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Let it go!

Rationalising medicines for patients with life limiting illness

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St. Benedict's Hospice
& Centre for Specialist
Palliative Care

Welcome

- After lunch!
  - Interactive
- Time limited
  - Assumptions
    - Polypharmacy
    - Limited life expectancy
- Further theoretical/didactic info
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Group Exercise 1

Barriers to Deprescribing

Meet Bob …

- 73 years old with a recent diagnosis of NSCLC
- He has stage IV disease
  - Disease progression with PemCarbo chemotherapy
- In and out of hospital over the last six months
- Attending day hospice for symptom control

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Let's hear from Bob…

Intro 1

Bob's Medicines

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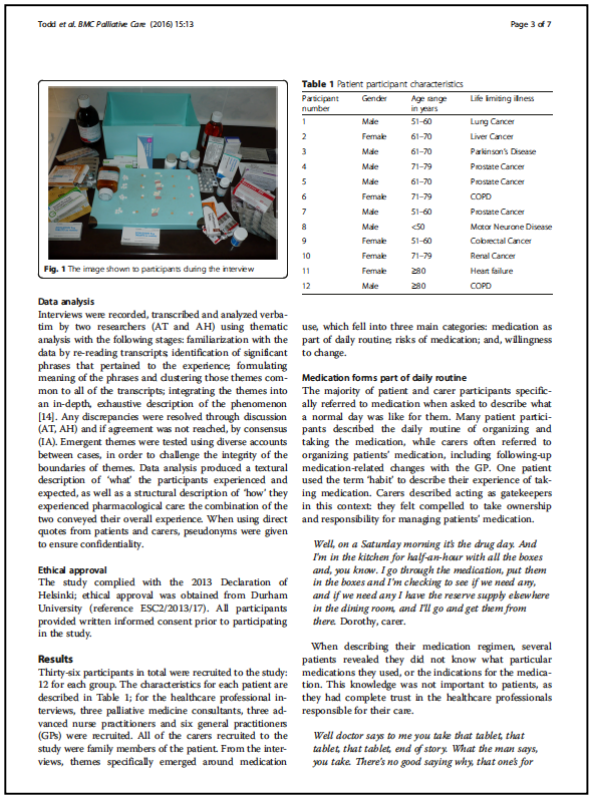
Patients reactions!...



Todd et al. BMC Palliative Care (2016) 15:13 Page 3 of 7

Fig. 1 The image shown to participants during the interview

Table 1 Patient participant characteristics

Participant number	Gender	Age range in years	Life limiting illness
1	Male	51–60	Lung Cancer
2	Female	61–70	Liver Cancer
3	Male	61–70	Parkinson's Disease
4	Male	71–79	Prostate Cancer
5	Male	61–70	Prostate Cancer
6	Female	71–79	COPD
7	Male	51–60	Prostate Cancer
8	Male	<50	Motor Neurone Disease
9	Female	51–60	Colorectal Cancer
10	Female	71–79	Renal Cancer
11	Female	≥80	Heart failure
12	Male	≥80	COPD

Data analysis

Interviews were recorded, transcribed and analyzed verbatim by two researchers (AT and AH) using thematic analysis with the following stages: familiarization with the data by re-reading transcripts; identification of significant phrases that pertained to the experience; formulating meaning of the phrases and clustering those themes common to all of the transcripts; integrating the themes into an in-depth, exhaustive description of the phenomenon [14]. Any discrepancies were resolved through discussion (AT, AH) and if agreement was not reached, by consensus (JA). Emergent themes were tested using diverse accounts between cases, in order to challenge the integrity of the boundaries of themes. Data analysis produced a textural description of 'what' the participants experienced and expected, as well as a structural description of 'how' they experienced pharmacological care; the combination of the two conveyed their overall experience. When using direct quotes from patients and carers, pseudonyms were given to ensure confidentiality.

Ethical approval

The study complied with the 2013 Declaration of Helsinki; ethical approval was obtained from Durham University (reference ESC2/2013/17). All participants provided written informed consent prior to participating in the study.

Results

Thirty-six participants in total were recruited to the study: 12 for each group. The characteristics for each patient are described in Table 1; for the healthcare professional interviews, three palliative medicine consultants, three advanced nurse practitioners and six general practitioners (GPs) were recruited. All of the carers recruited to the study were family members of the patient. From the interviews, themes specifically emerged around medication use, which fell into three main categories: medication as part of daily routine; risks of medication; and, willingness to change.

Medication forms part of daily routine

The majority of patient and carer participants specifically referred to medication when asked to describe what a normal day was like for them. Many patient participants described the daily routine of organizing and taking the medication, while carers often referred to organizing patients' medication, including following-up medication-related changes with the GP. One patient used the term 'habit' to describe their experience of taking medication. Carers described acting as gatekeepers in this context: they felt compelled to take ownership and responsibility for managing patients' medication.

