ASSESSING MEDICATION ADHERENCE

Patient-reported, clinical, pharmacoepidemiologic, and economic perspectives

Workshop objectives

• To review methods of adherence assessment, and barriers to accurately estimating adherence, from the patient-reported outcomes and pharmacoepidemiologic perspectives;

• To provide an overview of clinical impact and a case study of patient experience in CML;

• To review challenges in linking adherence estimates to other clinical, patient-reported, and economic outcomes; and

• To discuss common questions that arise when designing and implementing studies focusing on adherence.
Background

Non-adherence definitions

**Adherence / Compliance**
- Adherence is the preferred term; it refers to the extent to which patient behavior matches (agreed-to) health advice. Non-adherence should not be a reason to blame the patient
- Primary vs Secondary non-adherence
- Intentional vs Unintentional non-adherence

**Persistence**
- The LENGTH OF TIME the patient stays on treatment from prescribing date to discontinuation

**Concordance**
- Not the same thing as compliance or adherence. Refers to PROCESS of consulting with patients to elicit patients views and negotiating treatment options. Aim is to create a shared understanding and a shared decision-making
Extent of Non-adherence

**Overall average non-adherence rate**

- Overall (569 studies) 25%

**Chronic diseases**

- Diabetes (23 studies) 32%
- Pulmonary diseases (41 studies) 31%
- Hypertension & CVD (129 studies) 26%

**Life-threatening diseases**

- End-stage renal disease (20 studies) 30%
- Cancer (65 Studies) 21%
- HIV (8 studies) 12%

Non-adherence includes both over dosing & missing doses

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**Patient-reported outcome perspective**

- Research aims may be to:
  - Assess the extent of adherence/non-adherence
  - Understand reasons for non-adherence

- **Methods - self-report:**
  - Interview
  - Questionnaire
  - Simple 1-item questions, i.e. Visual Analogue Scale (VAS)

- **Definition of non-adherence?**
  - Varies widely!
    - <80% of medication taken, specific cut-point on scale
Self-report adherence measures

• Wide range of self-report measures:
  • No gold standard or consensus for research studies or clinical practice
  • Differences in what the measures are measuring:
    • Behavior, beliefs, reasons for non-adherence
  
• Generic vs. Disease-specific?
  • Generic are the most widely used
  • Most frequently validated in hypertension, asthma, and HIV patient populations (Nguyen et al, 2013)
  • Less frequently validated in COPD, rheumatoid and osteo-arthritis (Nguyen et al, 2013)
  • Some disease-specific measures:
    • E.g. Diabetes Self-Care Inventory, Immunosuppressant Therapy Adherence Scale, Maastricht Utrecht Adherence in Hypertension Questionnaire, Compliance Questionnaire Rheumatology.
Adherence measures: Generic examples

- Morisky Medication Adherence Scale (MMAS)
- Medication Adherence Report Scale (MARS)
- Medication Assessment Questionnaire (MAQ)
- Brief Medication Questionnaire (BMQ)
- Simple 1-item VAS

[note: measures can be adapted to specific conditions/treatment]

Assessing adherence using PRO measures

STRENGTHS

- Ease of use
- High acceptability and relevance to patients
- Economical
- Applicable to clinical practice
- Provides insight into why patients are non-adherent

LIMITATIONS

- Social desirability bias
- Recall bias
- Difficult to get detail on patterns of adherence
How should we ask patients about adherence?  

<table>
<thead>
<tr>
<th>Question Type</th>
<th>Question Content</th>
<th>Response Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>“Did you take all your medications all the time”?</td>
<td>None of the time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A little of the time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Some of the time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A good bit of the time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Most of the time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>All of the time</td>
</tr>
<tr>
<td>Percent</td>
<td>“What percent of the time were you able to take your medications exactly as your doctor prescribed”</td>
<td>11 categories: 0, 10, 20.... to 100%</td>
</tr>
<tr>
<td>Rating</td>
<td>“Rate your ability to take all your medications as prescribed”</td>
<td>Very poor</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fair</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Good</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Very good</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Excellent</td>
</tr>
</tbody>
</table>

