THE FAILURE OF THE PSA TEST

Implications (and Opportunities)

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COCHRANE SYSTEMATIC REVIEW 2013

- Author's Conclusions:
  - Prostate cancer screening with PSA/DRE showed no benefit PCa or all-cause mortality.
  - Meta-analysis of 5 RCTS.
  - Only two centres of one study (ERSPC) showed 21% decrease in PCa but not all-cause mortality.
  - Harms frequent and moderate in severity. **Common overdiagnosis and overtreatment (at least 50% of cases likely).**
- AUA surprisingly accept: for every 1000 men screened 0-1 less death PCa. Risks = 170 diagnoses of PCa, 2 serious CV events, one excess DVT/PE, 29 more men with erectile dysfunction, 18 more men with incontinence, and 0-1 will die from treatment. 'Shared decision-making'

WHAT EXACTLY HAS FAILED?

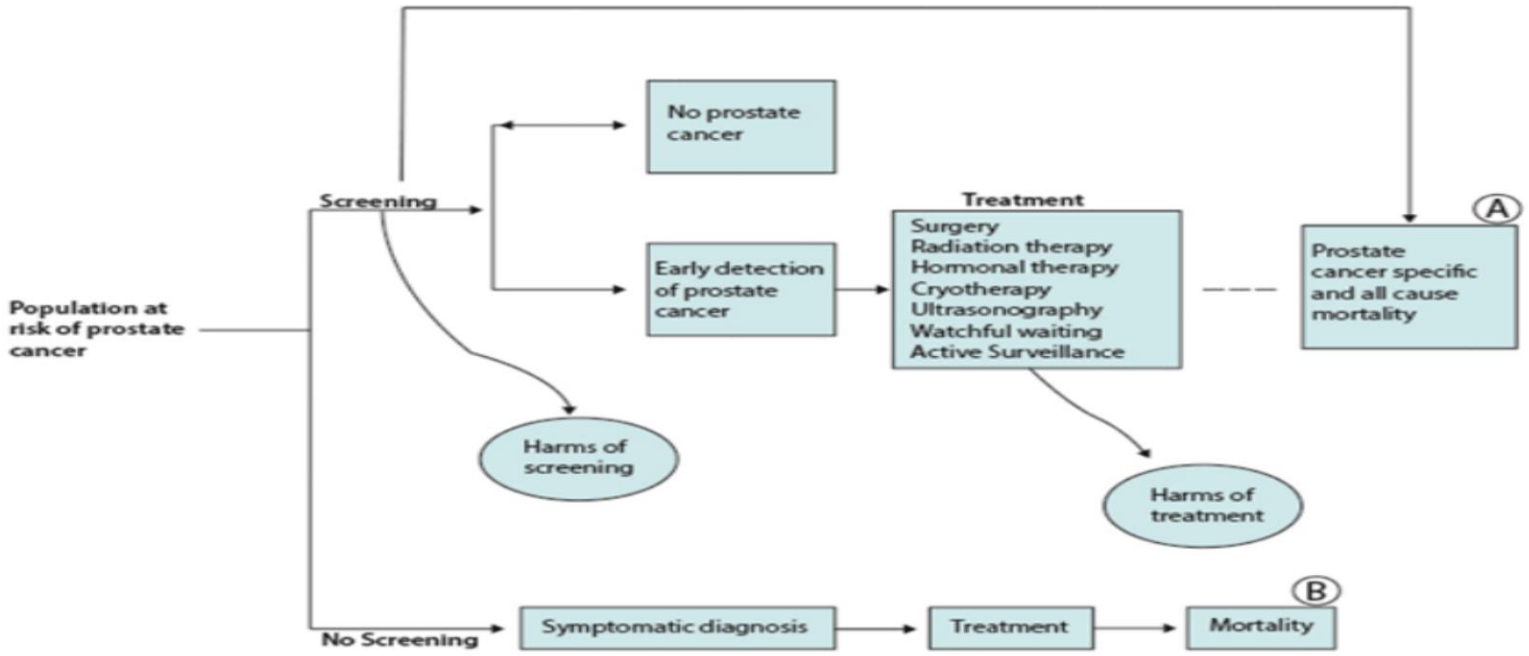


Figure 1

Screening tests give a unique testing of the entire program of care. Given the amount of effort and monies expended, expect mortality A << mortality B.

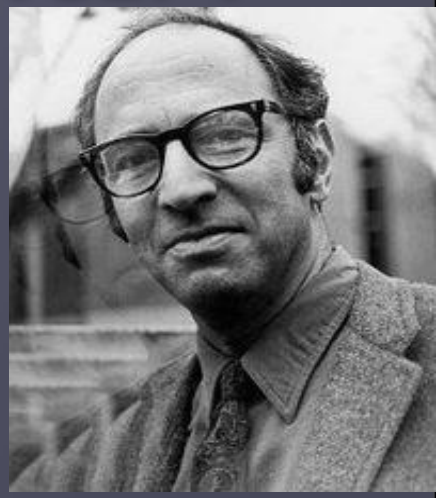
WHAT EXACTLY HAS FAILED?

