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From Medication Review to Integrated Medication Management

Dr BJF (Bart) van den Bemt,
pharmacist/clinical pharmacologist/senior reseacher

Sint Maartenskliniek, Nijmegen, The Netherlands
Radboud University Medical Center, Nijmegen, The Netherlands

Disclosures

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No conflict of interests

Content

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- Review on the effectiveness of medication review
- Outcome measures
- Selection of patients
- Interventions based on
  Medication management pyramid
- Time to follow up:
  From horizontal to longitudinal medication management

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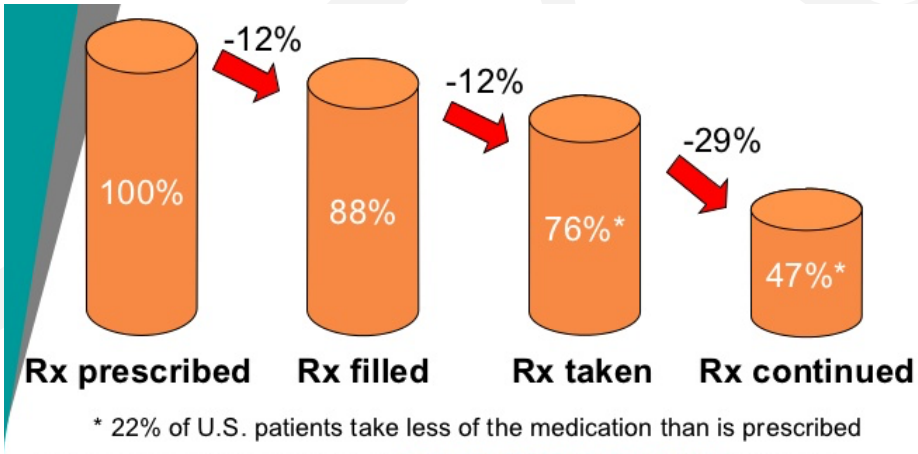
Drug deaths now outnumber traffic fatalities in U.S., data show

Fueling the surge are prescription pain and anxiety drugs that are potent, highly addictive and especially dangerous when combined with one another or with other drugs or alcohol.

September 17, 2011 | By Lisa Girion, Scott Glover and Doug Smith, Los Angeles Times

Medication Mistakes

Every year 2.5 billion prescriptions are filled by pharmacies and 3.75 billion drugs are administered at hospitals.
Every year approximately 1.5 million people suffer injuries because of prescription errors.



Dutch HARM study

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- 41.000 medication related hospital admissions NL[1]
  - 19.000 potentially avoidable
- On average 4 DRPs per patient[2]

[1] van den Bemt 2006

[2] Vinks 2008, Stuijt 2008, Kwint 2011

Definitions medicationreview

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Medicatie review: “a structured critical examination of a patient’s medicines with the objective of reaching an agreement with the patient about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste”

Room for review 2002 (UK); Clyne 2008

Primary care

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Allard 2001	RCT n=226	MAP	No difference DPRs/#pills
Bernsten 2001	RCT n=2454	MAP	Beter treatment, less costs
Krska 2001	RCT n=332	MAP	Less DRPs, no diff other outcomes
Zermansky 2001	RCT n=1188	MAP	Less drugs and costs
Meredith 2002	RCT n=259	MA	Better medication use
Sturgess 2003	RCT n=191	MAP	Increased adherence, less DRPs
Sorensen 2004	RCT n=400	MAP	No effect
Holland 2005	RCT n=872	MP	More hospital admission due to medication review
Bond 2007	RCT n=1493	MAP	No effect
Weber 2007	RCT n=620	MA	Decreased # falls
Denneboom 2007	RCT n=738	MA	Increased adaption therapy
Leendertse 2010	CT n=674	MAP	10 vs 6 hospital admission (ns)
Kwint 2011	RCT n=118	MA	Less DRPs

Hospital care

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Lipton 1992	RCT n=236	MAP	Less DRPs
Hanlon 1996	RCT n=208	MAP	MAI improves, less adverse events
Schmader 2004	RCT n=834	MAP	Less adverse events
Spinewine 2007	RCT n=203	MAP	MAI imporved
Gillespie 2009	RCT n=398	MAP	Less hospital admission

Nursing homes

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Furniss 2000	RCT n=330	MA	Decreased mortality, # drugs and # of DRPs
Roberts 2001	RCT n=3230	MA	Decreased # DRPs, no influence on mortality
Crotty 2004a	RCT n=154	MA	Improved MAI
Crotty 2004b	RCT n=110	MA	Less decrease quality of pharmacotherapy
Zermansky	RCT n=661	MAP	Less medication adaptions

However…

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- Are the medicationreviews in the literature representable for medication reviews performed in usual care?

