

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 rate¹

- 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

¹DiMatteo MR, et al. Med Care 2004;4:200–209;

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

What are validated self-report adherence scales really measuring?: a systematic review

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AIMS

Medication non-adherence is a significant health problem. There are numerous methods for measuring adherence, but no single method performs well on all criteria. The purpose of this systematic review is to identify self-report medication adherence scales that have been validated with comparison measures of medication taking behaviour (i.e. scales for these scales measure adherence and we explore how these adherence scales have been validated).

METHODS

Crossed and PubMed databases were used to search articles written in English on the development or validation of medication adherence scales dating to August 2012. The search terms used were medication adherence, medication use, adherence, medication compliance and terms of each scale. Data such as names identified, year published, comparison measures were utilised and compared.

RESULTS

Only articles were included in the review which contained at least 41 adherence items. Adherence scales include items that either elicit information regarding the patient's medication taking behaviour or beliefs, associated with adherence. The validation strategies employed depended on whether the focus of the scale was to measure medication taking behaviour or identify barriers to both.

CONCLUSIONS

Supporting patients to be adherent requires information on their medication taking behaviour (complex to adherence and beliefs about medication). Adherence scales have the potential to explore these aspects of adherence but currently there has been a greater focus on measuring medication taking behaviour. Selecting the 'right' adherence scale(s) requires consideration of what needs to be measured and how well or whether the scale has been validated.

RESEARCH ARTICLE

Open Access

Suitability of measures of self-reported medication adherence for routine clinical use: A systematic review

Sue Sarfield^{1*}, Sarah Clifford¹, Lisa Haines^{2,3}, Nick Sabin⁴ and Alan Wilton¹

Abstract

Background: There is a recognised need to build primary care medication adherence services which are tailored to patient needs. Continuous quality improvement of such services requires a regular working method of measuring adherence in order to monitor effectiveness. Self-report has been proposed the method of choice for clinical use. It is cheap, relatively unobtrusive and able to distinguish between intentional and unintentional non-adherence, which have different underlying causes and therefore require different interventions. A self-report adherence measure used in routine clinical practice would ideally be brief, acceptable to patients, valid, reliable, have the ability to distinguish between different types of non-adherence and be able to be completed by or in conjunction with others when necessary.

Methods: We systematically reviewed the literature in order to identify self-report adherence measures currently available which are suitable for primary care and evaluate the extent to which they met the criteria described above. We searched the databases Medline, Embase, International Pharmaceutical Abstract, Pharmline, CINAHL, PsycINFO and Health to identify studies reporting the development, validation or reliability of generic adherence measures. One reviewer screened all abstracts and assessed all relevant full text articles obtained and a second reviewer screened a random 10% to check reliability.

Results: Fifty eight measures were identified. While validation data were presented in support of the vast majority of self-reported measures (83%), data for a relatively small number of measures was presented for reliability (11/58) and few to compare (3/58). Few were designed to have the ability to be completed by or in conjunction with others and few were able to distinguish between different types of non-adherence which limited their ability to be used effectively in the continuous improvement of targeted adherence enhancing interventions. The data available suggested that systems find it easier to estimate general adherence than to report a specific number of doses missed. Visual analogue scales can be easier for patients than other types of scale but are not suitable for telephone administration.

Conclusions: There is a need for a measure which can be used in the routine, external quality monitoring of adherence services.

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

MMAS 4		
	No	Yes
Do you ever forget to take your medication?	(1)	(0)
Are you always at home when taking your medication?	(1)	(0)
When you feel better, do you sometimes stop taking your medication?	(1)	(0)
Sometimes, if you feel worse when you take your medicine, do you stop taking them?	(1)	(0)

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

1. Put a cross on the line below at the point showing your best guess about how much of your prescribed medication you have taken in the last 7 days

