Incorporating human behaviour in simulation models for breast cancer screening

Sally Brailsford
Outline of talk

- Modelling human behaviour – why do it, and is it possible?
- Postscript: some very recent work on evaluating mammography programmes (2010)
Why model behaviour?

- Operational Research models are widely used in evaluation of healthcare interventions
- Human behaviour can influence outcomes: e.g. adherence with medication, compliance with screening programmes
- Models which ignore human factors can give misleading or erroneous results
- But can we capture human behaviour adequately in a simulation model?
Is it even worth trying?

“What a chimera the human being is! What a novelty, what a monster, what a chaos, what a contradiction, what a prodigy! Judge of all things, powerless earthworm, dark room of uncertainty, the glory and the shame of the universe. When he praises himself, I will humble him; when he humbles himself, I will praise him; and I will go on contradicting him until he comprehends that he is incomprehensible.”

Pascal, *Pensées* (1670)
How I got interested in this

• NHS-funded project in mid 1990’s on diabetic retinopathy

• Led by Ruth Davies (School of Management) with Paul Roderick (School of Medicine) and Chris Canning, consultant ophthalmologist, Southampton University Hospitals Trust

• Developed discrete-event simulation models to evaluate different screening policies
Diabetic Retinopathy

- Two types of diabetes, Type 1 and Type 2; incidence of Type 2 increasing in developed countries due to ageing population and lifestyle changes

- Retinopathy is a serious complication of both types, and is the major cause of preventable blindness in developed countries

- Retinopathy can be detected before the patient is aware of any symptoms, and can be successfully treated by laser
Screening issues

- Who does it - GP, optometrist, ophthalmologist, technician, nurse, diabetologist?
- What is the best technology - camera, direct eye examination, with/without dilating pupils?
- In what setting - hospital, doctor’s office, optometrist’s shop, mobile van?
- What is the best interval between screens, and should it be a one-stage or two-stage process?
- Models were coded in Borland Delphi and used Davies’s POST methodology - Patient Oriented Simulation Technique (Davies and Davies, 1993)

POST - Patient oriented simulation technique

- Healthcare models often require patient entities to be in more than one place at a time
- Most off-the-shelf DES software cannot easily handle simultaneous and interacting activities or queues
- In POST patients can take part in more than one activity - the earliest one takes precedence over the others
- Patients can queue while taking part in activities
- Future events can be extracted from the calendar and terminated or changed and returned
- Pointers used to locate linked items rapidly
Central vision loss

Severe vision loss

Screen for any retinopathy

Detect background retinopathy

Visit ophthalmology clinic

Detect and treat PDR or CSMO

Screening & treatment

Disease progression

Death
The model

• Population-based model taking set of diabetic patients (including new cases) through their “life histories”, superimposing different screening policies

• Used natural history data from WESDR (the Wisconsin Epidemiologic Study of Diabetic Retinopathy – Klein et al 1985)

• Used NHS cost data to evaluate a range of policies in terms of cost per sight-year saved

• Decision parameters: screening intervals, test sensitivity and specificity
Main results

• Standard methods of screening save up to 50% of the potential sight years lost, giving up to 85% of the sight years saved by an idealised “gold standard” programme

• The mobile camera (sens = 61%; spec = 85%), used for both annual screening and six month follow-up after the detection of BDR, was the most cost-effective at £2,842 per sight year saved

• It is less efficient to screen Type 2, rather than Type 1 patients, but Type 2 contributed almost 75% of the sight years saved

Summary of findings

• Screening is worthwhile for all diabetic patients

• Remarkably little difference between methods in terms of sight saved: need to discriminate on other grounds, i.e. cost and convenience

• Crucial factors are coverage and compliance

• But what if we could model compliance......??
Modelling compliance

- Current approaches highly simplistic
- Model behaviour at a global level: e.g. a certain probability of showing up for screening, or taking a drug as prescribed
- Is this good enough? Can we obtain added insights by more detailed models of health-related behaviour?
- If yes, then we could provide useful information to health providers to increase compliance and adherence
Early ideas

- Worked for a while in the late 1990’s with Prof Bernd Schmidt of the University of Passau, Germany