Results – Lu et al (2008)  

![Fig. 1 Mean difference between self-report (SR) and MEMS adherence](image)
Pharmacoepidemiologic

- Specifically, using retrospective, pharmacy (+ more) data to assess adherence
  - In the US, traditionally/often insurer databases; restricted coverage, limited clinical data
  - Potential data sources expanding; EHR, registries and population-based admin data

- Potential research aims
  - To characterize adherence
  - To estimate the association between adherence, and other outcomes
  - To adjust for adherence while precisely estimating other parameters

How is adherence assessed using retrospective data?

- Through some type of counting (of days, meds), using records of dispensations
- Data are required on at least one refill to be able to calculate adherence
- BEWARE, definitions of common measures vary across studies

<table>
<thead>
<tr>
<th>MPR, Medication possession ratio</th>
<th>PDC, Proportion of days covered</th>
</tr>
</thead>
<tbody>
<tr>
<td># days of medication supplied/ # days in refill interval</td>
<td># days that medication is available/ # days in a time interval (vs. refill interval)</td>
</tr>
<tr>
<td>Intuitive, can be measured continuously over many refills</td>
<td>Because counting days, avoids double counting of MPR</td>
</tr>
<tr>
<td>However, estimate can &gt;1, when fills occur prior to completion of previous refill interval, or when switches occur; cannot account for discontinuation at the end of the refill interval</td>
<td>Can include periods of discontinuation</td>
</tr>
<tr>
<td>Tends to be &lt; than MPR</td>
<td></td>
</tr>
</tbody>
</table>

- Choice of measure impacts perception of adherence
  - Particularly, for using continuous vs. dichotomized measures
Assessing adherence using retrospective data

Limitations
- Relies on the validity of input data, collected for purposes other than research
- Records prescriptions or dispensations, not usage
- Often miss some medication use
  - In hospital
  - OTC/Physician samples
  - Non-linked pharmacies
- Cannot be used to understand patterns of adherence/non-adherence
- Unit of measurement for adherence limited by duration of the prescription refill

Strengths
- Economical
- Non-invasive
  - Avoids the Hawthorne effect, social desirability bias
- Real-world, potentially very large sample sizes with long follow-up
  - Some databases are population-based

- *Key strength: Other clinical, admin data can link adherence to downstream clinical and economic consequences*

Retrospective assessment of adherence to CML therapy

- Adherence measurement is no longer an issue just of chronic disease management
- For example, for CML: Oral therapy to achieve treatment response/prevent relapse, dispensed from community pharmacies

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Data source</th>
<th>Treatment</th>
<th>N</th>
<th>Mean MPR (%)</th>
<th>Mean PDC (%)</th>
<th>% with ‘poor adherence’</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darkow et al, 2007</td>
<td>US claims data</td>
<td>Imatinib</td>
<td>267</td>
<td>78</td>
<td>--</td>
<td>45% (MPR&lt;90%)</td>
<td>12</td>
</tr>
<tr>
<td>Wu et al., 2010a</td>
<td>US claims data</td>
<td>Nilotinib</td>
<td>521</td>
<td>--</td>
<td>79</td>
<td>--</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dasatinib</td>
<td>--</td>
<td>69</td>
<td>--</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Wu et al., 2010b</td>
<td>US claims data</td>
<td>Imatinib</td>
<td>592</td>
<td>79</td>
<td>--</td>
<td>41% (MPR&lt;85%)</td>
<td>12</td>
</tr>
<tr>
<td>Dicus et al., 2014</td>
<td>Canadian provincial cancer registry pharmacy data</td>
<td>Imatinib</td>
<td>91</td>
<td>90</td>
<td>--</td>
<td>18% (MPR&lt;80%)</td>
<td>12</td>
</tr>
<tr>
<td>Trivedi et al, 2014</td>
<td>US claims data</td>
<td>Nilotinib</td>
<td>377</td>
<td>84</td>
<td>77</td>
<td>36% (MPR&lt;85%)</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dasatinib</td>
<td>88</td>
<td>79</td>
<td>28% (MPR&lt;85%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ward et al, 2015</td>
<td>US claims data</td>
<td>Imatinib</td>
<td>237</td>
<td>--</td>
<td>77</td>
<td>48% (PDC&lt;85%)</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nilotinib or</td>
<td>131</td>
<td>--</td>
<td>68</td>
<td>53% (PDC&lt;85%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>dasatinib</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Adherence to CML therapy (2)

