Rapid critical appraisal
using GATE

Rod Jackson
University of Auckland, NZ
February 2011

GATE: Graphic Appraisal Tool for Epidemiology

One picture: the GATE frame

the shape of every epidemiological study

British doctors
smoking status measured
smokers non-smokers
Lung cancer yes no 10 years
Longitudinal (cohort) study

Cross-sectional study

British doctors
smoking status measured
smokers non-smokers
Lung function normal abnormal

British doctors
Randomised to aspirin or placebo
aspirin placebo
Myocardial infarction yes no 5 years
RCT
Middle-aged US women

Breast cancer

no Breast cancer

mammogram

positive

negative

Diagnostic test accuracy study

Clinical use of a diagnostic test

Test applied

Mammogram positive

Mammogram negative

Breast cancer

yes

no

One picture: the GATE frame

every epidemiological study hangs on the GATE frame

The 1st acronym = PECOT: the 5 parts of every epidemiological study

Participants

Exposure Group

Comparison Group

Time

Outcomes

1st critical appraisal task: describe study’s design by hanging on GATE frame using PECOT acronym

Participants

Study Setting

Eligible Participants
Participants

Study Setting: London, UK, ? 1990s

Eligible Participants: no previous DVT, > 50 yrs, planned economy air travel 2 sectors > 8 hours

Participants: 231, mean age 61-62 years

DVT in long-haul flights: Lancet 2001;357:1485-9

Exposure & Comparison Groups

Exposure or Intervention Group (EG):
Below knee compression stockings

Comparison or Control Group (CG):
no stockings

Outcomes (O)

Primary Outcome (O)

DVT

Outcomes (O)
Time (T)

incidence

prevalence

Outcome: e.g. death

T = time from take-off to 48 hours post final flight

Study design: GATE frame & PECOT

Participants

Exposure Group

Comparison Group

Outcomes

Every epidemiological study hangs on the GATE frame

Questions?
The 1st formula: study analyses

Occurrence (risk) of disease
= Numerator ÷ Denominator

All epidemiological studies involve measuring the OCCURRENCE of ‘outcomes’

Denominator (Participants)
Numerator (Outcomes)

Occurrence (risk) = Numerator ÷ Denominator

Denominator (Participants)
Numerator (Outcomes)

Occ = N÷D (?)

All epidemiological studies involve measuring the OCCURRENCE of ‘outcomes’

During what period of time (T) was N measured? (incidence)

At what point in time (T) was N measured? (prevalence)

Occ = N÷D (?)

The 1st formula: Occurrence (risk) = Numerator ÷ Denominator

2nd appraisal task: describe analyses by hanging numbers on the GATE frame and calculating occurrences in exposure & comparison groups

Denominator 1:
Exposure Group (EG)
Numerator 1: a

Denominator 2:
Comparison Group (CG)
Numerator 2: b
Occurrence = \( N \div D \)

Denominator 1: Exposure Group
\( EG \)

Numerator 1: \( a \)

Denominator 2: Comparison Group
\( CG \)

Numerator 2: \( b \)

Exposure Group Occurrence: \( EGO = a \div EG \)
Comparison Group Occurrence: \( CGO = b \div CG \)

Calculate EGO & CGO for the outcome ‘DVT’ post long-haul flight

Denominator 1: Exposure Group
\( EG = 115 \)

Numerator 1: \( a = 0 \)

Denominator 2: Comparison Group
\( CG = 116 \)

Numerator 2: \( b = 12 \)

\( EGO = 0/115 = 0\% \) at post flight assessment
\( CGO = 12/116 = 10\% \) at post flight assessment

ITT (intention to treat) analysis

Calculate EGO & CGO for the outcome ‘average platelet count’ pre-long-haul flight

Denominator 1: Exposure Group
\( EG = 115 \)

Numerator 1: \( a \)

Denominator 2: Comparison Group
\( CG = 116 \)

Numerator 2: \( b \)

\( EGO = average \ \text{platelet count} = 242 \times 10^9/L \)
\( CGO = average \ \text{platelet count} = 240 \times 10^9/L \)

Describing differences between occurrences

Relative difference or Relative Risk = EGO + CGO

Absolute Difference or Risk Difference = EGO - CGO

Number Needed To Treat (NNT) = 1 ÷ RD
Describing differences between occurrences

Relative difference or Relative Risk = \( \frac{EGO}{CGO} \)