- PECS architecture: physiological, emotional, cognitive and social aspects of human behaviour (agent-based models)

- Used PECS for diabetic retinopathy (EJOR, 2003)

- PECS assumed two types of behaviour for agents:
  - Reactive (instinctive, learned, drive-controlled, emotionally driven)
  - Deliberative (constructive or reflective)

Psychological models

- The Health Belief Model (Becker, 1974)
- The Theory of Planned Behaviour (Ajzen, 1991)
- Widely established and recognized in the field of health psychology for many years
- Not adopted to date by OR modellers

The Health Belief Model

Health behaviour

Health Motivation

Perception of illness threat
- Perceived susceptibility to illness

Evaluation of behaviours to counteract threat
- Perceived severity of illness
- Perceived benefits of behaviour
- Perceived barriers to behaviour

Cues to Action
The Theory of Planned Behaviour

- **behaviour**
  - Behavioural intentions
    - Attitude towards behaviour
      - Belief about outcomes
        - X
        - Evaluation of outcomes
    - Subjective norms
      - Normative beliefs
        - X
        - Motivation to comply
    - Perceived behavioural control
      - Perceived likelihood of occurrence
        - X
        - Perceived facilitating or inhibiting power
Details of the TPB

- Based on Fishbein & Ajzen’s “Theory of Reasoned Action”: they don’t suggest people consciously do these calculations!
- Looks mathematical – good candidate for modelling?
- Three main constructs: attitude, subjective norms and perceived behavioural control

<table>
<thead>
<tr>
<th>Belief about outcomes</th>
<th>Normative beliefs</th>
<th>Perceived likelihood of occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \sum_i b_i e_i )</td>
<td>( \sum_j c_j m_c_j )</td>
<td>( \sum_k d_k p_k )</td>
</tr>
</tbody>
</table>

**EXTERNAL VARIABLES**

Demographic variables: age, sex, occupation, socio economic status, religion, education

Personality traits: extraversion, agreeableness, conscientiousness, neuroticism, openness
Breast cancer

• Second only to lung cancer as cause of cancer death in US women: the most common cause in the UK

• In the UK in 2006 more than 45,500 women (and 300 men) were diagnosed with breast cancer

• Early detection greatly improves the prognosis

• Since the 1980’s death rates have declined due to introduction of population screening (mammography)

http://info.cancerresearchuk.org/cancerstats/types/breast/mortality/
UK screening programme

• Introduced in 1988 following trial evidence from many countries

• Initially offered to women aged 50-64, every 3 years

• From 2001, offered every 3 years from ages 50-70, and over 70 on request

• Over 1.4 million UK women screened every year, with approx 75% uptake of invitations

• 5-year survival has increased to 80%
Modelling cancer screening programmes

• One of the classic areas for the applications of simulation modelling in healthcare (e.g. Habbema et al, 1985 (MISCAN))

• All “microsimulations” i.e. individual-based models

• No interactions between entities, no resource constraints and no queues: i.e., not traditional DES models in the OR sense

Our model

• MSc dissertation project in 2006 by Jenni Sykes, co-supervised by me and Paul Harper

• Another microsimulation, coded in Microsoft Visual Basic for Applications, using a 3-phase discrete-event approach with five B-activities:
  – Develop cancer
  – Be invited for screening
  – Detect the cancer by means other than mammography
  – Die from breast cancer
  – Die from other causes
Breast Cancer Screening Model

- No Detectable Cancer
- Breast Cancer
- Screening
- Detection
- Self Detect/Other detection
- Death from Breast Cancer
- Cure
- Death From Other Causes

behaviour
Model parameters

• Physiological
  – Incidence, age of onset; tumour growth rate; death rates from breast cancer and from other causes; survival after treatment

• Screening
  – Start and end ages; interval; test sensitivity according to tumour size

• Psychological
  – Probability of attendance
Model outputs

- Number of screens performed
- Number of cancers detected
- Number of cancer and non-cancer deaths
- Statistics relating to tumour size at detection (for validation)
- Life years saved (calculated by comparing with baseline run)
- We did not include costs or perform cost-effectiveness analyses
Tumour growth