• Ranges of
  • MPR: 78-90% over 12 months
  • PDC: 69-79% over 12 months
  • ‘Poor adherence’ (by MPR): 18 to 45%

• Clinically-important thresholds for adherence may vary according to:
  • Disease
  • Population
  • Treatment
  • Outcome

When planning retrospective studies of adherence, consider

• What is the key research objective?
  • Describing adherence? Adjusting for it?

• What data are available and what are their limitations? Key assumptions?

• What measure should I use?
  • Is there evidence of clinically-relevant thresholds for classifying patients as adherent, or not?
  • Be aware of differences in definitions used when comparing results across studies

• Keep in mind what you can never know...
Non-adherence in Cancer

The example of Tyrosine Kinase Inhibitors
Cancer Treatment: A Paradigm in Transition

- Cancer prevalence is increasing
- Age specific death rates are decreasing
- Increasing use of Oral Cancer Treatments

Improved treatments & increased use of oral drugs mean cancer is becoming more of a chronic disease managed at home by the patient – thus non-adherence is likely to become more of an issue than it already is.

Extent of non-adherence to TKIs

- **Imatinib**
  - Belgium: 1/3 of patients non-adherent & only 14% took all doses\(^1\)
  - UK: 26% of patients took ≤90%\(^2\)
  - US: 31% patients had no imatinib for >30 days\(^3\)
  - US: 41% patients ≤85% MPR\(^4\)
  - US: 30% patients had ≥1 interruption of >1 week\(^5\)
  - IT: 47% of patients report suboptimal adherence (MMAS, n=413)\(^6\)

- **Dasatinib & Nilotinib 2nd line\(^7\)–\(^10\)**
  - Few reports and some conflicting results, but over all non-adherence rates are similar to that of 1st line imatinib

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Impact of poor adherence to TKIs

Negative impact on response of non-adherence to first line TKIs

• Patient with suboptimal response had lower adherence levels\(^1\)
• ≤90% no CMR\(^2\)
• ≤80% no MMR\(^2\)
• 2-year follow up: Patients taking ≤85% more likely to lose imatinib response / discontinue treatment\(^3\)
• Non-adherent patients less likely to reach 5-year EFS (59.8% vs 76.7%) & less likely to achieve CCyR at any point (26% vs 44%)\(^4\)

Increased health care costs\(^5,6\)

Predictors of Non-adherence to TKIs

• **Grade 1-2 side effects of BCR-ABL inhibitors in CML\(^1\)**
  • Lack of energy / feeling tired
  • Feeling sick / vomiting
  • Muscle cramps
  • Pain in bones or joints

• **Treatment characteristics\(^2\)**
  • Duration on first line TKI
  • Time lag between CML diagnosis and initiation
  • Starting dose

• **Low social support & desire for additional information\(^3\)**

• **Presence of co-morbidities (using Charlson Comorbidities Index)\(^4\)**

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Why are patients non-adherent?

To understand why we cannot just look at predictors – we need to listen to individuals.

What do CML patients say?

Unintentional non-adherence

And sometimes you just forget. It’s very strange. It’s almost a surprise when you don’t take it

They [the pharmacy] had no medication for me, so I went for nearly a week with no medication.
Intentional non-adherence

Oh I can’t be bothered tonight, it’s not going to kill me [to miss a dose] – sort of thing, so I’ll just go to sleep

I don’t want to take it, because it makes me feel sick. And the next day I’d feel a bit better. I sleep better when I don’t have it. So I consciously didn’t take it. Because I didn’t want to take it

I thought there was no way I was going [on holiday] and being tired. So I did actually stop taking the tablets for a week before I went, and I didn’t take them for the first half of the week I was there

Both Unintentional & Intentional

If I think I've missed it I will definitely wait until the next day…/… rather than overdose...