> *Well, on a Saturday morning it's the drug day. And I'm in the kitchen for half-an-hour with all the boxes and, you know. I go through the medication, put them in the boxes and I'm checking to see if we need any, and if we need any I have the reserve supply elsewhere in the dining room, and I'll go and get them from there.* Dorothy, carer.

When describing their medication regimen, several patients revealed they did not know what particular medications they used, or the indications for the medication. This knowledge was not important to patients, as they had complete trust in the healthcare professionals responsible for their care.

> *Well doctor says to me you take that tablet, that tablet, that tablet, end of story. What the man says, you take. There's no good saying why, that one's for*

Christ!

Good heavens! I take 11 in the morning and one at tea time and one at supper time, but that's a tremendous amount of drugs isn't it?

It horrifies me. That's my immediate reaction is fear, because I would hate to be on that much medication

Good God, yes!

All the tablets! I mean what are all these when they get inside your system, what are they doing?

Bob's medication

- Morphine sulphate MR 10 mg tabs
- Dexamethasone 4 mg tabs
- Levothyroxine 50 mcg tabs
- Simvastatin 40 mg tabs
- Ferrous sulphate 200 mg/5 mL syrup
- Ramipril 10 mg caps
- Aspirin 75 mg tabs
- Erlotinib 150 mg tabs
- Diazepam 2 mg tabs
- Amlodipine 10 mg tabs
- Gliclazide 60 mg tabs
- Prednisolone 5 mg tabs
- Salbutamol 100 mcg inhaler
- Metoclopramide 10 mg tabs
- Metformin 500 mg tabs
- Multivitamin caps
- Tiotropium inhaler
- Haloperidol 500 mcg caps
- Ibuprofen 400 mg tabs
- Lansoprazole 15 mg caps
- Amitriptyline 10 mg tabs

How did Bob end up on so many medicines?

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We are driven by Guidelines

Time	Medications†	Other
7:00 AM	Ipratropium metered dose inhaler 70 mg/wk of alendronate	Check feet Sit upright for 30 min on day when alendronate is taken Check blood sugar
8:00 AM	500 mg of calcium and 200 IU of vitamin D 12.5 mg of hydrochlorothiazide 40 mg of lisinopril 10 mg of glyburide 81 mg of aspirin 850 mg of metformin 250 mg of naproxen 20 mg of omeprazole	Eat breakfast 2.4 g/d of sodium 90 mmol/d of potassium Low intake of dietary saturated fat and cholesterol Adequate intake of magnesium and calcium Medical nutrition therapy for diabetes‡ DASH‡
12:00 PM		Eat lunch 2.4 g/d of sodium 90 mmol/d of potassium Low intake of dietary saturated fat and cholesterol Adequate intake of magnesium and calcium Medical nutrition therapy for diabetes‡ DASH‡
1:00 PM	Ipratropium metered dose inhaler 500 mg of calcium and 200 IU of vitamin D	
7:00 PM	Ipratropium metered dose inhaler 850 mg of metformin 500 mg of calcium and 200 IU of vitamin D 40 mg of lovastatin 250 mg of naproxen	Eat dinner 2.4 g/d of sodium 90 mmol/d of potassium Low intake of dietary saturated fat and cholesterol Adequate intake of magnesium and calcium Medical nutrition therapy for diabetes‡ DASH‡
11:00 PM	Ipratropium metered dose inhaler	
As needed	Albuterol metered dose inhaler	

Boyd C, *et al*. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. *JAMA.* 2005; **294**(6): 716-24.

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Homework exercise

Guidelines

Do Bob's medicines all live in harmony?

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Potential Drug-Drug Interactions

- The total number of medications prescribed for the cohort was 1,532 (mean per patient, 12; range 1–21)
- 267 potential drug interactions, categorizing 112 as clinically significant and 155 as not clinically significant
- Drug interactions further sub-divided as moderate and severe
- Severe drug interactions had the potential to result in hospitalization, irreversible harm or death

Severe Drug Interactions Identified	Description
Amisulpride and furosemide	Increased risk of prolongation of the QT interval resulting in ventricular tachycardia
Amlodipine and simvastatin (>20 mg daily)	Increased risk of myopathy and rhabdomyolysis
Aspirin and ibuprofen	Increased risk of bleeding and haemorrhage
Candesartan and spironolactone	Increased risk of developing severe hyperkalaemia
Clopidogrel and warfarin	Increased risk of bleeding and haemorrhage
Dexamethasone and methotrexate	Increased risk of acute hepatotoxicity
Diclofenac and fluoxetine	Increased risk of bleeding and haemorrhage
Digoxin and bendroflumethiazide	Increased risk of digoxin toxicity through loss of potassium
Digoxin and bumetanide	Increased risk of digoxin toxicity through loss of potassium
Digoxin and furosemide	Increased risk of digoxin toxicity through loss of potassium
Fenofibrate and simvastatin	Increased risk of myopathy and rhabdomyolysis
Haloperidol and quinine sulphate	Increased risk of prolongation of the QT interval resulting in ventricular tachycardia
Lisinopril and spironolactone	Increased risk of developing severe hyperkalaemia

Todd A, *et al*. Inappropriate prescribing in patients accessing specialist palliative day care services. *Int J Clin Pharm.* 2014; 36(3):535-43.