- Four models: exponential, generalized logistic, Gompertz, modified Gompertz
- Fitted to data from the literature
Age of cancer onset

- Fitted to data from UK South West Cancer Intelligence unit – database of 26,298 patients between 1981 and 2000

- Age at onset was back-calculated from tumour size at presentation, using all four tumour growth models
Mortality

- Natural death inferred from UK life tables
- Breast cancer cure and death are functions of tumour size and spread
Tumour detection

- Other detection (Erlang(0.85, 3))
- Mammography detection (Weibull(1.2, 1.03))
- Data from Tabar et al (2002)
- Data from Michaelson et al. (2003)

Data from Tabar et al (2002)
Data from Michaelson et al. (2003)
Attendance at Screening

- “Global” percentage
- “Local” percentage
- Theory of Planned behaviour
- Baker and Atherill model (2002): probability of attendance is a function of previous attendances

\[ P(n) = \frac{1}{1 + S(n)} \]

Data for the TPB

• Rutter (2000) tested TPB’s ability to predict attendance at breast cancer screening appointments

• 2058 women completed questionnaire before appointment date

• TPB scale variables significantly predicted attendance/non attendance

TPB probability of attendance

- Logistic regression found relationship between TPB variables and attendance

\[ \ln \left( \frac{\pi(\beta, X)}{1 - \pi(\beta, X)} \right) = \beta_1 + \beta_2 X_1 + \beta_3 X_2 + \beta_4 X_3 \]

- Assumed attendance result of Bernoulli trial and used maximum likelihood to find regression coefficients

- \( \pi = \) probability of attendance
Scenarios

- Four different growth models
- Four different behavioural models
- Five screening strategies

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Start Age</th>
<th>End Age</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>51</td>
<td>69</td>
<td>3 years</td>
</tr>
<tr>
<td>2</td>
<td>51</td>
<td>63</td>
<td>3 years</td>
</tr>
<tr>
<td>3</td>
<td>51</td>
<td>69</td>
<td>2 years</td>
</tr>
<tr>
<td>4</td>
<td>51</td>
<td>63</td>
<td>2 years</td>
</tr>
<tr>
<td>5</td>
<td>45</td>
<td>69</td>
<td>3 years</td>
</tr>
</tbody>
</table>
Numbers of tumours detected for different growth models

- Mod Gompertz
- Logistic
- Gompertz
- Exponential

Tumour Growth Pattern

- Screening 45:69 every 3 years.
- Screening 51:63 every 2 years.
- Screening 51:63 every 3 years.
- Screening 51:69 every 2 years.
- Screening 51:69 every 3 years.
Average life years saved

![Bar chart showing average life years saved for different tumor growth patterns and screening intervals.]

- **Mod Gompertz**
- **Logistic**
- **Gompertz**
- **Exponential**

**Tumor Growth Pattern**
- Screening 45:69 every 3 years.
- Screening 51:63 every 2 years.
- Screening 51:63 every 3 years.
- Screening 51:69 every 2 years.
- Screening 51:69 every 3 years.
Average number of attendances for different behaviour models

- **Average of Equation**: Screening 51:63 every 3 years.
- **Average of Local**: Screening 51:69 every 3 years.
- **Average of Global**: Screening 51:63 every 2 years.
- **Average of TPB**: Screening 51:69 every 2 years. Screening 45:69 every 3 years.
% change in tumours detected for a ±10% change in TPB variables

![Bar chart showing percentage change in tumours detected for a ±10% change in TPB variables. The chart compares the percentage change for Attitude, Subjective Norm, PBC, and All variables, with bars indicating the percentage detected for down 10%, up 10%, and base conditions.]
So what?