Eliasson, Thesis 2011

Patients’ views of consequences

I suppose, I’m not a doctor, but I don’t think missing one pill, or 3 pills, in a month affects me at all

I really noticed it when I didn’t take it for 2 months…/… I felt myself again

Health care providers’ influence on patients’ adherence

I’m tending to miss more now, because at first I thought it was sort of life or death if you miss a tablet, but now the doctors have told me, you know, it’s not a big thing if you miss one or two, so I tend to not worry about it as much as I did previously.

If I thought there was going to be any effect on [my response] then I guess that would make a big difference

I knew I was missing days, but I didn’t quite realise how many I was missing.

So it worked out that maybe I’d missed 20% of the doses over a three month period. So it wasn’t working quite as well as it could do, so they said, ‘We’ll bring your dose down instead, to 400 mg, make sure you take it every day’.

And the side effects haven’t been quite so bad. So it’s more manageable to do that ...

I haven’t missed any, because I know I am taking less, and I want it to work on less. I have been trying to make sure I take it every time.

Impact of adherence on clinical and economic outcomes: does non-adherence matter?

• Periodic non-adherence in very mild disease may have negligible consequences.
• Some medicines may be more ‘forgiving’ than others, such that partial adherence may still produce some clinical benefit.
• If a medicine has been prescribed appropriately, this represents a lost opportunity to improve or maintain a patient’s health status.
• Potential consequences of non-adherence:
  • health benefits forgone (poor health-related quality of life, increased hospitalisations and premature mortality)
  • wider economic burden (personal, health and social cost).

What do we know about the impact of adherence on clinical outcomes?

<table>
<thead>
<tr>
<th>Disease, country, cohort</th>
<th>Effect of adherence on outcomes</th>
</tr>
</thead>
</table>
| Diabetes, USA, 11 532 adults in a managed care organization (Ho et al 2006 (a)) | Non-adherent (<80% adherence) patients had:  
  • ↑ all-cause hospitalization (23.2% vs 19.2%, P<.001)  
  • ↑ higher all-cause mortality (5.9% vs 4.0%, P<.001)  
  MVA: non-adherence remained significantly associated with:  
  • all-cause hospitalization (OR, 1.58; 95% CI, 1.38-1.81; P<0.001)  
  • all-cause mortality (OR 1.81; 95% CI, 1.46-2.23; P<0.001). |
| Post MI, USA, 1521 adults discharged with aspirin, β-blocker, statin after MI hospitalization (Ho et al 2006 (b)) | Patients who discontinued use of all medications at 1 month had:  
  • ↓ 1-year survival (88.5% vs 97.7%; P<0.001) vs patients who took 1 or more medication(s).  
  MVA: medication discontinuation remained significantly associated with:  
  • ↑ higher mortality (HR, 3.81; 95% CI, 1.88-7.72).  
  Results were consistent across discontinuation of aspirin, β-blockers, and statins. |
| COPD, Multi-country, 6112 adults with moderate to severe COPD in an RCT (Vestbo et al 2009) | Non-adherent (<80% adherence) patients had:  
  • ↑ exacerbation-related hospitalization (27% vs 15%, P<.001)  
  • ↑ all-cause mortality (26.4% vs 11.3%)  
  MVA: adherence remained significantly associated with:  
  • exacerbation-related hospitalization (RR 0.58, 95% CI 0.44 to 0.73, p < 0.001).  
  • all-cause death (HR 0.40 (95% CI 0.35 to 0.46), p<0.001). |
What do we know about the impact of adherence on economic impact?

Estimating the impact of adherence on economic outcomes

- In England, the estimated opportunity cost of health gains foregone due to non-adherence: £930m p.a. in 5 key diseases:
  - Asthma (£130 million);
  - Type 2 diabetes (£100 million);
  - high cholesterol/coronary heart disease (statins for primary prevention and secondary prevention) (£120 million);
  - hypertension (£390 million);
  - schizophrenia (£190 million).