Literaturereview effect medicatiereview

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Study author	Date	Country	No. of patients	Mean age, years	% male	Type of pharmacist	No. of pharmacists	Intervention	Patient data	Ability to enact advice	Contact with prescriber	Setting	Extent of patient contact
Begley [1]	1997	UK	222	82	39.4	Research pharmacist	Unclear	Home visits and counselling by a pharmacist after hospital discharge	Discharge letter	Unable to enact	Unclear	Own home	Four detailed visits over a year
Bernsten [18]	2001	Europe	2454	74	42.4	Community pharmacist	104	Community pharmacy assessment of drug-related problems and implementation of a pharmaceutical care plan	Repeat prescribing data	Unable to enact	Unclear	Pharmacy	Unclear
Bolas [34]	2004	Northern Ireland	242	74	39.5	Hospital/ clinical pharmacist	1	Full history, preparation of discharge letter. Medication review (stated in abstract but not method).	Full notes	Unable to enact	Close contact	Hospital	Inpatient ward visit plus discharge plan
Bond [17]	2000	UK	3074	66	41.6	Community pharmacist	62	Pharmacist-controlled repeat prescription system where pharmacist checked if medication needed. Review of side-effects and interactions	Repeat prescribing data	Unable to enact	Contact by letter	Pharmacy	Limited contact, mainly review of repeat scripts
Carter [35, 36]	1998	USA	1054	66.7	96.3	Hospital/ clinical pharmacist		Medication assessment and adherence, change of nonformulary to formulary drugs, and education	Full notes			clinic	Detailed enquiry, mean 3.5 visits over a year
Furniss [37]	2000	UK	330	81.2	27	Research pharmacist	1	Medication review with patient	Drug chart in nursing home			Nursing home	Detailed review, with second brief visit at 8 months
Gourley [10]	1998	USA	231	68.05	97.8	Hospital/ clinical pharmacist	45	Pharmacists involvement in healthcare team in the management of patient's drug therapy	Full notes	Partly enact	Unclear	Hospital	Clinical, review, at least 5 visits over 6 months
Graffen [38]	2004	Australia	402	77.7	38.8	Research pharmacist	1	Clinic-based medication review	Full notes	Unable to enact	Close contact	Primary care or clinic	One visit with brief enquiry
Granas [14]	1999	UK	500	65	38	Community pharmacist	Probably 1	Community pharmacist identified a drug-related problem and this was then discussed with pt's GP	Full notes	Unable to enact	Close contact	Primary care or clinic	Review of repeat prescription only
Grymonpre [39]	2001	USA	135	77	20.74	Hospital/ clinical pharmacist	1	Home medication history taken by 'lay person' and reviewed by a pharmacy consultant	Lay person report			Primary care or clinic	Single visit over a year
Hanlon [9]	1996	USA	208	69.8	99	Hospital/ clinical pharmacist	1	Monitored drug therapy, patient outcomes, medication use & drug-related problems	Full notes	Unable to enact	Close contact	Primary care or clinic	At least two visits and option for multiple visits over a year

Co-interventions

Co-interventions

> 3 months

> 3 months

> 3 months

Holland 2007

Aim literature review

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- To assess the effectiveness of medication review as an isolated short-term intervention, irrespective of the patient population and the outcome measures used.