- Can we capture human behaviour adequately in this model?
- Can we obtain added insights by more detailed models?
- Can we provide useful information to health providers?
- Further work is required, e.g. cost-effectiveness analysis to study relative benefits of different interventions to increase compliance (public education campaigns, social marketing) compared with increase in test accuracy
- Work is about to begin on collecting data for this
Recent work: the problem of overtreatment

- MSc project (2010) by Jessica Ashong, co-supervised by me and James Raftery, School of Medicine, Southampton

- Raftery’s current work, based on Nordic Cochrane Review (Gottszche and Nielson, 2009), suggests that the benefits of mammography may be over-estimated in the literature

- Current controversy in the US about screening women aged 40-49

- Does screening do more harm than good?
Jessica’s model

• Simple 4-state Markov model coded in Excel

• Cohort of 2000 women aged 50, followed for 40 years, at 1-year cycles; screened every 3 years until the age of 70

• Data from two systematic reviews: Nelson et al (2009, Gottszche and Nielson (2009) and the UK National Breast Cancer Screening Programme

• QALY values taken from literature (Forrest 1986) and were also varied in sensitivity analysis
## Data

<table>
<thead>
<tr>
<th>Source</th>
<th>Variable</th>
<th>Value</th>
<th>Duration (y)</th>
<th>Cycle applicability (y)</th>
<th>Frequency (y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nelson (2009)</td>
<td>50-59y, RR for breast cancer mortality</td>
<td>0.86 (CI: 0.75-0.99)</td>
<td>10</td>
<td>1-10</td>
<td>1</td>
</tr>
<tr>
<td>Nelson (2009)</td>
<td>60-69y, RR for breast cancer mortality</td>
<td>0.68 (CI: 0.54-0.87)</td>
<td>10</td>
<td>11-20</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>70-89y, RR for breast cancer mortality</td>
<td>1.00</td>
<td>20</td>
<td>21-40</td>
<td>1</td>
</tr>
<tr>
<td>Gotzsche &amp; Nielsen (2009)</td>
<td>RR for surgical operations</td>
<td>1.35 (CI: 1.26-1.44)</td>
<td>20</td>
<td>1-20</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>RR for surgical operations</td>
<td>1.00</td>
<td>20</td>
<td>21-40</td>
<td></td>
</tr>
<tr>
<td>NHSBSP (2008)</td>
<td>Attendance rate</td>
<td>0.7380</td>
<td>20</td>
<td>1-20</td>
<td>3</td>
</tr>
<tr>
<td>NHSBSP (2008)</td>
<td>False positive rate</td>
<td>0.0363</td>
<td>20</td>
<td>1-20</td>
<td>3</td>
</tr>
<tr>
<td>Forrest (1986)</td>
<td>Operation QoL Loss</td>
<td>0.08 (range: 0.01-0.08)</td>
<td>1</td>
<td>1-40</td>
<td>1</td>
</tr>
<tr>
<td>Raftery (2010)</td>
<td>False positive QoL Loss</td>
<td>0.05</td>
<td>0.1</td>
<td>1-20</td>
<td>3</td>
</tr>
</tbody>
</table>
Sensitivity analyses

• The relative risk of requiring surgery was varied between the lower and upper CIs (1.26, 1.44), in steps of 0.01

• The loss in QoL due to surgery was varied between 0.01 and 0.08 (Forrest, 1986), in steps of 0.01

• The loss in QoL due to false positive results (unknown) was varied between 0 and 0.5, in steps of 0.1

• The duration of the loss in QoL due to a false positive result (also unknown) was varied between 0 and 1 year, in steps of 0.1
Findings

• Results depend on time period considered: over a 10-year period there was no QALY gain, but over 20+ years there was a QALY gain in most scenarios, apart from that in which the age-related mortality rates from breast cancer are assumed to be at the high end of the CI’s from the Nelson review (see next slides)

• Under the current UK programme, for this cohort, over a 10-year period one woman’s life is prolonged and 200 women have false positive results
Uncertainty in the Nelson data: four scenarios

1. The lower CI value (0.75 and 0.54) for both age groups (best case scenario)

2. The lower CI value (0.75) for the 50-59 age group and the upper CI value (0.87) for the 60-69 age group.

3. The upper CI value (0.99) for the 50-59 age group and the lower CI value (0.54) for the 60-69 age group.

4. The upper CI values (0.99 and 0.87) for both age groups (worst case scenario).
Impact of age-related BC mortality
Further work

• Raftery’s work on overtreatment is continuing

• Also developing the behavioural work, e.g. to establish the relative costs & benefits of a more accurate test against increasing attendance through a social marketing campaign
Questions?