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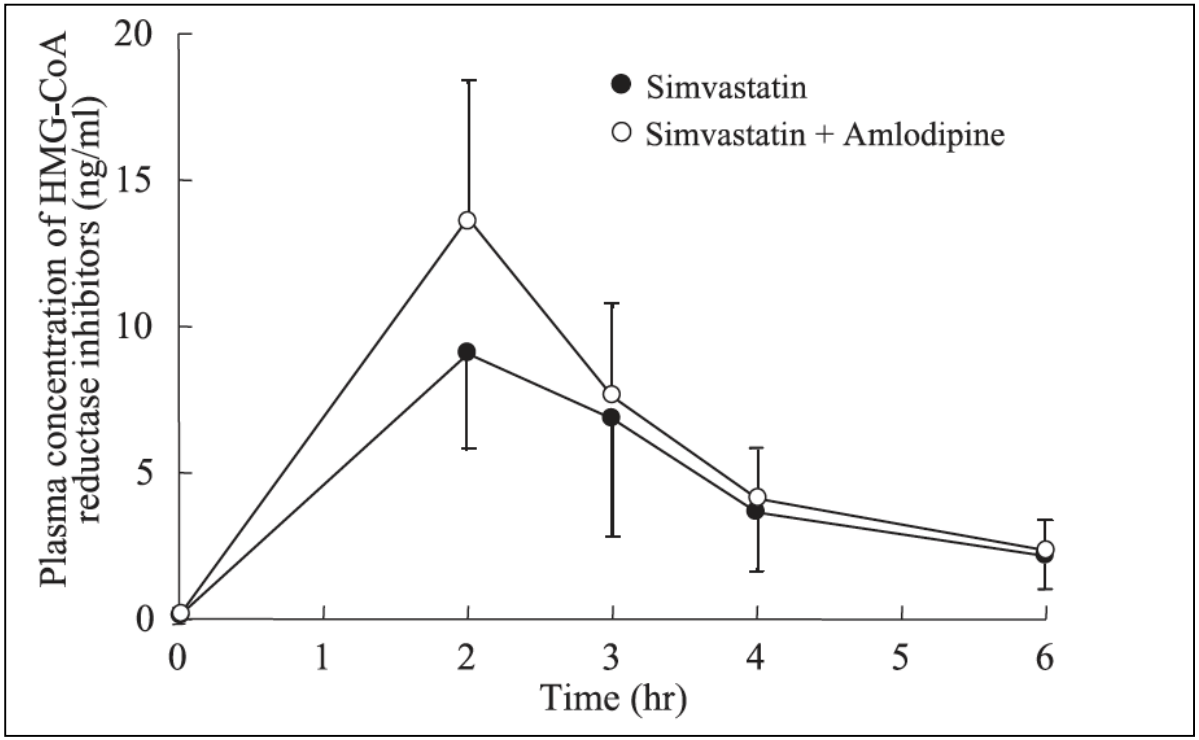
Group Exercise 2

Drug Interactions

Statin Drug Interactions



Nishio S, *et al*. Interaction between amlodipine and simvastatin in patients with hypercholesterolemia and hypertension. *Hypertens Res.* 2005;**28**(3):223-7.

So which tools are available to help us deprescribe?

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1. The patient!

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What does it feel like for patients?

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1. Medication forms a significant part of a patient's routine

- *Well, on a Saturday morning it's the drug day. And I'm in the kitchen for half-an-hour with all the boxes and, you know. I go through the medication, put them in the boxes and I'm checking to see if we need any, and if we need any I have the reserve supply elsewhere in the dining room.*

2. The risks of medication

- *I used to check my blood pressure every day and religiously take my tablets. And I thought eh, and I would say it is higher than yesterday, and this used to worry me. Now I don't worry about it.*

3. Willingness to change

- *So when it like sort of melts in your mouth that's when I feel sick. And I'll say oh I'm not taking them. I'm always changing, telling the doctors like.*

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Todd A, *et al*. 'I don't think I'd be frightened if the statins went' a phenomenological qualitative study exploring medicines use in palliative care patients, carers and healthcare professionals. *BMC Palliative Care.* 2016; **15**(1): 13.

