



Defining exposure periods based on dosage information - examples and discussion

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Outline

- Examples of different strategies
 - Using dosage
 - Using number of days supply
- Assumptions
- Choice of study period
- Issues to bear in mind
- What is available? Some examples

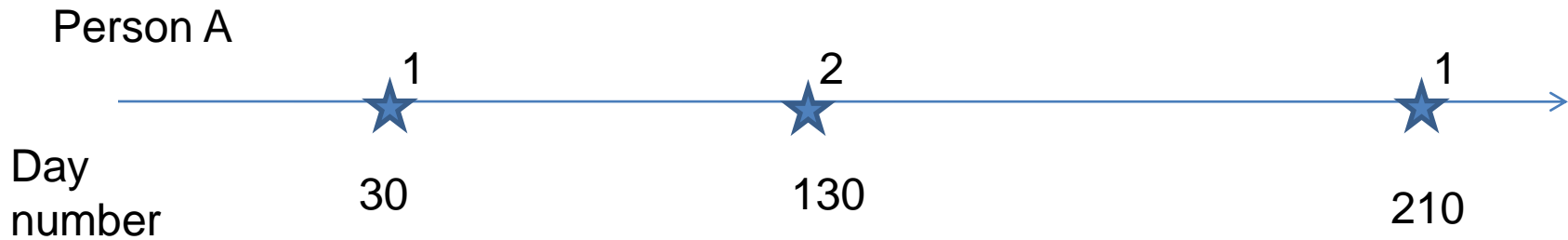


The core

- Exposure assessment
- Defining when a person is a user of a drug either at a specific day or during a period of time based on records on purchased medicines



When is someone a user?



How long should the purchased medicine last?

- How much was purchased?
- Consumption rate



Defining exposure – dosage (1)

- Dosage recorded in a structured manner
i.e. a dosage code
- PHARMO- recorded dose on label
tranferred to standard codes from text
- Estimated duration of use
→ (number of dispensed units)/(prescribed
number of units/day)



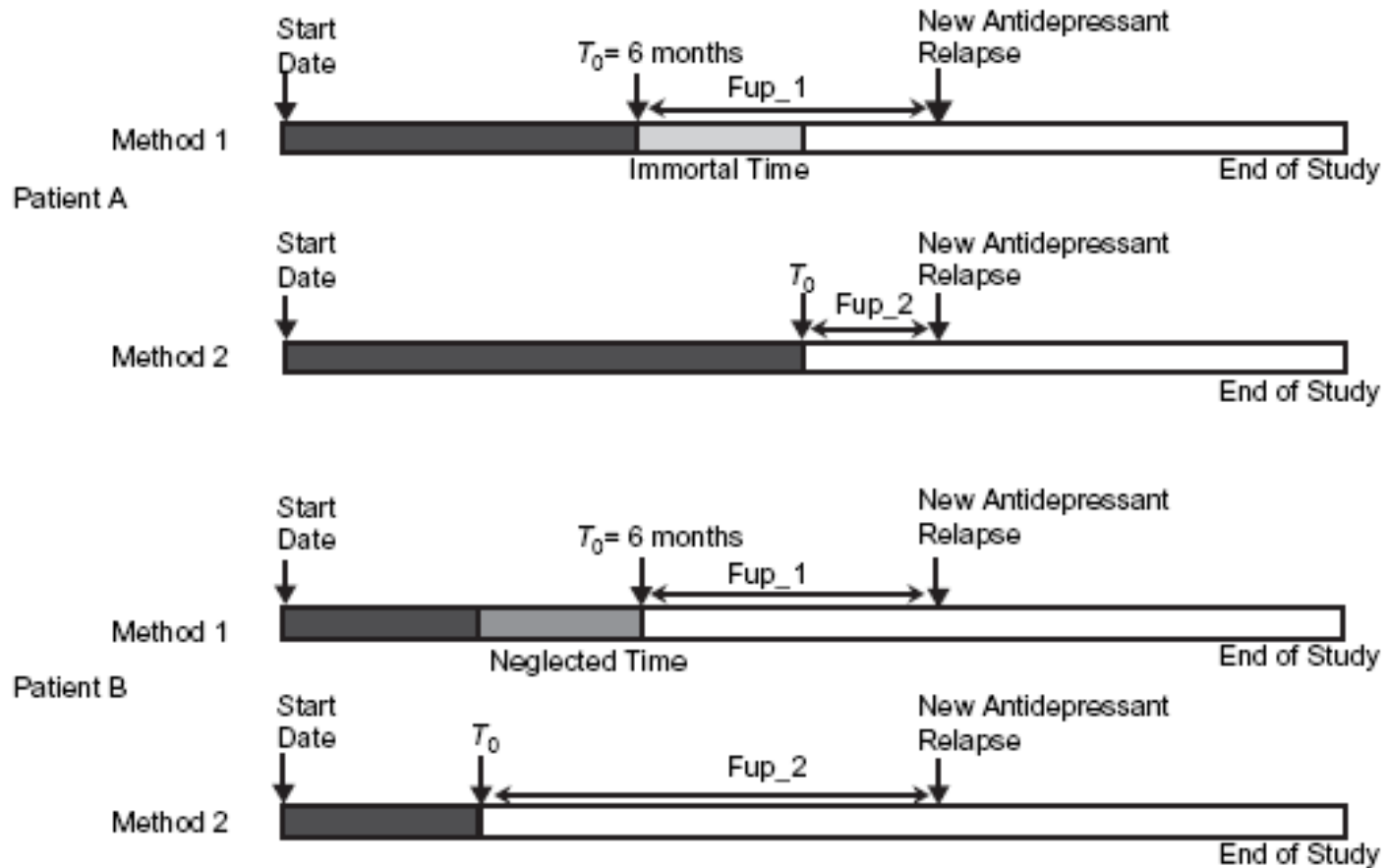
Example II Gardarsdottir et al 2009

- Duration of antidepressant drug treatment and its influence on risk of relapse/recurrence: immortal and neglected time bias. *Am J Epidemiol*.
- Compares two methods of exposure assessment
- New users of antidepressants with depression as diagnosis/indication
- Run-in period 6 months, follow-up at least 12 months
- Dispensing data for GPs in DNSGP-2 1999-2003
- Outcome: recurrence or relapse