0% means you have taken none of the medication

100% means you have taken every single dose of the medication

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

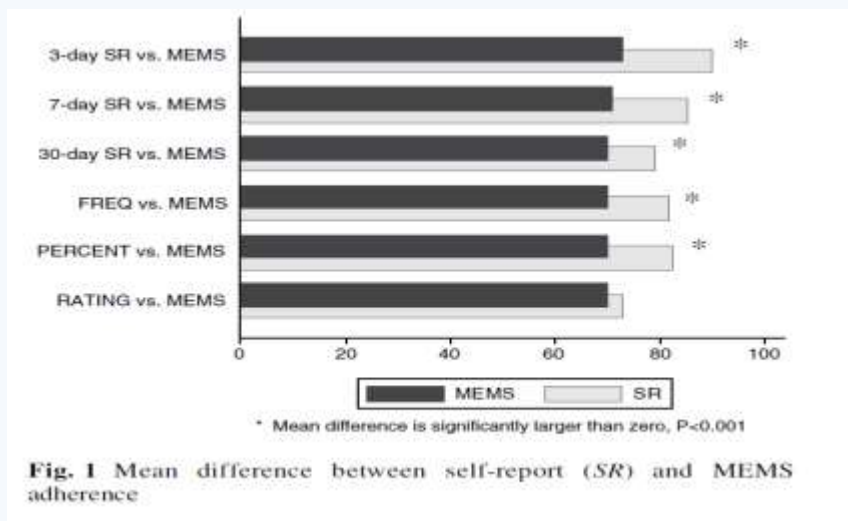
- Social desirability bias
- Recall bias
- Difficult to get detail on patterns of adherence

How should we ask patients about adherence?

Lu et al, 2008

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

Results – Lu et al (2008)



Pharmacoepidemiologic

- Specifically, using retrospective, pharmacy (\pm 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

MPR, Medication possession ratio

- # days of medication supplied/ # days in refill interval
- Intuitive, can be measured continuously over many refills
- However, estimate can >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

PDC, Proportion of days covered

- # days that medication is available/ # days in a time interval (vs. refill interval)
- Because counting days, avoids double counting of MPR
- Can include periods of discontinuation
- Tends to be $<$ than MPR

- 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*

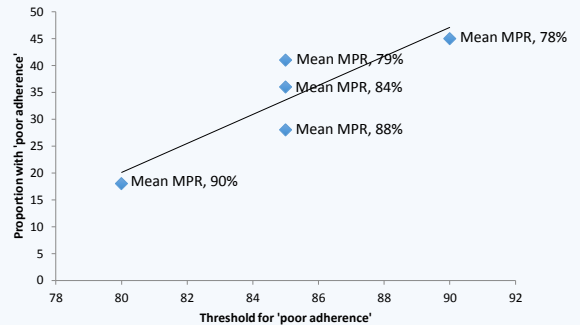
Retrospective assessment of adherence to CML therapy

- 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

Author, year	Data source	Treatment	N	Mean MPR (%)	Mean PDC (%)	% with 'poor adherence'	Follow-up (months)
Darkow et al, 2007	US claims data	Imatinib	267	78	--	45% (MPR<90%)	12
Wu et al., 2010a	US claims data	Nilotinib	521	--	79	--	6
		Dasatinib		--	69	--	6
Wu et al., 2010b	US claims data	Imatinib	592	79	--	41% (MPR<85%)	12
Dicus et al., 2014	Canadian provincial cancer registry pharmacy data	Imatinib	91	90	--	18% (MPR<80%)	12
Trivedi et al, 2014	US claims data	Nilotinib	377	84	77	36% (MPR<85%)	12
		Dasatinib		88	79	28% (MPR<85%)	
Ward et al, 2015	US claims data	Imatinib	237	--	77	48% (PDC<85%)	12
		Nilotinib or dasatinib	131	--	68	53% (PDC<85%)	

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 doses¹
- UK: 26% of patients took $\leq 90\%$ ²
- US: 31% patients had no imatinib for >30 days³
- US: 41% patients $\leq 85\%$ MPR⁴
- US: 30% patients had ≥ 1 interruption of >1 week⁵
- IT: 47% of patients report suboptimal adherence (MMAS, n=413)⁶

Dasatinib & Nilotinib 2nd line⁷⁻¹⁰

- Few reports and some conflicting results, but over all non-adherence rates are similar to that of 1st line imatinib

