Introduction to Translational Cancer research:

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Session objective

- To provide an introduction to translational research
- Define the translational research stages
- Provide some operational definitions.
Translational research

- A relatively recent term...
- The concept of research utilisation in nursing emerged in the 1970s and 80s
- More prominent in the last decade
- Describes the steps between a fundamental discovery and its application in clinical medicine
- Involves moving knowledge gained from the basic sciences to its application in clinical and community settings
- ‘Bench to Bedside’ and increasingly ‘Bedside to Community’ (or bookshelf to bedside)
  - Generating new research paradigms
Broadly – three types of research

- Basic research
- Clinical research
- Translational research
  - Knowledge translation research
  - Implementation research
  - Dissemination research
  - Program science
Definition: Translational Research

- JAMA, 2002 Editorial – coined the term translational research, which they defined as:
  
  - ‘translation of the new knowledge, mechanisms, and techniques generated by advances in basic science research into new approaches for prevention, diagnosis, and treatment of disease’
  
  - Translational research was declared essential for improving health

(Fontanarosa & De Angelis, 2002, p. 178).
“Translational research means different things to different people, but it seems important to almost everyone.”

Steven H. Woolf, MD, MPH, JAMA Commentary, 2007
Translational Research

Two areas of focus

- Translational research fosters the multidirectional and multidisciplinary integration of basic research, patient orientated research, with the long-term aim of improving the health of the public.

- The process of applying lab research discoveries & pre-clinical studies to the development of trials and studies in humans.

- Research aimed at enhancing the adoption of best evidence based practices.

A very long lead time....

- “It takes 17 years to turn 14 per cent of original [applied] research to the benefit of patient care”

Balas, 1995
Improving health outcomes

- “The application of what we know already will have a bigger impact on health and disease than any drug or technology likely to be introduced in the next decade.”
- J A Muir Gray, Director of Clinical Knowledge, Process and Safety - Connecting for Health, NHS

Improved knowledge management can help prevent and minimise:

- Errors and mistakes
- Poor quality healthcare
- Waste
- Variations in policy and practice
- Poor patient experience
- Overenthusiastic adoption of interventions of low value
- Failure to get new evidence into practice
Setting the scene

- One of the most critical issues impeding improvements in public health today is the enormous gap between what we know can optimize health and healthcare and what actually gets used and implemented in every day practice.
Bridging the “valleys of death” between research and outcomes
Translational Research Model

- Dynamic interplay
- Research – continuing cycle
- Bi-directional arrows – new knowledge and hypotheses generated at each step
- Some basic research and population-based research is translational, but neither type of research is by definition translational.
- In contrast, patient-oriented research fundamentally addresses issues that have the potential to translate to clinical practice and, therefore, affect health

Translation Research: T1

T1: Translational Research

- Bench to Bedside
- Research that expedites the movement between basic research and patient orientated research, that leads to new or improved scientific understanding or standards of care.

Phase 1-11 Studies

<table>
<thead>
<tr>
<th>Phase</th>
<th>What happens</th>
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<tbody>
<tr>
<td>Phase I</td>
<td>• After the treatment has been tested in the laboratory and on animals (and is deemed safe), phase I trials are the first studies that involve people.</td>
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<tr>
<td>Phase II</td>
<td>• Are continuations of phase I trials, although usually involving more people. They monitor the safety of treatment.</td>
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<tr>
<td>Phase III</td>
<td>• Compare the new treatment with current standard treatment and investigate which treatment works the best. People who take part in these trials are usually allocated to either (a) the group that receives the new treatment or (b) the group that receives the current standard treatment.</td>
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Taking scientific discoveries from the lab bench to bedside
T1: Clinical Research
Translation Research: T2

T2: Translational Research

- Research that facilitates the movement between patient orientated research and population based research that leads to better patient outcomes, the implementation of best practices, and improved health status in communities.

Examples

- Examples of T2 are clinical epidemiology, health services (outcomes) research, and the newly developing methodology of community-based participatory research.
Translation Research: T3

T3: Translation Research

- T3 research promotes interaction between laboratory-based research and population-based research to stimulate a robust scientific understanding of human health and disease.

Examples of T3

- Emerging disciplines such as molecular and genetic epidemiology.
- T3 research highlights, for instance, how research in populations informs hypotheses that can be tested in basic science laboratories and how biomarkers in animal models can translate into population-based screening tools.
What is translation research?

The road less traveled?