- Method 1(Melfi et al 1998)- fixed periods
 - 6 months pre-treatment
 - 6 month treatment
 - 18 month follow-up
- Method 2
 - 6 months pre-treatment
 - Individual treatment period (n months following start date)
 - A follow-up period (24- n months)

Method 2 - Estimation of individual treatment periods

- Start date- the first dispensed antidepressant drug
- End date – expected end date of the last prescription of the treatment episode
- Expected end date/prescription – dispensing date + estimated duration of use
- Succeeding prescriptions considered part of the episode if time between expected end date and dispensing date less than 6 months



Patient A- continuing user
 Patient B- early discontinuer

Defining exposure –dosage (2)

- Analyzing dosage text strings
- By standardizing/grouping text strings into categories with prescribed daily dose
 - I.e. 1 tablet once daily is translated to 1
- Requires soft-ware that can interpret text strings / programming skills
- Have been used in the national open comparisons of drug use among the elderly



Defining exposure periods based on number of days supply

- Usually based on administrative reasons
- Number of days supply registered



Example Valuck et al 2009

- Antidepressant discontinuation and risk of suicide attempt: a retrospective, nested case-control study. J Clin Psychiatry.
- Cohort of patients with new depression episodes
- Outcome suicide attempt
- PHARMetrics 1999-2006 - 47 million patients

- Cases: index date - time of event
- Controls: event date – equal number of days after start of depression as their matched case
- Number of days supply given for each dispensed prescription medicine
- Ever use – ≥ 1 filled antidepressant prescription
- Start date - first prescription fill date
- Stop date – last fill + last days' supply

- Current therapy – the antidepressant interval contains the outcome event date
 - Short term – <90 days
 - Long-term – >90 days
 - Initiation – the first 55 days
 - Maintenance – early 56-179 days vs. late ≥ 180 days
 - Titration up /down - the daily dose is changed from previous daily dose in the maintenance phase
- Past therapy - ≥ 1 day gap between stop and event date
 - Recent /distant past - < 90 days / ≥ 90 days
 - Abbreviated trial – last fill date within 56 days of initiation
 - Discontinuation –14 days after stop, no preceding titration down
 - Prior therapy – any days after the stop of therapy and not included in the categories above

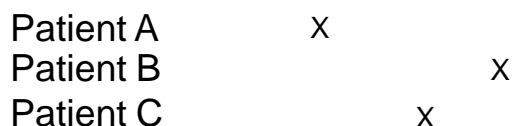
Some issues to consider

- Dosage regimen "As prescribed"
- Multi-dose dispensed drugs
- Drugs used "as needed" and variable dosage
- Adherence and irregular drug use patterns
- What is the focus? The drug itself vs a marker of patients with a specific health problem?
- Recurrent vs first-time users
- Benefit scheme structure
 - Amounts supplied
 - Co-payments
 - Listed products

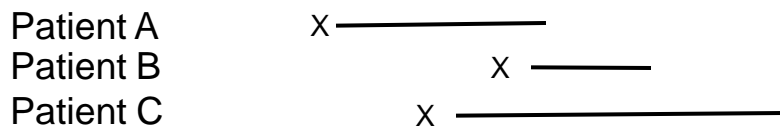


Levels of classifying drug exposure

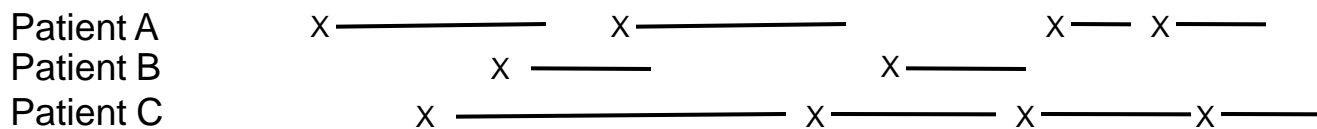
Level 1



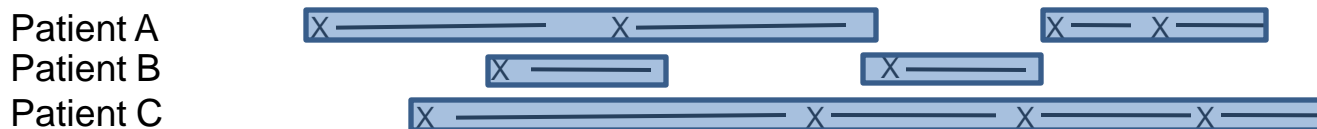
Level 2



Level 3



Level 4



After Leufkens and Urquhart. J Pharm Pharmacol 1994 and Gardarsdottir H. Drug treatment episodes in pharmacoepidemiology – antidepressant use as a model 2009



Thanks for your attention!