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How's Bob feeling today?…

2

Bob's biochemistry

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BIOCHEMISTRY REPORT NHS

SURNAME	FORNAME	DoB	NHS NUMBER
JOHNSON	BOB	22/10/1943	113665591

REQUESTS	RESULTS	RANGE	UNITS
HAEMOGLOBIN	11.9	13.5-17.7	g/dL
WBC (TOTAL)	7	4-11	$x10^9/L$
SODIUM	140	135-146	mmoL/L
MAGNESIUM	0.7	0.7-1.1	mmoL/L
POTASSIUM	5.0	3.5-5.0	mmoL/L
CALCIUM	2.60	2.20-2.67	mmoL/L
BILIRUBIN	16	<17	µmol/L
UREA	7.5	2.5-6.7	mmol/L
CREATININE	150	79-118	µmol/L
eGFR	43	90-140	$mL/min/1.73m^2$
CPK	560	30-200	U/L
ALK PHOS	259	39-117	U/L
GGT	122	11-58	U/L
ALT	75	<40	U/L
AST	60	12-40	U/L

- Renal insufficiency is common in patients with advanced cancer
- Changes in body fat distribution also evident
- Reduction in blood flow to the liver
- Many patients have cachexia
- Then there's the polypharmacy!

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What's Bob's blood pressure?…

3a and 3b

Hypertension

Int J Clin Pharm
DOI 10.1007/s11096-016-0327-0

SHORT RESEARCH REPORT

Blood pressure evaluation and review of antihypertensive medication in patients with life limiting illness

Felicity Dewhurst[1] · Lisa Baker[1] · Inga Andrew[1] · Adam Todd[2]

Received: 23 September 2015 / Accepted: 26 May 2016

Threshold for treatment

- **Stage 1 hypertension** Clinic blood pressure is 140/90 mmHg or higher **and** subsequent ambulatory blood pressure monitoring (ABPM) daytime average or home blood pressure monitoring (HBPM) average blood pressure is 135/85 mmHg or higher.
- **Stage 2 hypertension** Clinic blood pressure is 160/100 mmHg or higher **and** subsequent ABPM daytime average or HBPM average blood pressure is 150/95 mmHg or higher.
- **Severe hypertension** Clinic systolic blood pressure is 180 mmHg or higher **or** clinic diastolic blood pressure is 110 mmHg or higher.

Monitoring treatment and blood pressure targets

1.5.4 Use clinic blood pressure measurements to monitor the response to antihypertensive treatment with lifestyle modifications or drugs. **[new 2011]**

1.5.5 Aim for a target clinic blood pressure below 140/90 mmHg in people aged under 80 years with treated hypertension. **[new 2011]**

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Bob's worried about you deprescribing… "Blood pressure tablets were for the rest of my life"

So which tools are available to help us deprescribe?

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1. The patient! ✓
2. Lists/criteria

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Tools already in existence

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1. Beers list
    1. 1991: Older persons. Delphi, consensus panel, updated 2012

2. Medicines Appropriateness Index
    1. 1992: Older persons. Clinical pharmacist intervention (RCT), narrative review 2014

3. Screening Tool of Older Person's Potentially Inappropriate (STOPP) criteria
    1. 2008: Older persons. Delphi, expert panel, updated 2015

Not specifically for patients with limited life expectancy

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Group Exercise 3

Beers Criteria

Beer's Criteria

- Morphine sulphate MR 10 mg tabs
- Dexamethasone 4 mg tabs
- Levothyroxine 50 mcg tabs
- Simvastatin 40 mg tabs
- Ferrous sulphate 200 mg/5 mL syrup
- Ramipril 10 mg caps
- Aspirin 75 mg tabs
- Erlotinib 150 mg tabs
- Diazepam 2 mg tabs
- Amlodipine 10 mg tabs
- Gliclazide 60 mg tabs
- Prednisolone 5 mg tabs
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- Metformin 500 mg tabs
- Multivitamin caps
- Tiotropium inhaler
- Haloperidol 500 mcg caps
- Ibuprofen 400 mg tabs
- Lansoprazole 15 mg caps
- Amitriptyline 10 mg tabs

So which tools are available to help us deprescribe?

1. The patient! ✓
2. Lists/criteria ✓
3. Specific to limited life expectancy
    1. Framework model (all)
    2. OncPal (cancer)
        1. Tool+Pharmacist vs Medical Expert: 94% match
    3. STOPPFrail (elderly)
        1. 27 criteria