- ? concerned with the inability of the totality of our best cancer diagnostic and clinical care to improve PCa and all-cause mortality when delivered at the earliest possible time?
- The amount of overdiagnosis and over treatment in any nation could be staggering i.e. all the cancer clinic visits, surgical costs, GP visits etc.
- Program of care = Pubmed filters ‘prostate cancer’ = broad therapy 43,528 articles, broad etiology 53,135 articles, broad diagnosis 49,684 articles, broad prognosis 38,591 articles, broad clinical prediction guides 43,872 articles. Tremendous effort!
  - Can it be possible that all of these articles have failed?

WHERE IS THE CRISIS?

- If we are surprised that all of the research effort underlying our PCa program of care may have failed – we may be willing to consider that our present research methods won't fix the problem, since they caused the problem in the first place i.e. the production of a huge mass of research articles, potentially without measurable benefit.
- 'More of the same' – it is possible that producing another 228,810 articles will fix the problem … but is this reasonable?
- I have not discovered evidence of a Kuhnian crisis in PCa field.

NEW TOOLS TO HELP US?? PARADIGM CONCEPT

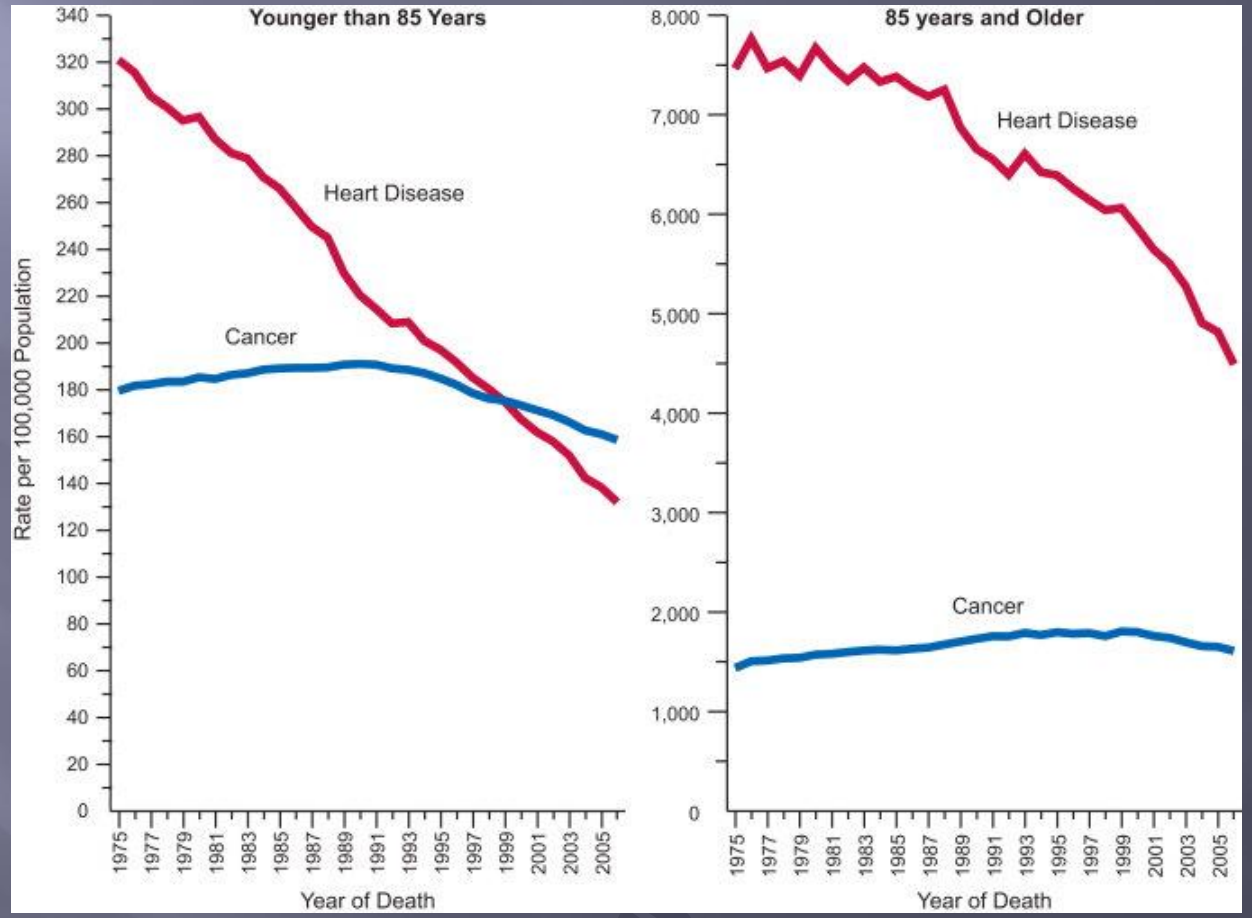


- Thomas Kuhn a physicist and eventually an historian of science. Precursor physician = Ludwig Fleck (syphilis).
- A paradigm represents that totality of the beliefs (both expressed and tacit) and all the tools used in the field. EBM is a tool used in our present PCa paradigm so it may need reconceptualization as well.
- widely used in social science but suffered criticism within philosophy.
- Nevertheless, research with professionals, including physicians, has shown that they use a **theory-in-use** to interact with clients and cannot act without such a theory. So we seem to use the paradigm concept in our daily work and this concept changes i.e. h.pylori and duodenal ulcers. This concept makes sense for Medicine.