¹Noens L, et al. Blood 2009;113:5401–1541; ²Marin D, et al. J Clin Oncol 2010;28:2381–2388; ³Darkow T, et al. Pharmacoeconomics 2007;25:481–496; ⁴Wu EQ, et al. Curr Med Res & Opin 2010;26(1):61–69; ⁵Ganesan P, et al. Am J Hematol 2012;86:471–474; ⁶Efficace et al 2012: Abstract 1026; ⁷Wu EQ, et al. Curr Med Res & Opin 2010;26(12):2861–2869; ⁸Guerin, et al. Blood (ASH Annual Meeting Abstracts) 2010;116(21): Abstract 3437; ⁹Ulickas Yood M, et al. J Clin Oncol 2012;29: Abstract 6589; ¹⁰Guerin, et al. Curr Med Res & Opin 2012;28:1155-1162

Impact of poor adherence to TKIs

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

- Patient with suboptimal response had lower adherence levels¹
- ≤90% no CMR²
- ≤80% no MMR²
- 2-year follow up: Patients taking ≤85% more likely to lose imatinib response / discontinue treatment³
- 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}

¹Noens L, et al. Blood 2009;113:5401–1541; ²Marin D, et al. J Clin Oncol 2010;28:2381–2388; ³Ibrahim AR, et al. Blood 2012;117(14):3733–3736; ⁴Ganesan P, et al. Am J Hematol 2012;86:471–474; ⁵Wu EQ, et al. Curr Med Res & Opin 2010;26(1):61–69; ⁶Darkow T, et al. Pharmacoeconomics 2007;25:481–496.

Predictors of Non-adherence to TKIs

- **Grade 1-2 side effects of BCR-ABL inhibitors in CML¹**
 - Lack of energy / feeling tired
 - Feeling sick / vomiting
 - Muscle cramps
 - Pain in bones or joints
- **Treatment characteristics²**
 - Duration on first line TKI
 - Time lag between CML diagnosis and initiation
 - Starting dose
- **Low social support & desire for additional information³**
- **Presence of co-morbidities (using Charlson Comorbidities Index)⁴**

¹Marin D, et al. J Clin Oncol 2010;28:2381–2388; ²St Charles M, et al. Blood (ASH Annual Meeting Abstracts) 2009;114(22): Abstract 2209; ³Efficace F, et al. Blood (ASH Annual Meeting Abstracts) 2012: Abstract 1026. ⁴Fogliatto L, et al. Blood (ASH Annual Meeting Abstracts) 2010;116(21): Abstract 2296

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?