A model for prescribing late in life

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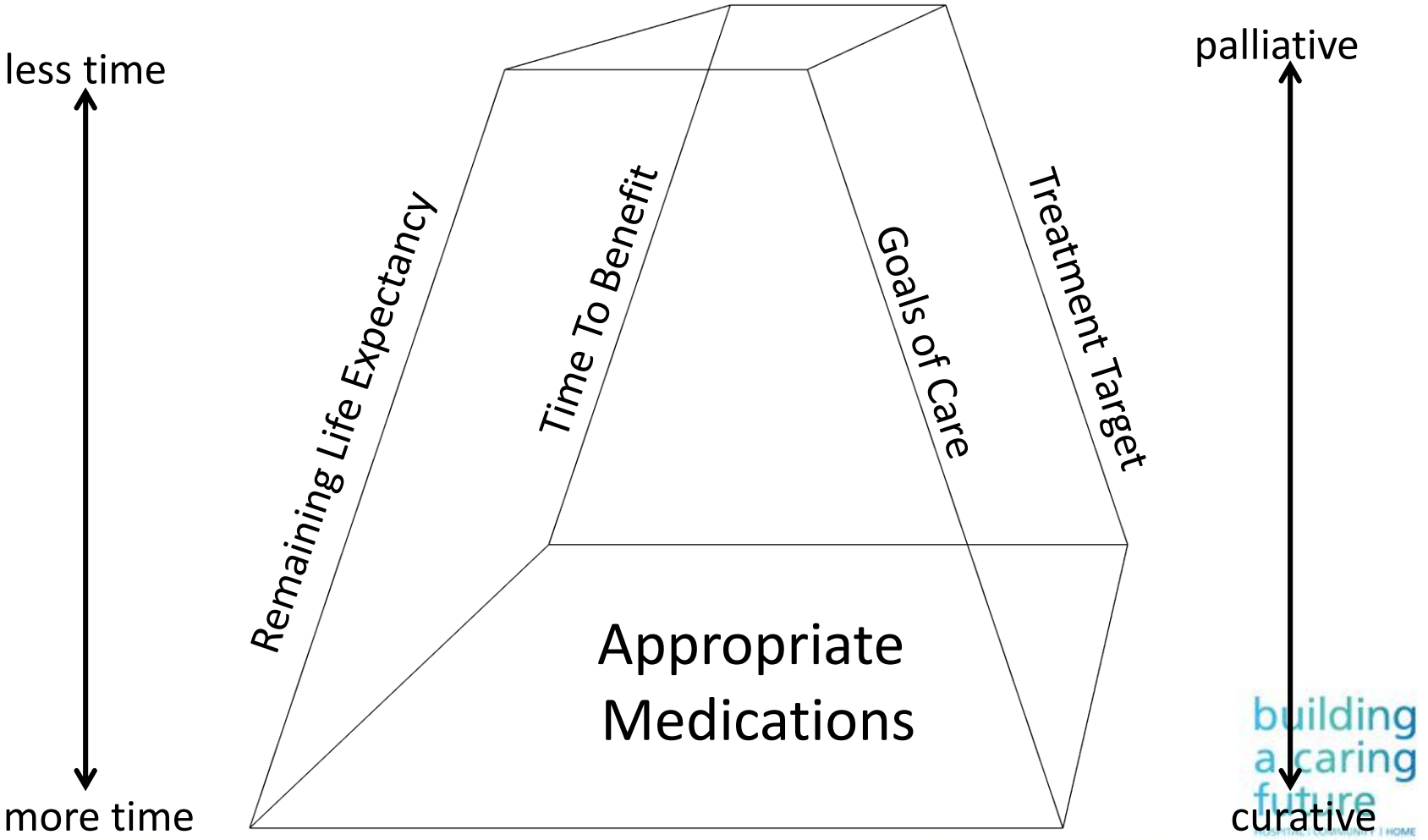

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Holmes HM, Cox Hayley D, Alexander C, Sachs GA. Reconsidering medication appropriateness for patients late in life, *Arch Int Med* 2006; 166: 605-9.

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Group Exercise 4

Framework approach

Framework approach

- Morphine sulphate MR 10 mg tabs
- Dexamethasone 4 mg tabs
- Levothyroxine 50 mcg tabs
- Simvastatin 40 mg tabs
- Ferrous sulphate 200 mg/5 mL syrup
- Ramipril 10 mg caps
- Aspirin 75 mg tabs
- Erlotinib 150 mg tabs
- Diazepam 2 mg tabs
- Amlodipine 10 mg tabs
- Gliclazide 60 mg tabs
- Prednisolone 5 mg tabs
- Salbutamol 100 mcg inhaler
- Metoclopramide 10 mg tabs
- Metformin 500 mg tabs
- Multivitamin caps
- Tiotropium inhaler
- Haloperidol 500 mcg caps
- Ibuprofen 400 mg tabs
- Lansoprazole 15 mg caps
- Amitriptyline 10 mg tabs

EBM: Can Bob stop his Statin?

