPhail et al *2013*
  - **Patient-reported delays**: Neal & Allgar *2005* (X2); Lyratzopoulos et al *2012*
  - **First UK audits in primary care**: Baughan P et al, BJC *2009*; Rubin et al *2011*
We cannot measure early / late diagnosis effectively in the population without....

- A high quality cancer registration system and the data linkages it enables

- Critical role of
  - And its predecessors since 2008 and ‘peers’ in Scotland, Northern Ireland and Wales

- Large amounts of innovation and intellectual property generated ‘in-house’
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Timely diagnosis matters – beyond improving survival

- Treatment-related morbidity / side-effects
- Cost of treating advanced disease
- Patient safety incidents (complaints)
- Efficiency
- Patient experience

Covered by Professor Peter Johnson
Timely diagnosis matters – beyond improving survival

- Treatment-related morbidity / side-effects
- Cost of treating advanced disease
- Patient safety incidents (medico-legal complaints)
- Efficiency

Patient experience
Patients with 3+ pre-referral consultations more likely to report negative experience of subsequent cancer care compared with patients with 1-2 consultations.

Stronger associations for care aspects relating to/involving primary care...

Measures in early diagnosis epidemiology

Direct (time) measures
- Patient interval
- Primary care int.
- ‘System’ interval

Surrogate markers
- Emergency presentation
- Stage at Dx

Dx activity metrics
- Endoscopy
- Imaging
- Referrals

Relate to patients with cancer

Adapted from Lyratzopoulos G Cancer Epidemiol 2014

Patients with/without cancer
Correlations between measures-markers-activity metrics

Direct measures
- Patient interval
- Primary care int.
- ‘System’ interval

Surrogate markers
- Emergency presentation
- Stage at Dx

Dx activity metrics
- Endoscopy
- Imaging
- Referrals
Direct (time) measures

Surrogate markers

Dx activity metrics

Patient level

Organisational (geographical) level
Examples of recent / current research in respect of...

- **Direct measures**
  - Patient interval

- **Surrogate markers**
  - Emergency presentation

- **Dx activity metrics**
  - Referrals
Examples of recent / current research in respect of...

Direct measures

Surrogate markers

Dx activity metrics

Referrals
The ‘wrong demographic’ problem

2WW referral **less likely** in low cancer incidence groups (where PPV is low)

Dx referral guidelines work but for the ‘common’ patient

Complementary approaches needed
- Active follow-up (‘safety netting’)
- New Dx tests / services - “ACE / MDC”

Examples of recent / current research in respect of...

- **Direct measures**
- **Surrogate markers**
  - Emergency presentation
- **Dx activity metrics**
Map of evidence on Emergency Presentations (circa 2016)

- Algorithmic definitions in administrative or electronic health record datasets
  - Abel, Bottle, Comber, Elliss-Brookes, McPhail, Nouraei, Palser, Raine, Renzi, Shawihdi, Sheringham, Sikka, Tataru, Tsang, Wallace and all routes to diagnosis data online reports
- Emergency services used?
  - Clinical criteria (whether life-threatening symptoms present, or emergency treatment used)
    - Dejardin
  - Contextual criteria (whether patient presented to emergency services)
    - Cleary, Gunnarsson
    - Gunnarsson 2013, Mc Ardle
- Patient critically ill?
  - Medical record review used to define emergency presentations

Map distils 13K abstracts in multiple data sources

Zhou Y et al, 2016 Nat Rev Clin Oncol
Emergency presentation: A complex, multi-factorial phenomenon

Zhou Y et al, 2016 Nat Rev Clin Oncol
Model relates to Walter & Scott “Pathways to treatment” model

Nature Reviews | Clinical Oncology
Likelihood of *no* prior GP consultation in emergency presenters (adjusted for cancer site)

1/3 of emergency presenters did not see a GP with relevant symptoms

More frequent in patient groups with greater psychosocial barriers to presentation

Challenges simplistic interpretations / identifies target for improvement

Examples of recent / current research in respect of...

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<tr>
<th>Direct measures</th>
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<td>Patient interval</td>
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Understanding variation by symptom in the patient interval could help to target awareness campaigns....

......but hard to measure patient intervals in populations

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<th>Method</th>
<th>Strengths</th>
<th>Limitations</th>
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| Patient interview (or questionnaire) studies | Potentially highly accurate and detailed  
Can allow for detailed (‘in-depth’) appreciation of relevant symptoms and their time of onset. | Limited representativeness (generalisability)  
Patients dying soon after symptom onset/diagnosis and those ‘too ill to take part’ are unlikely to be included. |
| Studies of medical consultation records | High representativeness (generalisability)  
Information about all cancer patients can be included, even for those with poor prognosis/only short-term survival. | Potential limitations in completeness and accuracy  
Rely on doctors appropriately eliciting the timing of symptom onset as part of history taking and accurately interpreting and recording this information. Patient interval information may be missing. |

Keeble et al, *IJC* 2014
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Diagnostic challenges / late presentations an ubiquitous problem in medicine...

Examples of diseases where emergency presentation a problem: Acute liver failure / Acute kidney injury / AIDS defining-illness (in the context of chronic undiagnosed condition)

RHEUMATOLOGY

Services for people with ankylosing spondylitis in the UK—a survey of rheumatologists and patients
Louise Hamilton¹, Annie Gilbert², Jane Skerrett², Sally Dickinson² and Karl Gaffney¹

Opportunities to diagnose chronic obstructive pulmonary disease in routine care in the UK: a retrospective study of a clinical cohort
Rupert C M Jones, David Price, Dermot Ryan, Erika J Sims, Jukka van Zuylen, Lawrence Mascarenhas, Anne Buxton, David M G Holgate, Robert Whiteman, Matt Keenan, Kevin Holford, Anne Moir, Paul Freeman, Alison Chisholm, Eric O Buttimer, on behalf of The Respiratory Effectiveness Group

COPD: 5/6 patients had missed Dx opportunities in last 5 years

Ankylosing Spondylitis: Median diagnostic interval = 6 years

American Cutaneous Leishmaniasis in U.S. Travelers
Barbara L. Herwaldt, MD, MPH; Susan L. Stokes; and Dennis D. Juranek, DVM, MSc

Intervals
Appraisal
Help-seeking
Primary care
Referral
Treatment planned / start

Cancer treatment: a cancer research problem
Cancer diagnosis: a medical research problem
Key priorities for early diagnosis epidemiology

Pre-presentation

Examining under-studied risk modifiers
- Symptoms
- Comorbidity
- False re-assurance from ‘prior all clear’ (Renzi et al, BJGP 2016)

Post-presentation

Understanding pre-diagnostic consultation / investigation / prescription patterns and related symptoms to select patients for:
- Referral (if risk above referral threshold)
- Surveillance / ‘safety netting’ (if below)

Develop more efficient instruments to routinely survey “awareness” and symptoms in populations
Key priorities for performance indicator development in early diagnosis....

We need informative measurement of organisational variation

Robust processes required for developing indicators, including profiling of their validity and reliability

Need to learn from other disciplinary traditions (e.g. health policy / health services research) and countries
In conclusion...

Diagnosing (cancer) earlier poses great challenges.

Epidemiological approaches can help to target interventions (or their evaluations)
- But inadequate in themselves re translation.

Broad alliances across disciplines and disease areas can accelerate progress
- Psychology, epidemiology, human factors engineering, primary care, Dx technology sciences; multi-disease big data or basic science initiatives.
Thank you

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