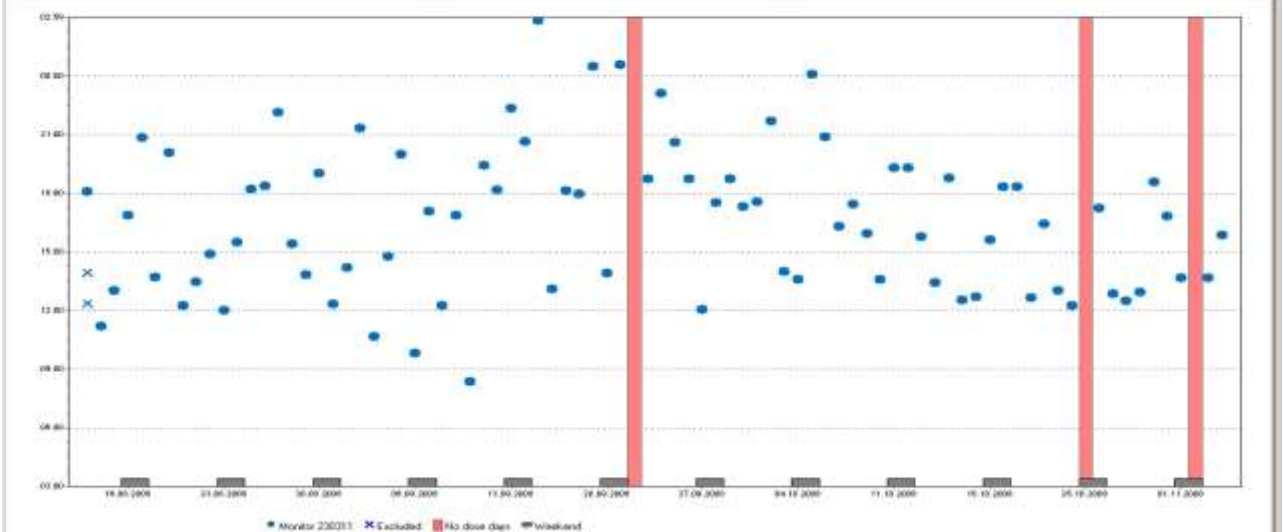
Unintentional non-adherence

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

Patient	7315 94 400d 400	General	Number of monitored days	94	Taking	% Prescribed number of doses taken	96.4%	Hour	Interval intervals	Shortest	10.3
Monitor	230211		Number of prescribed doses	94		% Days correct rate of doses taken	96.4%		Longest	3 Prescribed doses taken on schedule	93.0
Drug	Orvir 500mg		Number of doses taken	91							67.9%
Phase (1)	12/03/2008 03:00 - 05/11/2008 02:59										

Calendar plot | Chronology | Patient info | Days (stats) | Intervals (stats) | Timing (stats) | Drug holidays | Therapeutic coverage | Event list

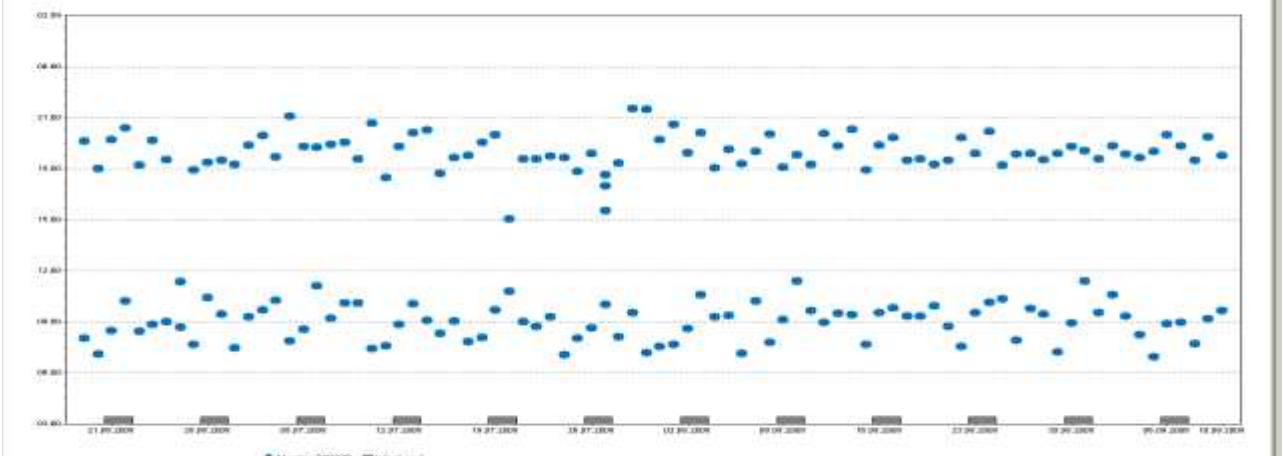


With doses taken
 With wrong doses
 With missed events
 With non-monitored periods
 With none
 With no dose days
 With excluded events
 With errors

© Lina Eliasson

Patient	7030 5P 2008d 100	General	Number of monitored days	94	Taking	% Prescribed number of doses taken	100.0%	Hour	Interval intervals	Shortest	0.7
Monitor	230230		Number of prescribed doses	100		% Days correct rate of doses taken	99.0%		Longest	30.0	30.0
Drug	(Twice a day)		Number of doses taken	100							75.0%
Phase (1)	10/05/2008 03:00 - 11/09/2008 02:59										

Calendar plot | Chronology | Patient info | Days (stats) | Intervals (stats) | Timing (stats) | Drug holidays | Therapeutic coverage | Event list



With doses taken
 With wrong doses
 With missed events
 With non-monitored periods
 With none
 With no dose days
 With excluded events
 With errors

© Lina Eliasson

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

Eliasson L, et al. Leuk Res 2011;35(5):626–630.



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

Eliasson L, et al. Leuk Res 2011;35(5):626-630.

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

Eliasson L, et al. Leuk Res 2011;35(5):626–630. and data on file.

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.