Methods

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- Systematic review MEDLINE, EMBASE and Web of Science t/m 2015

- Inclusion criteria
  - RCT's
  - Medication review as isolated intervention

- No exclusion criteria

- Quality assessment two reviewers -> best evidence synthesis

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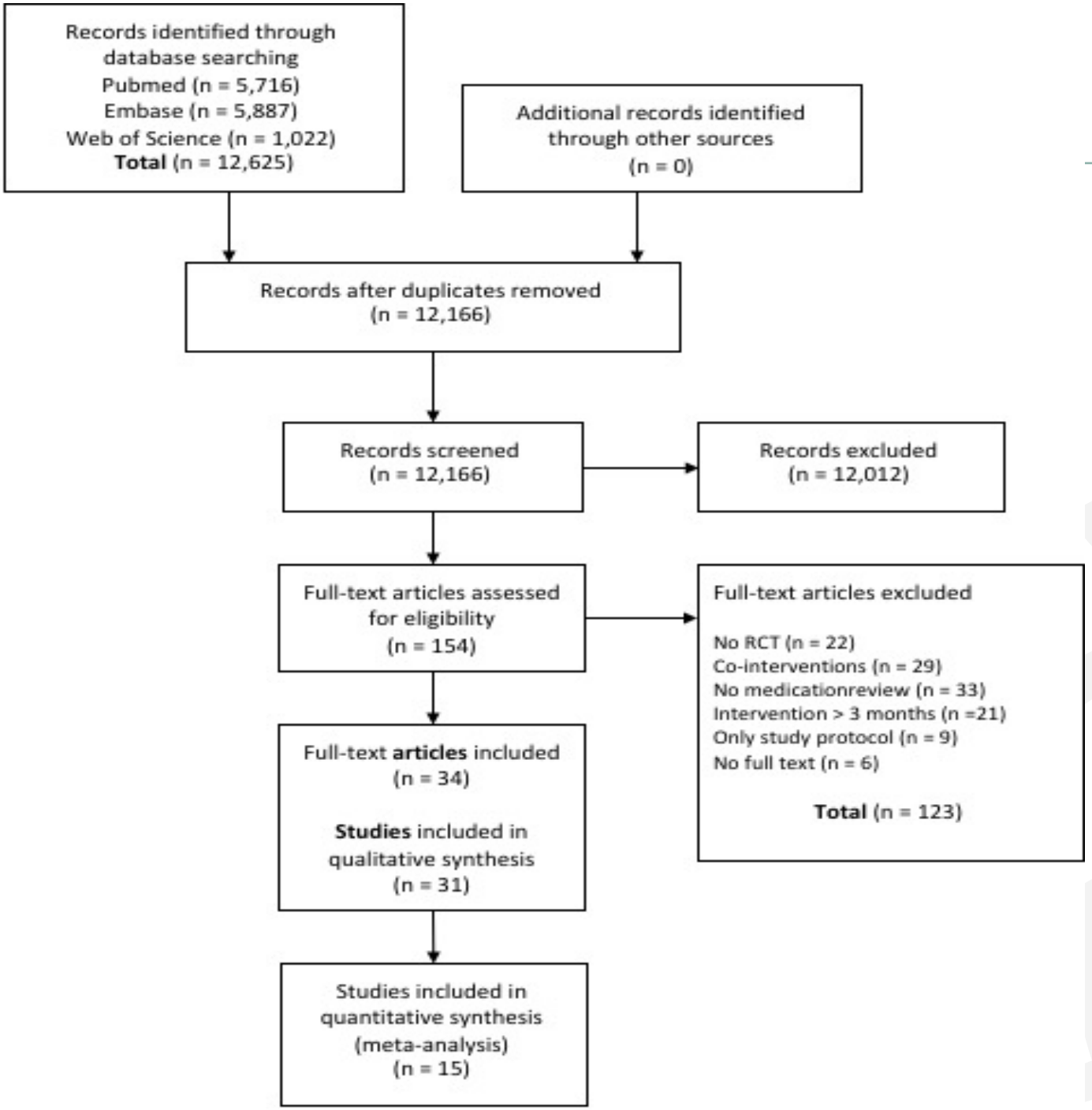

Best evidence synthesis (1)

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Example: number of emergency visits

6 Studies

1190 Interventionpatients (IP) in these 6 studies

415 interventionpatients with positive findings included

775 interventionpatients with negative findings included

= **35%** intervention patients with effect

Best evidence synthesis (2)