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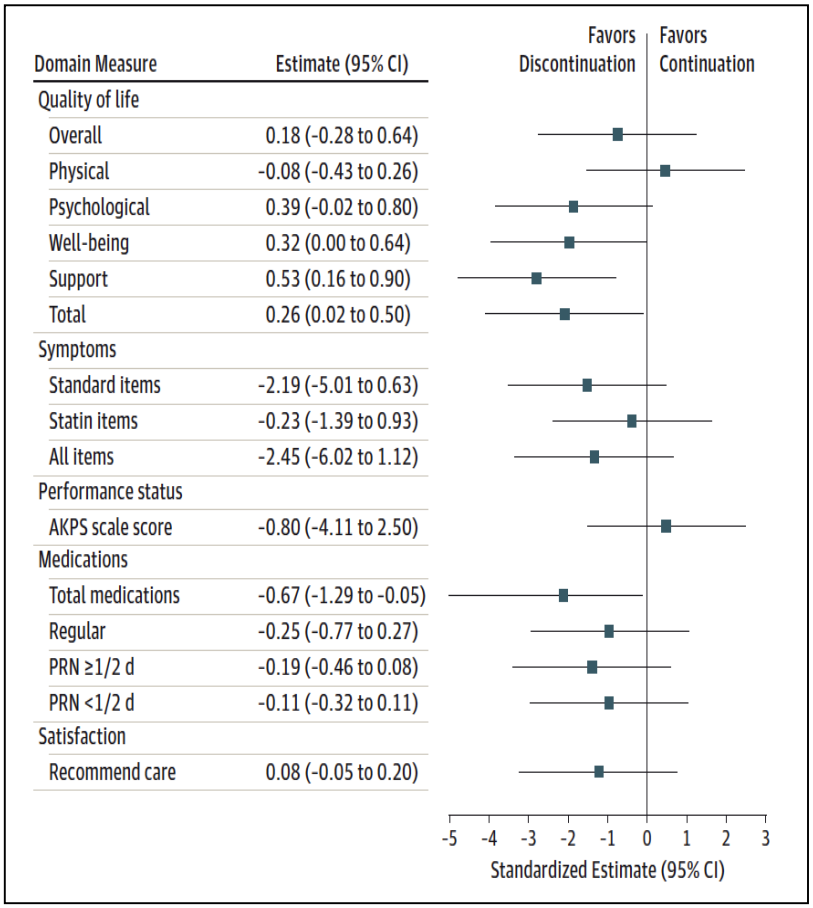
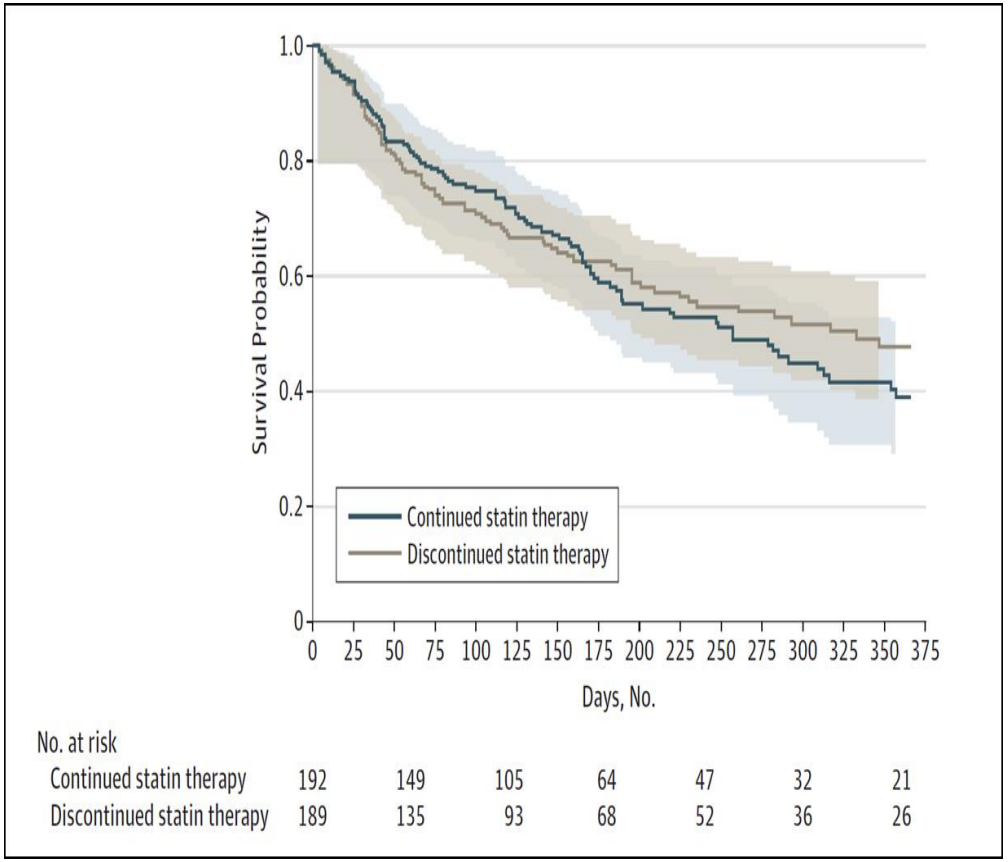