Eliasson L: data on file

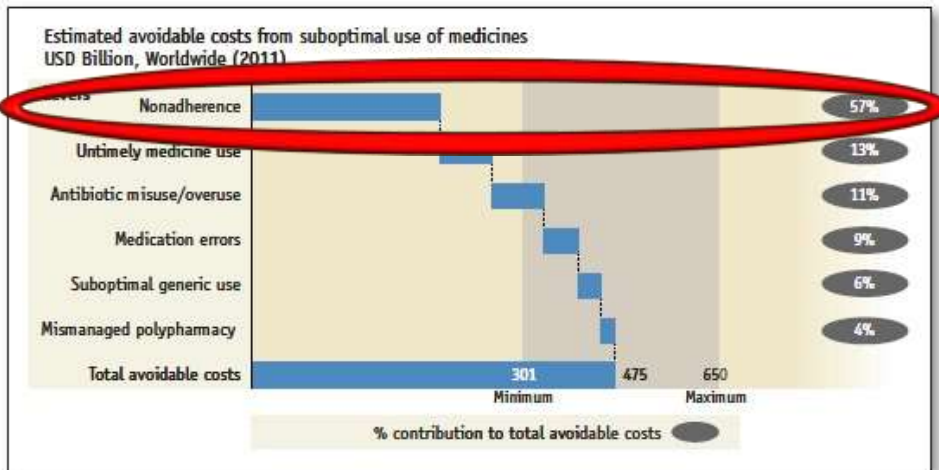
Impact of adherence on clinical and economic outcomes: does non-adherence matter?

- 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?

Disease, country, cohort	Effect of adherence on outcomes
Diabetes, USA, 11 532 adults in a managed care organization (Ho <i>et al</i> 2006 (a))	Non-adherent (<80% adherence) patients had: <ul style="list-style-type: none"> • ↑ all-cause hospitalization (23.2% vs 19.2%, P<.001) • ↑ higher all-cause mortality (5.9% vs 4.9%, P<.001) • 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, 1522 adults discharged with aspirin, beta-blockers, and statins after hospitalization (Ho <i>et al</i> 2006 (b))	<ul style="list-style-type: none"> • ↑ higher mortality (HR, 3.81; 95% CI, 1.88-7.72). Medication discontinuation remained significantly associated with ↑ mortality. Results were consistent across discontinuation of aspirin, beta-blockers, and statins.
COPD, Multi-country 6112 adults with moderate to severe COPD in an RCT (Vest <i>et al</i> 2009)	Non-adherence remained significantly associated with ↑ risks for: <ul style="list-style-type: none"> • ↑ exacerbation-related hospitalization (27% vs 15%, P<.001) • ↑ all-cause mortality (RR 1.46, 95% CI 1.18-1.81, p<.001). • 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?

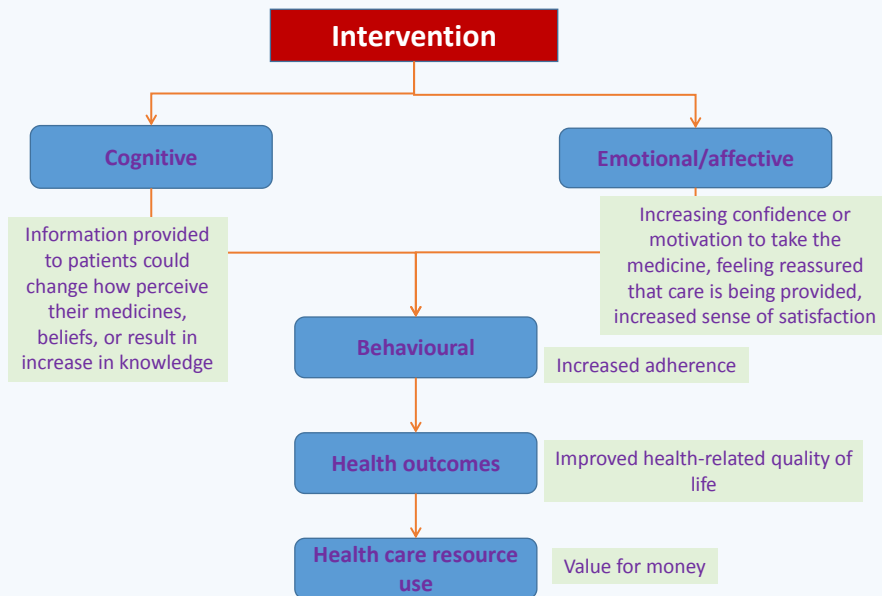


Advancing the responsible use of medicines, IMS Institute for Healthcare Informatics, October 2012.

