Screening and Test Evaluation Program

Overview  Les Irwig
Screening  Glenn Salkeld
Diagnosis  Petra Macaskill
Monitoring  Les Irwig and Kirsten McCaffery

Disciplines cover epidemiology, biostatistics, health economics and psychosocial research
STEP people

- Les Irwig
- Jonathan Craig
- Glenn Salkeld
- Petra Macaskill
- Kirsten McCaffery
- Kirsten Howard
- Nehmat Houssami
- Andrew Hayen
- Robin Turner
- Gabrielle Williams

Partly based in Edward Ford Building, partly at Westmead Children’s Hospital
Some STEP people

- Sian Smith
- Sally Lord
- Barbara Ann Adelstein
- Elizabeth Davey
- Katy Bell
- Siew Chan
- Angela Webster
- Jesse Jansen
- Kevin McGeechan
- Clement Loy
- Miriam Codarini
- Kathy Flitcroft
- Michelle Cunich
- Nick Cross
- Nic Lucas
- Germaine Wong
- Luke Marinovitch
- Meagan Brennan
- Meagan Brennan
- Ruth Mitchell
STEP people working with others in the School

- Alex Barratt
- Bruce Armstrong
- Lyndal Trevena
- Philip Clarke
- Alison Hayes
STEP
University-wide collaboration

- George Institute: Bruce Neal, Chris Maher, Rob Herbert
- CeMPED: Alex Barratt, Phyllis Butow, Martin Tattersall, Lyndal Trevena
STEP national and international links

- Paul Glasziou - University of Oxford
- Patrick Bossuyt – Amsterdam Medical Centre
- Stephen Walter – McMaster University Ontario
- Jack Dowie – London School of Hygiene and Tropical Medicine
- Jon Deeks – University of Birmingham
- Cochrane Collaboration
- Tien Wong - Centre for Eye Research Australia
<table>
<thead>
<tr>
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Disciplines cover epidemiology, biostatistics, health economics and psychosocial research
Downsides of tests

Irwig, Irwig, Trevena and Sweet
Smart Health Choices

I'M DYING!

THEY'VE MADE A FAULTY DIAGNOSIS
I'M NOT DYING!
Irwig, Irwig, Trevena and Sweet
Smart Health Choices
Screening - a framework

Screening and choice

Informed choice for screening: implications for evaluation

Les Irwig, Kirsten McCaffery, Glenn Salkeld, Patrick Bossuyt

Evaluation of screening should reflect consumer priorities. We need to make more effort to find out what they really are

Value all benefits and harms

Enable participation in informed choice

Concordance between preferences and actions
Communicating about screening

Informed choice is important for screening, but not everyone wants or is able to analyse research data. **Vikki Entwistle and colleagues** propose a new approach to communication.

Patients offered screening can be helped to consider whether a test is appropriate.
PSA testing for prostate cancer 60 year old ...

Scores
- PSA test: 0.58448
- No test: 0.75000

Weightings
- Absolute Risk Reduction: 0.25000
- Avoid Unnecessary Biopsy: 0.25000
- Avoid Overdiagnosis: 0.25000
- Avoid Bowel Problems: 0.25000

Ratings
- PSA test:
  - 0.00090
  - 0.89500
  - 0.46000
  - 0.98200
- No test:
  - 0.00000
  - 1.00000
  - 1.00000
  - 1.00000
## Breast cancer screening for women on dialysis

<table>
<thead>
<tr>
<th></th>
<th>Costs ($)</th>
<th>Incremental costs ($)</th>
<th>Benefits (LYs)</th>
<th>Incremental benefits (LYS)</th>
<th>Incremental cost-effectiveness ratio (ICER $/LYS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No screen</td>
<td>4402</td>
<td></td>
<td>5.97318</td>
<td>0.00366</td>
<td>109,852 /LYS</td>
</tr>
<tr>
<td>Screen</td>
<td>4805</td>
<td>403</td>
<td>5.97685</td>
<td>0.00366</td>
<td></td>
</tr>
</tbody>
</table>

**1.3 days of life**
# Colorectal cancer screening for kidney transplant recipients

<table>
<thead>
<tr>
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<th>Costs ($)</th>
<th>Incremental costs ($)</th>
<th>Benefits (LYs)</th>
<th>Incremental benefits (LYS)</th>
<th>Incremental cost-effectiveness ratio (ICER $/LYS)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No screen</strong></td>
<td>3606</td>
<td></td>
<td>7.85160</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Screen</strong></td>
<td>5076</td>
<td>1470</td>
<td>7.91786</td>
<td>0.06626</td>
<td>22,185 /LYS</td>
</tr>
</tbody>
</table>

24.1 days of life saved
The future

• Multi criteria decision analytic approaches to weighing up the benefits, harms and costs of screening

• Consumer and patient preferences

• Value of screening amongst patients with chronic disease
Diagnosis

How accurate is a diagnostic test?
Should I use it?
Which patients should I use it for?