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High Quality	No effect	No effect	Inconclusive	Effect	Effect
Low Quality	No effect	Inconclusive	Inconclusive	Inconclusive	Effect

25% 40% 60% 75% 100%

Percentage intervention patients
in trials showing effect

Best evidence synthesis (3)

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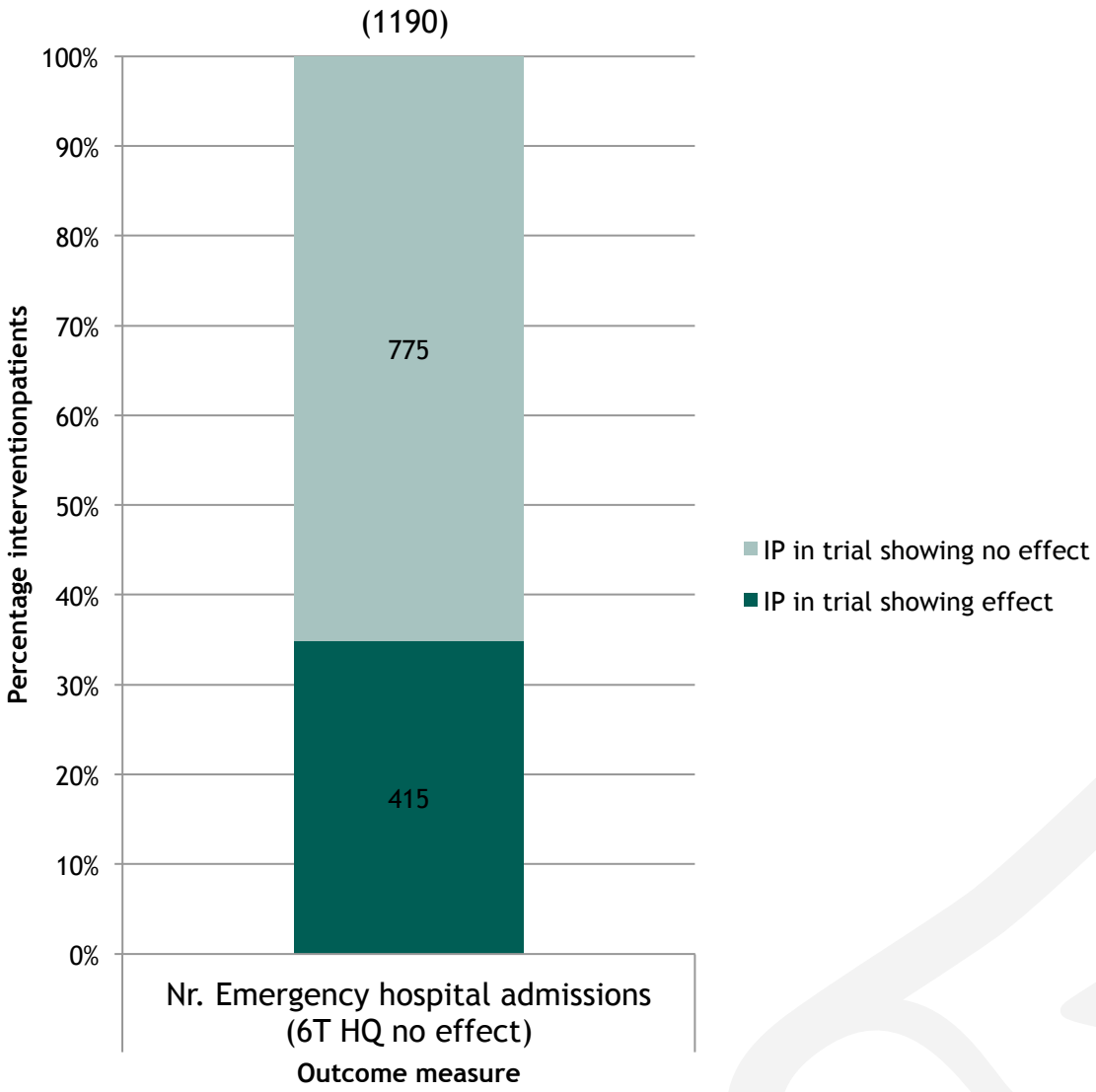