Domain Measure	Estimate (95% CI)
Quality of life	
Overall	0.18 (-0.28 to 0.64)
Physical	-0.08 (-0.43 to 0.26)
Psychological	0.39 (-0.02 to 0.80)
Well-being	0.32 (0.00 to 0.64)
Support	0.53 (0.16 to 0.90)
Total	0.26 (0.02 to 0.50)
Symptoms	
Standard items	-2.19 (-5.01 to 0.63)
Statin items	-0.23 (-1.39 to 0.93)
All items	-2.45 (-6.02 to 1.12)
Performance status	
AKPS scale score	-0.80 (-4.11 to 2.50)
Medications	
Total medications	-0.67 (-1.29 to -0.05)
Regular	-0.25 (-0.77 to 0.27)
PRN ≥1/2 d	-0.19 (-0.46 to 0.08)
PRN <1/2 d	-0.11 (-0.32 to 0.11)
Satisfaction	
Recommend care	0.08 (-0.05 to 0.20)



Kutner JS. *et al*. Safety and benefit of discontinuing statin therapy in the setting of advanced, life-limiting illness: a randomized clinical trial. *JAMA Intern Med.* 2015; **175**(5): 691-700.

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Evidence synthesis

Review

Inappropriate prescribing of preventative medication in patients with life-limiting illness: a systematic review

Adam Todd,[1] Andy Husband,[1] Inga Andrew,[2] Sallie-Anne Pearson,[3] Laura Lindsey,[1] Holly Holmes[4]

▸ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/bmjspcare-2015-000941).

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ABSTRACT

Objectives To systematically review the literature to examine the methods used to identify inappropriate prescribing of preventative medication in patients with life-limiting illness and to detail the nature of medications prescribed.

Methods A systematic literature search of 4 databases was undertaken (MEDLINE, EMBASE, CINAHL, PsycINFO) from inception to April 2015 to identify peer-reviewed, observational studies assessing inappropriate prescribing of preventative medication in patients with life-limiting illness. Inclusion criteria were: participants had a life-limiting illness; prescribed/dispensed/using preventative medication; medication appropriateness assessed as a specific study aim or outcome.

Results We found 19 studies meeting our eligibility criteria. The methods used to assess medication appropriateness included criteria developed for the elderly such as the Beers Criteria, and Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) criteria, Delphi consensus and expert clinical opinion. Lipid-regulating drugs (12 studies), antihypertensive (11 studies) and antidiabetic medications (9 studies) were the most common classes of inappropriate medication identified.

Conclusions Patients with life-limiting illnesses are prescribed preventative medications considered inappropriate in the context of diminished life expectancy. The way in which preventative medication appropriateness is assessed in patients with life-limiting illness varies considerably—with some methodologies utilising criteria previously developed for elderly populations. Given this lack of standardisation, improving the prescribing in this context requires an approach that is specifically designed and validated for populations with life-limiting illness.

INTRODUCTION

Polypharmacy and pill burden are common in patients with life-limiting illness such as cancer, heart failure, renal disease and dementia.[1] A key priority for healthcare professionals, when caring for these patients, is balancing chronic disease management and palliation of acute symptoms. An important element of this process is ensuring that the benefit of any prescribing decisions outweighs the potential risks. This can be particularly challenging, as many comorbidities are treated with chronic medications to maintain, or are prescribed to prevent further worsening of the disease state. Such preventative medications may not treat symptoms of the underlying disease; however, stopping preventative medications could, in theory, further worsen the comorbidity, resulting in the exacerbation of symptoms.[2]

In the context of diminished life expectancy, prescribing preventative medications may be inappropriate given the time until benefit can be several years and patients are at increased risk of developing a drug-related toxicity due to their altering pharmacokinetic and pharmacodynamic profiles.[3 4] To assist healthcare professionals in making prescribing decisions for this patient population, a series of frameworks have been developed to promote rational prescribing and reduce the use of unnecessary and potentially harmful care.[5 6] However, despite these approaches, and the policy drivers advocating the use of preventative medication,[7] it is unclear to what extent preventative medications are prescribed for patients with life-limiting illness.

Conclusions Patients with life-limiting illnesses are prescribed preventative medications considered inappropriate in the context of diminished life expectancy. The way in which preventative medication appropriateness is assessed in patients with life-limiting illness varies considerably—with some methodologies utilising criteria previously developed for elderly populations. Given this lack of standardisation, improving the prescribing in this context requires an approach that is specifically designed and validated for populations with life-limiting illness.