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.
- (Trueman P, et al. *Evaluation of the Scale, Causes and Costs of Waste Medicines*. London: YHEC/School of Pharmacy, 2010.)

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?

We need a bigger trial!



“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.”

(Haynes RB, Ackloo E, Sahota N, et al. Interventions for enhancing medication adherence (Review). Cochrane Database of Systematic Reviews 2008(2)

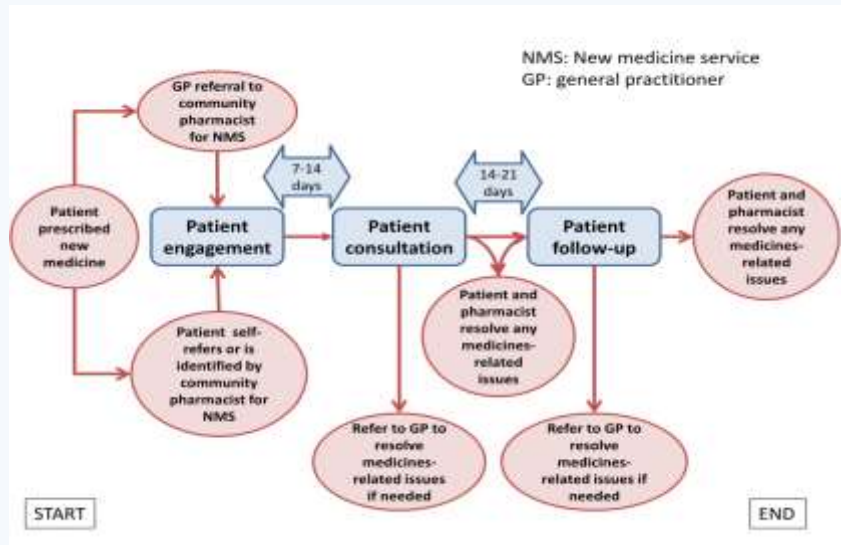
effective



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/>)



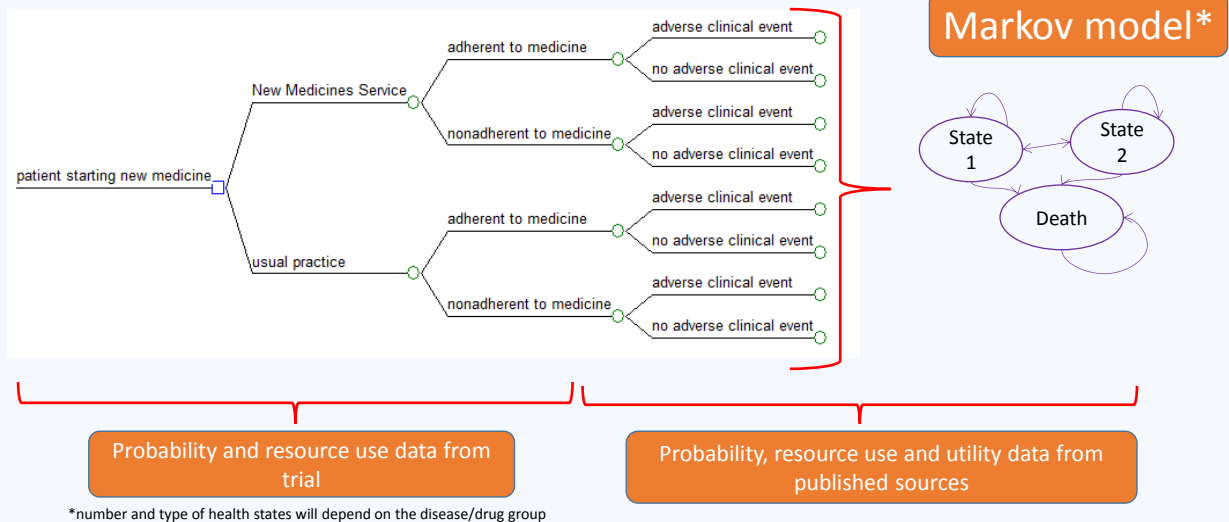
New Medicine Service evaluation (RCT)