- The authors estimated that improving adherence from current levels to 80% across these five areas would save the NHS £500m p.a.
Measuring outcomes of interventions to improve adherence

What are the key challenges for researchers in assessing the impact of adherence on clinical and economic outcomes?

- Assumption that prescription was appropriate
- Assumption that the medicine has an effect on outcome
- Assumption that adherence measure used is valid
- What outcome should be measured?
  - Is there a proven causal link between adherence and the outcome measure?
  - What about confounders?
- Is the study sufficiently powered to detect a difference in outcome?
- Can all resource use be captured (what about interoperability of data capture systems)?
- Will follow-up be long enough to capture the effects of non-adherence on patient health and resource use?
What are the key challenges for researchers in assessing the impact of adherence on clinical and economic outcomes (2)?

- Adherence: implicit assumption that taking prescribed medicines is a “good thing”
- Most patients take some medicines some of the time
- So improving adherence is about assessing the effect of patients taking slightly more medicines slightly more of the time
- $P_{\text{effectiveness}}$ isn’t 100% even when adherence is 100%

We need a bigger trial!

Impact of adherence on clinical and economic outcomes

- Present a case for targeting the area (i.e. economic impact of non-adherence)
- To show an intervention is effective (or not)
- To show an intervention is cost-effective (or not)
- Poor study design may show erroneously that an intervention isn’t effective/cost-effective

“36 of 81 interventions reported in 69 RCTs were associated with improvements in adherence, but only 25 interventions led to improvement in at least one treatment outcome. Even the most effective interventions did not lead to large improvements in adherence and treatment outcomes.”

Impact of adherence on clinical and economic outcomes: the case of the New Medicine Service

The New Medicine Service (NMS) is a national community pharmacy service to support medicines-taking in people starting a new medicine for asthma/COPD, hypertension, type 2 diabetes or an anticoagulant/antiplatelet agent.

(http://psnc.org.uk/services-commissioning/advanced-services/nms/)

New Medicine Service evaluation (RCT)

• 504 participants from 47 pharmacies (East Midlands, South Yorkshire, London) randomised to NMS or current practice.

• **Main outcomes:**
  • Adherence to new medicine 10 weeks post recruitment.
  • The NMS question: ‘Since we last spoke have you missed any doses of your new medicine, or change when you take it (prompt: when did you last miss a dose)?’

• **Analysis:** ITT, outcome adjusted for pharmacy clustering, NMS disease category, age, sex and medication count, multiple imputation for missing data.

• **Follow up:** At 10 weeks 85% patients contacted by telephone (n=443), 60% of questionnaires were returned (n=321), 52 patients withdrawn from study.

• **Adherence (NMS question):** OR (95% CI) 1.64 (1.08, 2.50, p=0.02), p [adherence] CP: 0.67 (0.60, 0.74) vs. p [adherence] NMS: 0.78 (0.72, 0.84)
NMS Economic evaluation

Markov model*

State

1

State

2

Death

Probability and resource use data from trial

Probability, resource use and utility data from published sources

*Numer and type of health states will depend on the disease/drug group

NMS economic models of impact of nonadherence

• The six treatment pathway models are:
  • Hypertension-amlodipine
  • Hypertension-ramipril
  • Asthma-inhaled corticosteroid (beclometasone)
  • COPD-tiotropium
  • Diabetes-metformin
  • Anticoagulants-aspirin

• Lifetime time horizon, NHS perspective, 3.5% discount rate, deterministic and probabilistic models

• Combined with
  • Effect size, age, disease severity, drug being prescribed and health status from NMS RCT
  • Proportion of disease groups covered by NMS
  • Intervention costs
New Medicine Service economic evaluation