6 Studies

1190
Intervention patients

415 (35%) intervention patients included in studies with effect

Quality evidence: high

Conclusion:
no effect

Results – clinical outcomes

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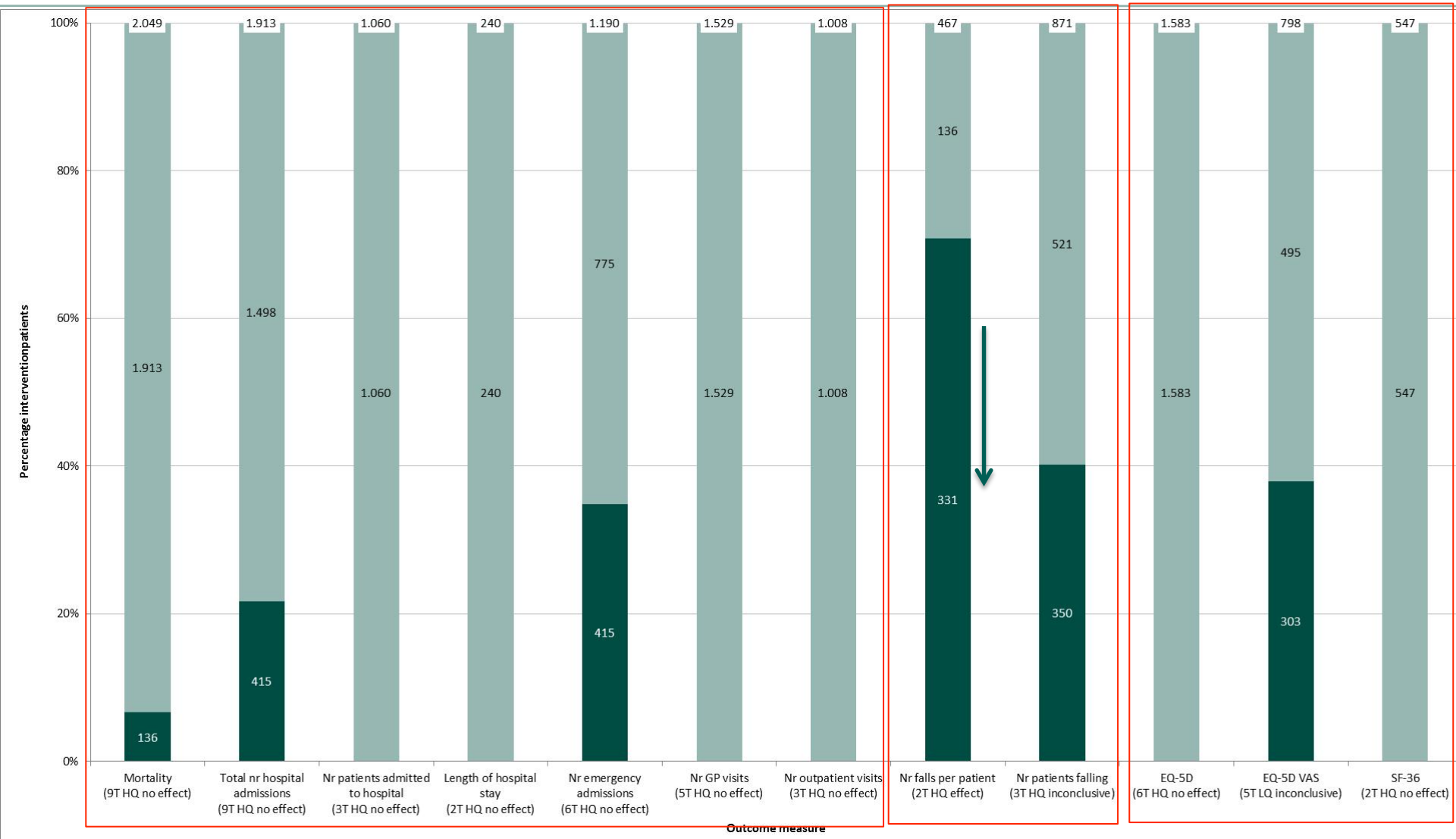