Todd A. *et al*. Inappropriate prescribing of preventative medication in patients with life-limiting illness: a systematic review. *BMJ Supportive & Palliative Care*. 2016

Reducing Inappropriate Polypharmacy
The Process of Deprescribing

Ian A. Scott, MBBS, FRACP, MHA, MEd; Sarah N. Hilmer, MBBS, FRACP, PhD; Emily Reeve, BPharm (Hons), PhD; Kathleen Potter, PhD, FRACGP; David Le Couteur, PhD, FRACP; Deborah Rigby, BPharm, GradDipClinPharm, FASCP, FACP, FAICD; Danijela Gnjidic, PhD; Christopher B. Del Mar, MB, BChir, MD, FRACGP; Elizabeth E. Roughead, PhD; Amy Page, MClinPharm; Jesse Jansen, MPsych, PhD; Jennifer H. Martin, MB, ChB, FRACP, PhD

1. Ascertain all drugs the patient is taking
2. Consider overall risk of drug-induced harm in individual patients in determining the required intensity of the intervention
3. Assess each drug for its eligibility to be discontinued
4. Prioritise drugs for discontinuation
5. Implement and monitor drug discontinuation regimen

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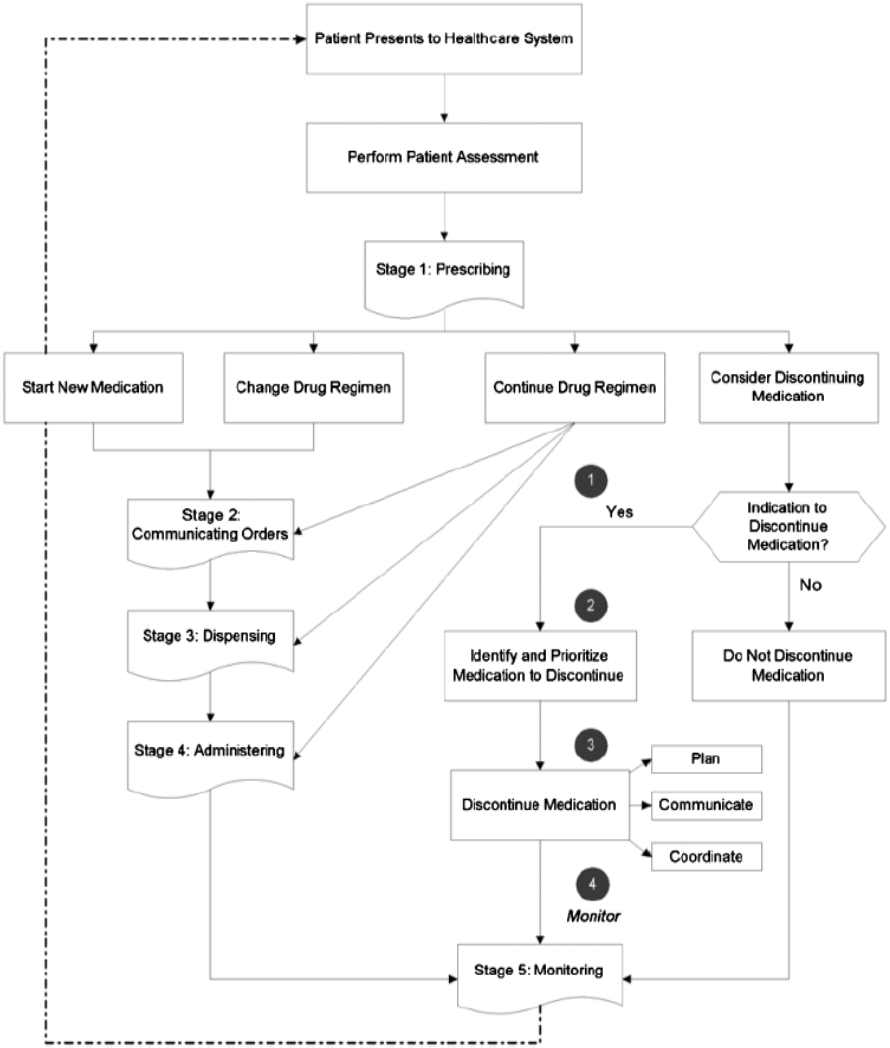
Bob's worried about you deprescribing… "But the hospital never mentioned it…"

An example

- Female patient, aged 85 years, NSCLC (stage IV), hospitalised 3 times over last 6 months of life, last event she was in hospital for 3 days
- *Medication on admission:* **aspirin**, levothyroxine, **lisinopril**, paracetamol, omeprazole, docusate, prednisolone, **atorvastatin**
- *Medication on discharge:* **aspirin**, levothyroxine, **lisinopril**, paracetamol, omeprazole, docusate, prednisolone, **atorvastatin**, salbutamol inhaler
- Numbers from discharge to death: **2 days**

Recommendations

1. Shared decision-making is also about prescribing medications
2. Not prescribing a medication should be presented as a reasonable alternative for patients late in life, when appropriate
3. Deprescribing is part of prescribing
4. Prescribers have to embrace uncertainty
5. Difficult discussions now simplify difficult decisions in the future



Conclusion

- Inappropriate medication use in life limiting illness is common
- Appears to be an issue in primary, secondary and tertiary care
- Need to develop evidence-based approaches toward deprescribing medication in life limiting illness
- Deprescribing strategies should include all healthcare professionals with responsibility for prescribing medication

Recommendation References

- Todd A and Holmes HM. Recommendations to support deprescribing medications late in life. *Int J Clin Pharm.* 2015; **36**(3) :535-43
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