Absolute Difference or Risk Difference = \( EGO - CGO \)

Number Needed To Treat (NNT) = \( \frac{1}{RD} \)

\( \frac{0/115}{12/116} = 0/10\% = 0 \)

\( \frac{0/115}{12/116} = -10\% = -10/100 \)

\( 1 \div (-10/100) = -100/10 = 10 \)

"If 10 people wore compression stockings 1 DVT would be prevented"
3rd appraisal task: assess the degree of bias by applying the RAMBO acronym

**Recruitment**
- Study setting & eligibility criteria well described?
- Recruited volunteers from advertisements; eligibility criteria well described
- Participants representative of eligibles?

**Allocation**
- Was Allocation to EG & CG successful?
- RCT: Allocate randomly by investigators (e.g., drugs)
- Cohort: Allocate by measurement (e.g., smoking)
- Were EG & CG similar at baseline?

**Maintenance**
- Were Recruitment processes appropriate to study goals?
- Study setting & eligibility criteria well described?
- Recruited random/representative sample or consecutive eligibles or volunteers from advertisements
- Participants representative of eligibles?
- Prognostic/risk profile appropriate to study question?

**Blind or Objective assessment of outcomes**

Successful randomisation depends on 2 inter-related processes
- Generating a random number sequence to allocate participants
- Concealing those involved (participants & investigators) from knowing to which group a participant will be allocated

Allocation concealment & double blinding
- RCTs

Concealment happens during randomisation, blinding happens after
RCT: Allocated randomly by investigators using sealed envelopes

EG & CG similar at baseline except more women in stocking group

? Allocation bias

Inadequate allocation concealment
& estimates of treatment effects

• Study of 250 randomised control trials of pregnancy and childbirth (Schulz et al. JAMA 1995;273:408)
• Results: studies with inadequate or unclear allocation concealment overestimate Rx effects by 30-40%
• Moher et al. 1998-Other trials on heart disease, stroke, mental health.
• Results: On average inadequate concealment yields 37% larger estimates of effect
(Moher et al. Lancet 1998;352:609)

RAMBO: A is for Allocation

were Participants Maintained as allocated?
did most participants remain in allocated groups (EG & CG)

Participants &/or investigators blind to exposure (and comparison exposure)?

Compliance high & similar in EG & CG?
Contamination low & similar in EG & CG?
Co-interventions low & similar in EG & CG?
Completeness of follow-up high & similar in EG & CG?

Were outcomes assessed Blind or Objectively?

If outcome assessments not Objective (eg, automated or definitive) were investigators Blind to exposure (and comparison exposure)

115 116
100 100

Participants &/or investigators blind to exposure (and comparison exposure)? no

Compliance high & similar in EG & CG? dk
Contamination low & similar in EG & CG? dk
Co-interventions low & similar in EG & CG? ok
Completeness of follow-up high & similar in EG & CG? ok, lost < 15%

* dk = don’t know
Outcome measurements reasonably objective (ultrasound)
Technician was blind to exposure (although some participants may have had a stocking line)

**The 4 (GATE) study biases**
- Recruitment bias
- Allocation bias
- Maintenance bias
- Outcomes assessment bias

**DVT in long-haul flights: Lancet 2001;357:1485-9**
- Recruitment ok
- Allocation ok
- Maintenance ok
- Outcomes assessment ok

**Questions?**

**The 2nd formula: assessing random error**

Random error = 95% Confidence Interval
(1.96 x Standard Error)

**4th appraisal task: assess degree of random error in study findings using the 2nd formula**

Random error = 95% Confidence Interval
EGO = 0%; 95% CI = 0% - 3%
CGO = 10%; 95% CI = 4.8% - 16%

Nine trials studying participants using KL stockings were analyzed. Forty-six of 1261 participants randomly assigned to the control group developed deep vein thrombosis (DVT), compared with two of 1237 participants (0.16%) in the KL stockings group. There was an absolute difference of 3.4% in the incidence of DVT, in favour of KL stockings. The number needed to treat with KL stockings to avoid one case of DVT was 29.4. However, there was significant heterogeneity among trials. The RR for DVT was 0.08 in high-risk participants and 0.14 in low- to medium-risk participants.