Finding the answer(s):
   Meta-analysis
   Primary studies

STEP is known for its methodological and applied research in both of these areas.
Diagnosis: Meta Analysis

Recent influential diagnostic reviews include:

- Dermoscopy compared to naked eye examination for the diagnosis of primary melanoma (*British Journal of Dermatology*, 2008)

Systematic reviews can have a major influence on policy and practice.
Diagnosis: Meta-Analysis

STEP expertise has a major influence on:

- methodology and framework now used for Cochrane systematic reviews of studies of diagnostic accuracy
- extensions to Cochrane software (Revman 5)
- use of more advanced rigorous methods for summary ROC analysis

STEP CIs currently hold leadership roles in the Cochrane Collaboration.
When feasible, full data on individual patients in each study is preferable to summary (published) data.

Kevin McGeechan has obtained IPD to:

- assess the value of retinal signs in the prediction of coronary heart disease and stroke.
- assess the incremental value of eye signs after accounting for known risk factors (age, smoking etc).

Complex statistical modeling is required.
Diagnosis: Primary Studies
Methodology

Major STEP contributions to methodology include:

- STARD – standards for the reporting of diagnostic test studies
- Statistical methods for evaluating the gain in using tests in combination
- Study design for diagnostic test evaluation, e.g. taking account of the intended purpose of a new test (replacement, add-on, triage)
Fever Phase 1:

The development of an algorithm to predict the probability of serious bacterial illness using multiple “tests” (signs and symptoms) in children presenting to Emergency Dept (Westmead) with unexplained fever (n=15,781).
Other major studies/evaluations include:

**Fever Phase 2:** Cluster randomised trial to evaluate the algorithm developed in Phase 1. *(data for 16,000 children currently under analysis)*

**CRISP:** Investigation of the value of symptoms in the diagnosis of colorectal cancer *(8000 participants).*

**Imager:** Comparison of the accuracy of computer-assisted reading of liquid based cytology (Thin-Prep Imager) with conventional Pap smear reading demonstrated the potential for cost savings in using this technology for screening programs *(55,000 split sample slides)*
Diagnosis: Future Directions

Improved framework for diagnostic meta-analysis:
- to reflect the intended purpose of the test
- to provide accessible statistical methods to allow for multiple thresholds per study

A greater focus on IPD meta-analysis and related methodology

Developing simple clinical prediction rules:
- evaluating their transferability/generalizability
- investigating barriers to their adoption
Estimated true and false positive rates for a 10 mmHg increase in diastolic blood pressure

<table>
<thead>
<tr>
<th>Initial level achieved on treatment</th>
<th>True positive rate %</th>
<th>False positive rate %</th>
<th>Ratio FP:TP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial level = 85 mmHg (so 5 mmHg increase needed)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>1.8%</td>
<td>19.8%</td>
<td>11</td>
</tr>
<tr>
<td>33 months</td>
<td>16.0%</td>
<td>12.4%</td>
<td>0.8</td>
</tr>
<tr>
<td>Initial level = 80 mmHg (so 10 mmHg increase needed)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>0.005%</td>
<td>5.8%</td>
<td>&gt;1000</td>
</tr>
<tr>
<td>33 months</td>
<td>4.4%</td>
<td>8.3%</td>
<td>1.9</td>
</tr>
</tbody>
</table>

Keenan BMJ 2008
New Zealand cardiovascular risk prediction charts

Jackson, R. BMJ 2000;320:709-710

Men

Risk level
5 year cardiovascular risk
(non-fatal and fatal)

Very high
>30%

High
25-30%

Moderate
20-25%

Mid
15-20%

Low
10-15%

<5%

Benefit (1)
Cardiovascular events prevented per 100 treated for 5 years*

>10

9

7.5

6

4

2.5

1.25

<0.8

Benefit (2)
Number needed to treat for 5 years to prevent 1 event**

<10

11

13

16

25

40

80

>20

* Record no <20% reduction in total cholesterol or a reduction in blood pressure of 10-15 mm Hg systolic or 5-8 mm Hg diastolic, which reduces risk of cardiovascular disease by about one third over five years

