Evidence-Based Practice

Prognostic studies

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Five steps in EBM

1. Formulate an answerable question
2. Track down the best evidence
3. Critically appraise the evidence for:
   - Validity
   - Impact (size of the benefit)
   - Applicability
4. Integrate with clinical expertise and patient values
5. Evaluate our effectiveness and efficiency
   keep a record; improve the process

The “ideal” prognostic study

Entire population of patients who ever lived who developed the disease followed up from the instant it developed!
Doll and Hill 1956

- 59600 questionnaires to all on the medical register October 1951
- Few simple questions
  - Age, M/F
  - current smoker?
  - Ex smoker?
  - Non (never)-smoker?
- Followed up 4 years and 5 months

- Mr. Wilson (age 68) and his wife come to see you. Two months ago you found he had a raised PSA and referred him to Urology.
- He has been told he has prostate cancer Stage T1
- They are both very anxious and asks you what this means for the future...

Doll and Hill 1956

- All cause death rate roughly same non-smoker and smokers
- Death from lung cancer 12x higher in smokers than non-smokers
- Death rate in smokers increases in those with highest tobacco consumption

Prostate Ca Staging

T01 implies < 5% tumour tissue in the specimen, and T0d > 5%.

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Lung Cancer and other Causes of Death in Relation to Smoking
A Study Report of the British Medical Research Council

Richard Doll, M.D., M.A.C.P.
Director of the British Medical Research Council

A. Bradford Hill, C.B.E., F.R.S.
Professor of Medical Research, London School of Hygiene and Tropical Medicine, University of the British Medical Research Council

On the 23rd of April, 1954, we made a final analysis of all death certificates of all causes recorded by our medical officers for the period October 1951 to October 1953. The results of this analysis are given in Table 1. In general, the highest death rates from lung cancer occurred in men who had smoked heavily for a long time. All smokers, and smokers with recent, absolute, or new onset of smoking. The death rate from cancer of the lung in men who had never smoked cigarettes was only slightly higher than the death rate from all other causes of death. However, this difference was statistically significant.
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Are The Results Valid?

2. Follow-up of patients sufficiently long and complete.
   - Too long? Too short?
   - Were all patients accounted for?
   - "5 and 20" rule:
     - <5% loss little bias
     - >20% loss threatens validity

Are The Results Valid?

1. Assembled a defined, representative sample of patients at a common point in course of disease.
   - Early in disease? "Inception Cohort"
   - Were they all at the same stage of disease at baseline?
   - Were they representative of a normal population?

Are The Results Valid?

3. Objective outcome criteria applied in a "blinded" fashion
   - How were outcomes measured?
   - Were any of the investigators "blinded" to the outcome?
   - Did they need to be?
Are The Results Valid?
4. Were there any subgroups with different prognoses identified?
   - was there adjustment for important prognostic factors?
   - Demographics?, Age?, Baseline characteristics?
   - validation in an independent, "test set" of patients?
   - Reference to a second independent study validating the predictive power of these prognostic factors.

How precise are the results?
6. What are the confidence intervals?
   - How early are the follow up periods?

What are the results?
5. How likely are the results over time?
   How are results reported?
   1. % of survival at a particular point in time (1-year or 5-year survival rates)
   2. Median survival (length of follow-up by which 50% of study patients have died)
   3. Survival curves e.g Kaplan-Meier curves

Can I apply these results to my patient?
   - Does their baseline characteristics fit with this study?
   - Are they at a similar stage in their disease?
   - What will I tell my patient?