Probability and resource use data from trial

Probability, resource use and utility data from published sources

*number and type of health states will depend on the disease/drug group

Results from individual models

<table>
<thead>
<tr>
<th>Model</th>
<th>Mean dQALY (95% CI), £</th>
<th>Mean dCost (95% CI)/£</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adherent</td>
<td>Non-adherent</td>
</tr>
<tr>
<td>CCB*</td>
<td>14.32</td>
<td>13.92</td>
</tr>
<tr>
<td></td>
<td>(11.76, 16.53)</td>
<td>(11.12, 16.18)</td>
</tr>
</tbody>
</table>

*Hypertension models: CCB and ACE
Combining the data from the RCT and the treatment pathway models

Cost & QALY caused by non-adherence from models

<table>
<thead>
<tr>
<th>Model</th>
<th>% NMS cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCB*</td>
<td>25.3%</td>
</tr>
<tr>
<td>ACE*</td>
<td>24.1%</td>
</tr>
<tr>
<td>Aspirin</td>
<td>8.5%</td>
</tr>
<tr>
<td>Asthma</td>
<td>17.5%</td>
</tr>
<tr>
<td>COPD</td>
<td>5.8%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>18.9%</td>
</tr>
<tr>
<td>Overall</td>
<td>100%</td>
</tr>
</tbody>
</table>

Adherence: 10-week ITT analysis incorporating imputed missing values, for NMS adherence outcome: odds ratio, SD (NMS vs. current practice): OR: 1.64 (1.08, 2.50).

p [adherence] NMS group: 78%
p [adherence] current practice: 67%

Cost of NMS intervention: £24.60

Composite economic evaluation

NMS Economic analysis: disaggregated and aggregated results

<table>
<thead>
<tr>
<th>Model</th>
<th>Mean cost (95% CI), £</th>
<th>Mean QALY (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NMS**</td>
<td>CP</td>
</tr>
<tr>
<td>CCB*</td>
<td>1 535 (516, 2 317)</td>
<td>1 562 (500, 2 398)</td>
</tr>
</tbody>
</table>
**Conclusions**

- NMS generated a mean of 0.06 (95%CI: 0.00, 0.16) more QALYs per patient, at a mean reduced cost of £190 (95%CI: -929, 87).
- NMS dominates current practice, with an ICER (95% credibility range) of £3 005 (-17 213, 4 543).
- The probability that NMS dominates current practice is 0.81. NMS has a high probability (0.97) of cost-effectiveness at a willingness-to-pay of £20,000 for one QALY.
- NMS increased health gain at a cost per QALY well below most accepted thresholds for technology implementation, usually about £20,000 to £30,000 in the UK.

**A 65 year old man (woman) with moderate hypertension and mild to moderate renal failure will gain 0.10 (0.06) QALYs from taking a statin**

Q&A

Scenarios
Linking adherence, clinical, and economic outcomes in CML

- There is some evidence from large retrospective studies in US CML populations, that better adherence results in lower healthcare resource use
- However, the links between adherence and resource use, and hard clinical outcomes (e.g. complete response to therapy), are lacking
  - We did not identify a retrospective study on adherence with access to the clinical data required to assess responsiveness
- Actual estimates of adherence from those studies differ
  - Due to variability in outcome measures selected, and thresholds used to classify patients as adherent
- How those with CML fared over longer periods of time was unclear, due to studies being limited to one year of follow-up per individual

- What kind of design and data could avoid these limitations?

Linking adherence, clinical, and economic outcomes in CML

**Population Health Data BC**

- Large, linked, population-based datasets
- ~4 M people

- Data included
  - Demographics
  - Medical services (diagnoses and procedures)
  - Acute care discharge data
  - Population-based prescription dispensations
    - Including oncology medications dispensed by community pharmacies
  - Vital statistics

- Linkages
  - Cancer registry
    - Treatment history, response to therapy, risk/prognostic factors
  - Some labs data

Linked data could be used to estimate clinical outcomes and healthcare resource use, while accounting for individual patient adherence

Similar data options available in other Canadian provinces, some US EHR datasets linked to claims data, Scandinavia, ??
Wrap-up

Assessing adherence