**
# Monitoring – the future

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MEASUREMENT:</strong>&lt;br&gt;Develop methods to improve Signal-Noise ratio of total CV risk&lt;br&gt;1-2 yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>COMPREHENSIVE OUTCOMES</strong>&lt;br&gt;Identify objectives and quantify benefits and harms of ‘monitoring’ for patients and clinicians [e.g. reassurance, education]&lt;br&gt;1-2 yrs</td>
<td></td>
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</table>
Understanding comprehensive outcomes in monitoring

- Monitoring serves many functions for patients and clinicians – it is not only about taking clinical measurements.
  - E.g. For clinician, to check patient understands and is adhering to medical advice
  - E.g. For patient, to get reassurance from clinician

- To develop optimum monitoring strategy we need to consider these broader functions and effects

- Important to understand these for both patients and clinicians before changes to follow-up are recommended.
Examples from the screening literature

- Patients’ desire to avoid regret as a determinant of CaCx screening (Sandberg et al BJSP 2008)
- Desire for reassurance motivated cardiology patients to undergo a stress test (Petrie et al BMJ 2007)
- Guilt and strained family relationships following a normal genetic test if other family members test positive (Biesecker et al JAMA 1993)
- Changes in diet and exercise (improved diet, less exercise) following bowel cancer screening (Larsen et al CGH 2007; Miles et al Cancer Epi Bio Prev 2003)
Framework for comprehensive outcomes

Quality of life/PRO
- Functional health status
- Social wellbeing
- Emotional / psychological wellbeing

Health psychology
- Illness representations/ belief domains\(^1,2\)
  - Cognitive
  - Emotional
  - Behavioural

Effects of screening, testing & monitoring
- Cognitive
- Emotional
- Social
- Behavioural

\(^1\) Leventhal et al, 1993, \(^2\) Petrie et al 1997
Monitoring & Mgmt

**Patient**
- Cognitions: Risk perceptions
- Emotions: Anxiety
- Social: Relationships
- Behaviour: Adherence

**Clinician**
- Cognitions: Confidence
- Emotions: Giving reassurance
- Social: Dr-patient relationship
- Behavioural: testing

**Primary Health outcome**

**Additional Patient Outcomes**

**Additional Clinician Outcomes**

Comprehensive effects of monitoring and mgmt
Example: CVD risk monitoring
Regularly checking my patients blood pressure helps me to:
... check whether their medication is working and give my patient further education about CVD risk (cognitive)
… feel confident I am treating my patient appropriately (emotional)
… maintain a positive and trusting relationship with my patient (social)
… check that my patient is adhering to treatment (behavioural)
Going for my routine blood pressure check-up helps me to:

... keep track of what my BP is and provides an opportunity to ask my Dr questions about my health (cognitive)

... feel like I am being looked after by my Dr (emotional)

... show my children I am doing everything I can to reduce my risk (social)

... check that I am keeping on top of my diet (behavioural)
<table>
<thead>
<tr>
<th>Doctor / patient</th>
<th>Perceived function of monitoring</th>
<th>Alternative ways of monitoring mgmt</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Checking use of correct treatment</td>
<td>1. Clear evidence to reassure Dr and patient treatment is effective without need of regular checks</td>
</tr>
<tr>
<td></td>
<td>Giving Dr confidence he is doing the right thing for the pt</td>
<td>2. Dedicated health education session with practice nurse</td>
</tr>
<tr>
<td></td>
<td>Maintaining a positive dr-pt relationship</td>
<td>3. Dr-pt consultation to discuss lifestyle change</td>
</tr>
<tr>
<td></td>
<td>Checking treatment and lifestyle change is working</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Getting further information</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Getting reassurance from Dr</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Showing my family I am taking my BP seriously</td>
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The future

- CVD risk monitoring
- Follow-up and management of melanoma
Monitoring – the future

Stage 1

MEASUREMENT:
Develop methods to improve Signal-Noise ratio of total CV risk
1-2 yrs

COMPREHENSIVE OUTCOMES
Identify objectives and quantify benefits and harms of ‘monitoring’ for patients and clinicians [e.g. reassurance, education]
1-3 yrs

Stage 2

Design strategies to meet all Measurement and Comprehensive Outcome objectives
2 yrs
Several iterations

Small RCTs to test components, e.g. different risk communication formats, decision support strategies, patient satisfaction

Stage 3

START RCT of final monitoring strategy [2 or 3 arms]
4 yrs +
Monitoring – the future

We aim to make monitoring more evidence-based in major areas of health care

Research consist of:

- Further development of concepts and methods, for example extending our approach to cancer surveillance
- Applying them widely in collaboration with content experts
STEP: screening, diagnosis and monitoring
how to ensure continuing success?

- Continually strive to identify new areas where our methodological expertise can make a difference to health
- People not just projects and papers