NEW TOOLS TO HELP US?? PARADIGM CONCEPT

- paradigm concept = allows us to appreciate that our ideas are often tested together and an error often exists somewhere within the paradigm.
  - diagram all of the components of the paradigm, including required tacit components, to root out error.
- Many medical arguments suffer from **circular reasoning**, which is fallacious. i.e. using the tools of prostate cancer paradigm to test itself. The paradigm concept allows us to step outside and avoid many circularities. i.e. measure all-cause mortality not PCa-specific mortality.
- Committed action occurs within the structure of a theory-in-use / paradigm.
  - So we need to create new paradigms to compete with our existing beliefs and allow us to abandon a failing paradigm. If our research doesn't have a cognitive space for the development of new paradigms, considered beside the old ones, then substandard paradigms will survive due to absent competition.

Cancer Statistics, 2010



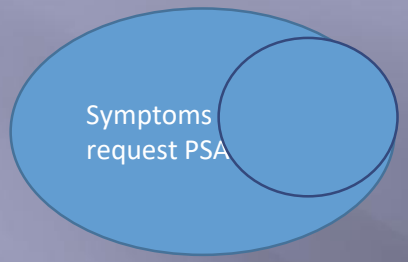
Is this another signal that our cancer paradigm contains severe error?

We can see the value of a paradigm-level evaluation.

Certain research behaviours may be OK in ischemic HD, which is succeeding, but inappropriate in cancer research.

CA: A Cancer Journal for Clinicians
Volume 60, Issue 5, pages 277-300, 7 JUL 2010 DOI: 10.3322/caac.20073
http://onlinelibrary.wiley.com/doi/10.3322/caac.20073/full#fig6

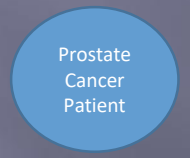
NEW TOOLS TO HELP US?? INDUCTIVE BEHAVIOUR MENTAL MODEL



S t

Enter
PARADIGM:
PSA Biopsy
Grade Stage

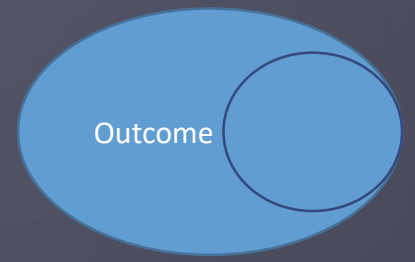
Categorization



S' t

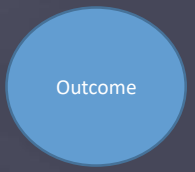
Transition Function,
natural development
of symptoms and
mortality

Transition Function,
Outputs of therapy in all
patients



S t+1

Leave the
PARADIGM:
people only
experience
symptoms
and mortality



S' t + 1

Induction. Holland, Holyoak, Nisbett, Thagard

NEW TOOLS TO HELP US?? BAYES' THEOREM

- If P(A) = 0 i.e. our beliefs are wrong, or the P(A) is very low, then any new evidence B does not much increase the P(A|B).
- So if the failure of the PSA test has supported a P(A) for the field as zero or very low, then no further studies using the theory may help us.
  - ? need to switch to inductive mode to generate new ideas and rules and categories.

Bayes' Theorem:

$$P(A|B) = \frac{P(B|A)\ P(A)}{P(B)}$$

NEW TOOLS TO HELP US?? CONTEXTUAL EMPIRICISM

- Helen Longino suggests that these social factors actually determine Science's validity – allow a research community to escape presuppositions. Assess a research community:
- Avenues for criticism.
- Shared public standards.
- Responsiveness to criticism.
- Tempered equality of authority.
- So we should look at our cancer communities to assess whether these communities can be trusted to produce empirically valuable work given the inevitable effects of background assumptions.

SCIENTIFIC ANALYSIS

- The failure of the PSA test = may show us the dangers of continued circular argumentation. An interesting case study.
- Possible 228,810 studies contaminated by an ineffective paradigm. I have made some preliminary suggestions to disinfect.
- Means Radical Prostatectomy, for instance, which has some trial evidence of efficacy ACM, may only work intra-paradigm.
- Create a support structure to EBM to prevent a naïve view of evidence i.e. that it can exist on its own, unencumbered by the rest of our beliefs.
- 'Hierarchy of Evidence' doesn't appear adequate in this case study as most modern studies would follow appropriate evidence guidelines. Doesn't appear possible that rigorous method can fully separate a fact from its entire support structure. **No Fact Stands Alone**. (Pierre Duhem)
- Should we 'switch modes' to a more inductive mode for cancer research but not ischemic heart disease research.

COMMENTS / QUESTIONS

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