T= trials; IP = intervention patients; HQ = high quality; LQ = low quality

Results – drug related outcomes

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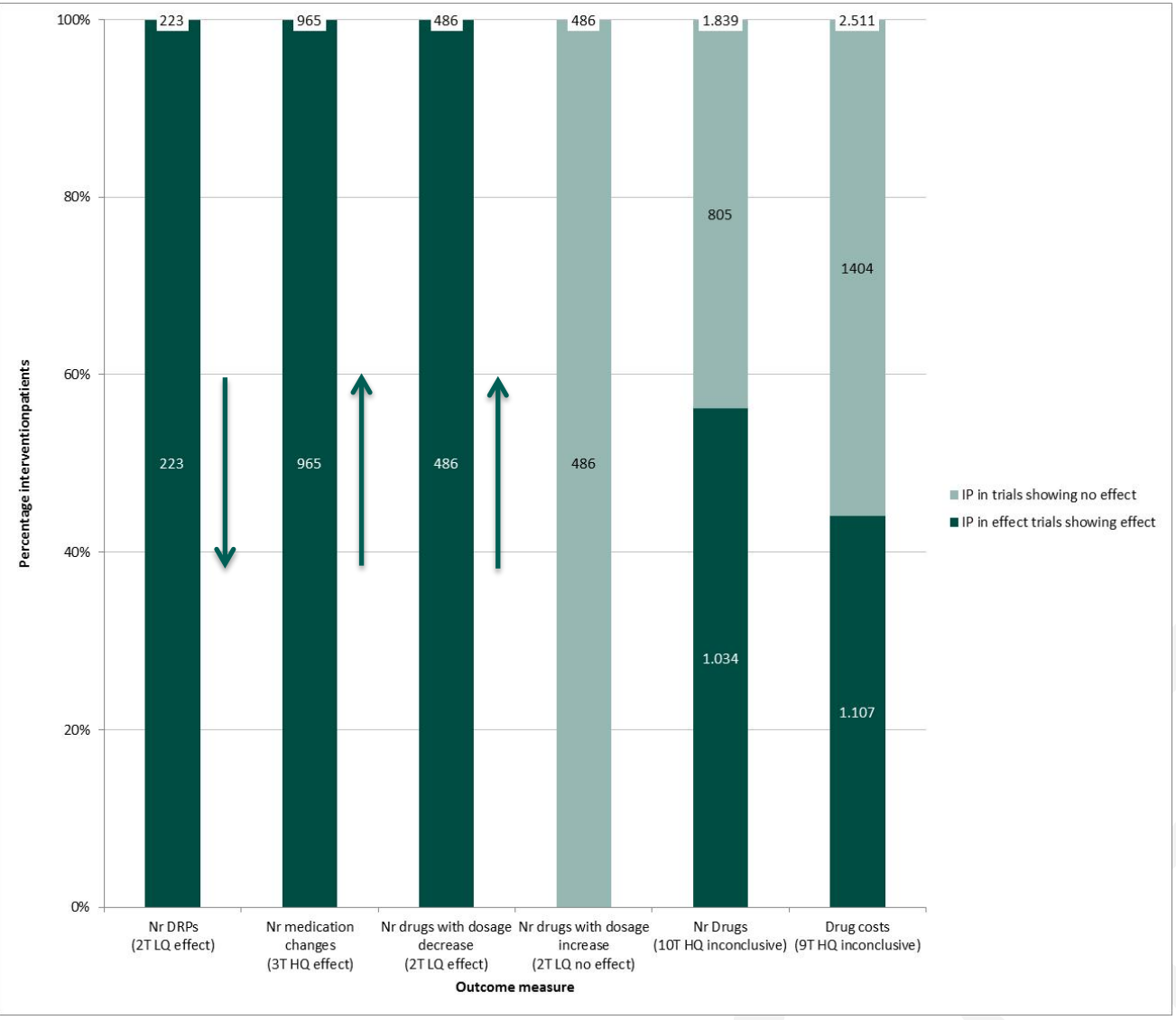

T= trials; IP = intervention patients; HQ = high quality; LQ = low quality

Summary

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Medication review as isolated intervention:

- Decreased number of DRPs/falls

- Increased number of medication changes/number of drugs with dose decrease

- No effect on:
- mortality
- Hospital admissions, gp-/outpatient visits
- Quality of live scores (SF-36 and EQ-5D)

Discussion

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- 12/26 trials low quality (v Tulder)
- Interventions not standardised
- Different setting
- Heterogeneous outcome measures

Explanation?