Rachel A Elliott, Matthew J Boyd, Nde-Eshimuni Salema, James Davies, Nick Barber, Rajnikant Mehta et al. Effectiveness of the New Medicine Service in community pharmacies in England. *BMJ Quality and Safety in print*

- 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



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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

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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

Model	Mean dQALY (95% CI), £		Mean dCost (95% CI)/£	
	Adherent	Non-adherent	Adherent	Non-adherent
CCB*	14.32 (11.76, 16.53)	13.92 (11.12, 16.18)	1379 (462.5, 1 968.9)	1739 (526, 2 833)

*Hypertension models: CCB and ACE



Combining the data from the RCT and the treatment pathway models

Cost & QALY caused by non-adherence from models



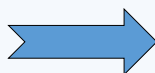
Model	% NMS cohort
CCB*	25.3%
ACE*	24.1%
Aspirin	8.5%
Asthma	17.5%
COPD	5.8%
Diabetes	18.9%
Overall	100%



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

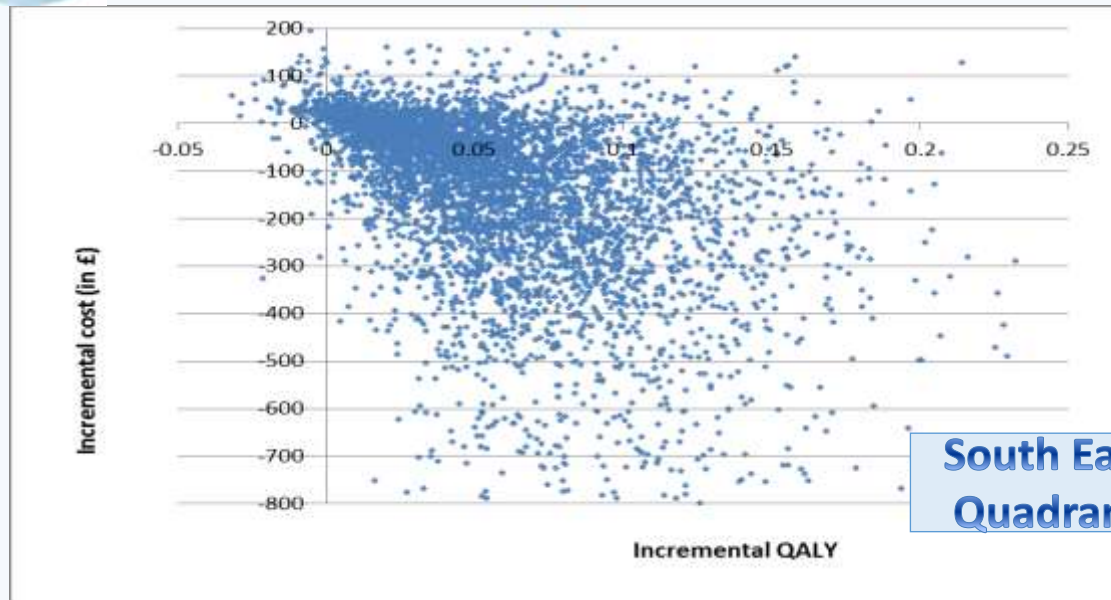


NMS Economic analysis: disaggregated and aggregated results

Model	Mean cost (95% CI), £			Mean QALY (95% CI)			
	NMS**		CP	NMS		CP	
CCB*	1 535 (516, 2 317)	1 562	(500, 2 398)	14.18	(11.55, 16.38)	14.12	(11.46, 16.35)



NMS: Incremental cost effectiveness ratio



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)

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

(Kevin F. Erickson et al. Cost-Effectiveness of Statins for Primary Cardiovascular Prevention in Chronic Kidney Disease. J Am Coll Cardiol. 2013;61(12):1250-1258. doi:10.1016/j.jacc.2012.12.034)

- NMS for technology implementation, usually about £20,000 to £30,000 in the UK

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