From the president's Cancer Panel's 2004-2005 Report
Translating Research into Cancer Care: Delivering on the Promise

NCI, Translational Research Working Group
Translational research – 4 phases

Four Phases \( T_0 \cdot T_4 \)

- \( T_0 \) characterised by the identification of opportunities and approaches to health problems
- \( T_1 \) seeks to move basic discovery into a candidate health application
- \( T_2 \) assess the value of application for health practice leading to the development of evidence based guidelines
- \( T_3 \) moves evidence based guidelines into health practice via dissemination and diffusion research
- \( T_4 \) seeks to evaluate the ‘real world’ health outcomes of population health practice
<table>
<thead>
<tr>
<th>Research Phase</th>
<th>Definition</th>
<th>Type of Research</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_0$</td>
<td>Identification of opportunities and approaches to health problem.</td>
<td>Basic research question</td>
<td>Are there specific gene mutations associated with breast cancer?</td>
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<tr>
<td>$T_1$</td>
<td>Discovery of candidate health application</td>
<td>Phase I and II clinical trials; observational studies</td>
<td>Is there an association between BRCA mutations and breast cancer?</td>
</tr>
<tr>
<td>$T_2$</td>
<td>Health application to evidence-based practice guidelines</td>
<td>Phase III clinical trials; observational studies; evidence synthesis and guidelines development</td>
<td>What is the positive predictive value of BRCA mutations in at-risk women?</td>
</tr>
<tr>
<td>$T_3$</td>
<td>Practice guidelines to health practices</td>
<td>Dissemination research; implementation research; diffusion research Phase IV clinical trials</td>
<td>What proportion of women who meet the family history criteria are tested for BRCA and what are the barriers to testing?</td>
</tr>
<tr>
<td>$T_4$</td>
<td>Practice to population health impact</td>
<td>Outcomes research (includes many disciplines); population monitoring of morbidity, mortality, benefits, and risks studies</td>
<td>Does BRCA testing in asymptomatic women reduce breast cancer incidence or improve outcomes?</td>
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Focus

- PRODUCT DRIVEN: What occurs from bench-to-bedside in the development of new drugs, devices, and treatment options for patients;

  VS.

- COMMUNITY AND POLICY FOCUSED: “translating research into practice.”
New research paradigms

- **Knowledge translation research** is a dynamic and iterative process that includes synthesis, dissemination, exchange and ethically sound application of knowledge to improve people’s health, provide more effective health services and products, and strengthen the health care system.

- **Dissemination and implementation research** seeks to address this gap by understanding how to best ensure that evidence-based strategies to improve health and prevent disease are effectively delivered in clinical and public health practice.
Implementation ‘Science’

What outcome gap(s) are we looking at?

What is the evidence to support practice change?

What are the barriers and enablers to change?

What intervention is most suitable to apply at this time?

How will we evaluate its impact?
PICO Format

- **P**atient population/disease
- **I**ntervention (diagnostic or treatment)
- **C**omparisons
- **O**utcome
Problem and population

- **PROBLEM:**
  - Pain is almost universally experienced by people with cancer.
  - People living with cancer have multiple health care encounters (GP, Community Nurse, Cancer Care – ambulatory, inpatients, and for some palliative care)
  - Cancer pain is frequently unrecognised and under treated. Rarely comprehensively assessed.

- **POPULATION:**
  - Cancer and palliative care clinicians
Intervention: Spaced Education, plus Audit and Feedback

Built around two evidence-based theories:

- The testing effect
- The spacing effect
Comparisons and Outcome

- CONTROL:
  - Sample too small to randomise (approximately 100)
  - Pre-post test design
  - Nested wait listed control – at one site

- OUTCOME:
  - 50% increase in evidence of a comprehensive pain assessment for patients with cancer related pain (chart audit).
    - 20% increased pain assessment knowledge (survey)
# Study design

- Pre-post test quasi-experimental study design
  - Nested case wait-listed control

<table>
<thead>
<tr>
<th>Time 1 (T1)</th>
<th>Intervention</th>
<th>Time 2 (T2)</th>
<th>Time 3 (T3)</th>
<th>Time 4 (T4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Survey</td>
<td>• Spaced Education (over 6 weeks)</td>
<td>• Survey</td>
<td>• Survey</td>
<td>• Survey</td>
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<tr>
<td>• Chart Audit</td>
<td></td>
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- **Survey:** pain assessment capabilities
- **Chart audit:** pain assessment practices
- **Impact:** Patient reported pain outcomes
Thank you

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