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- Outcome measures?
- Patient selection?
- Intervention/time to follow up

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Outcome measures

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- What is the aim of medication review?
- What is the corresponding outcome measure?

What is in fact our goal?

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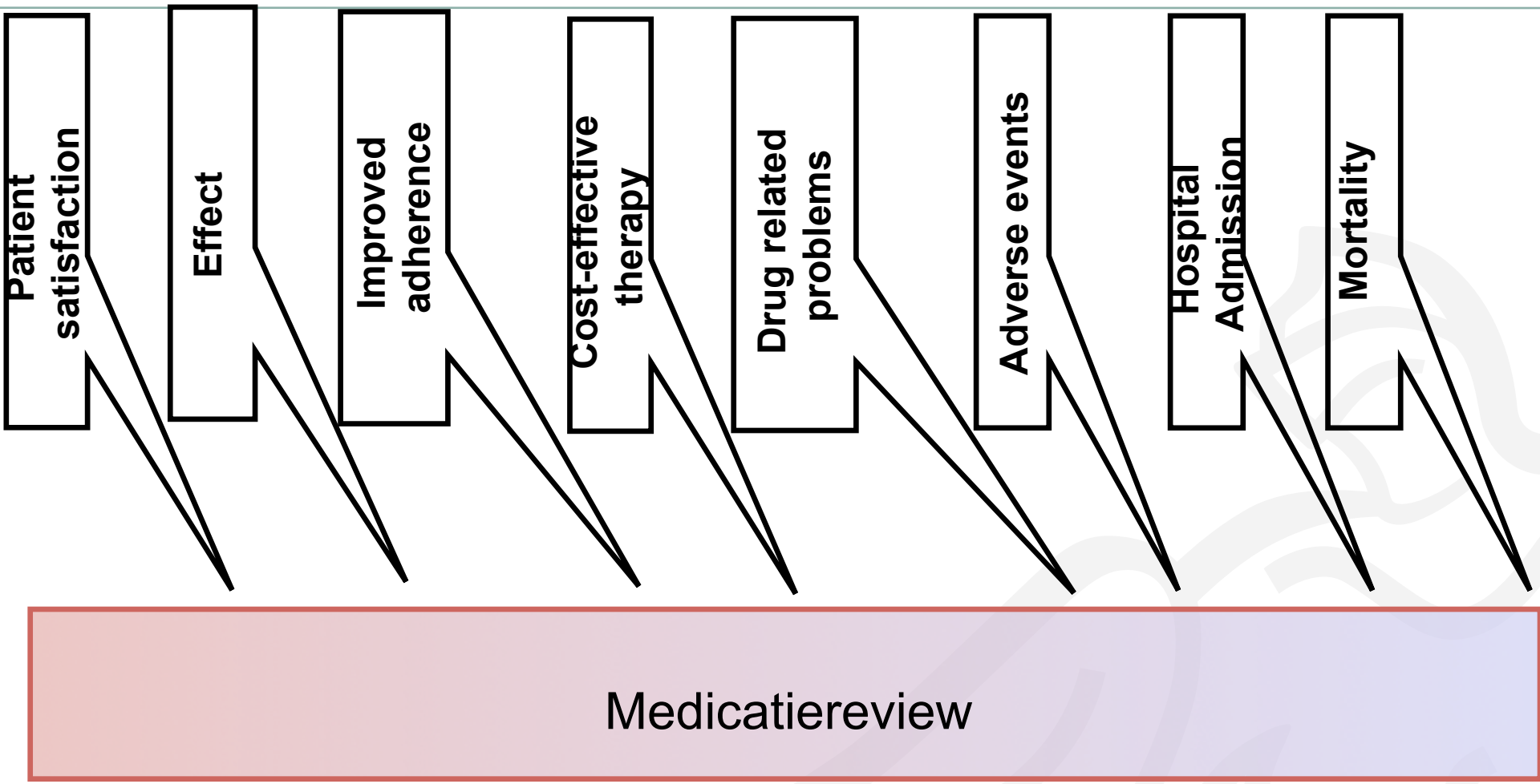

What is in fact our goal?

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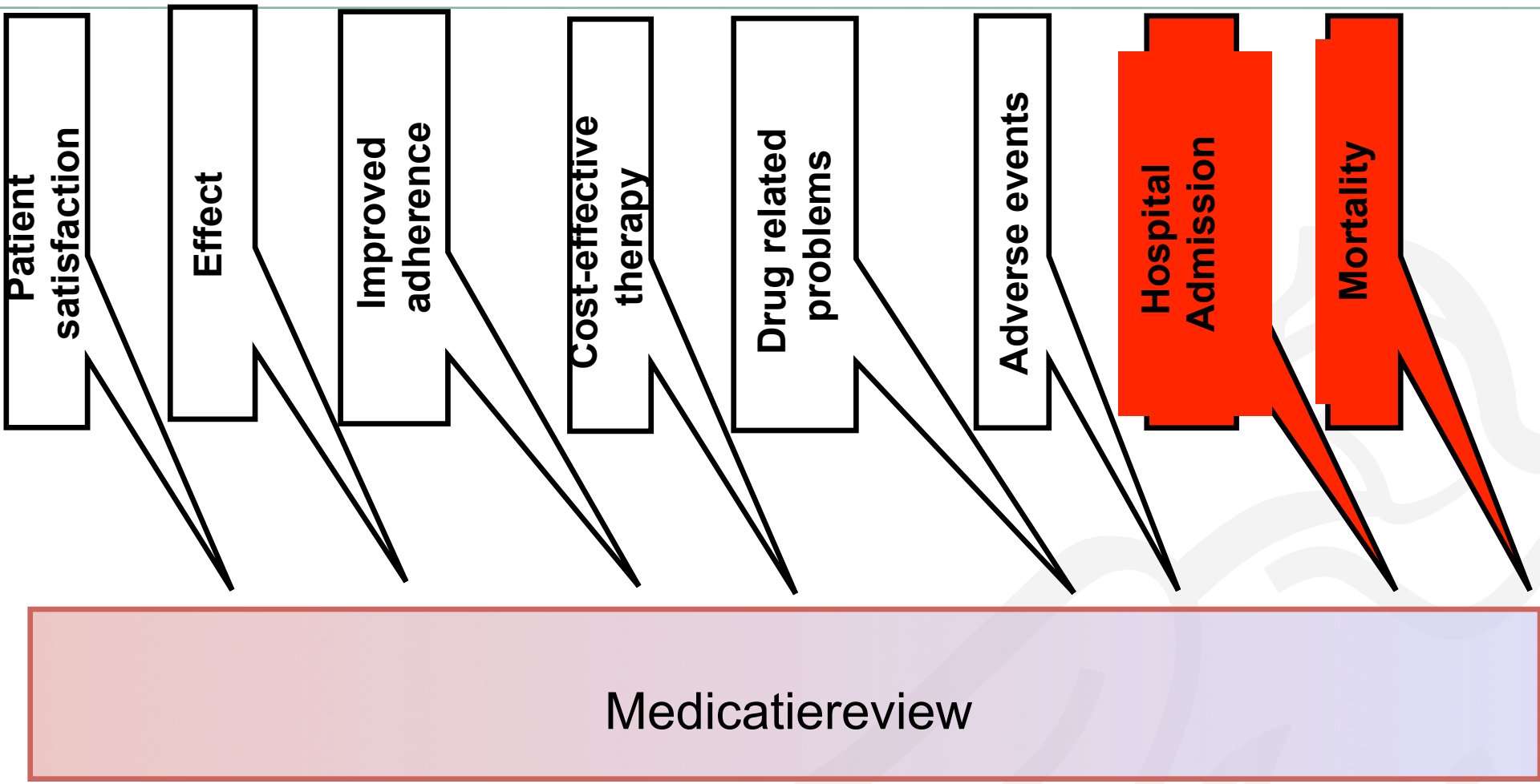

Medication review and hospital admission

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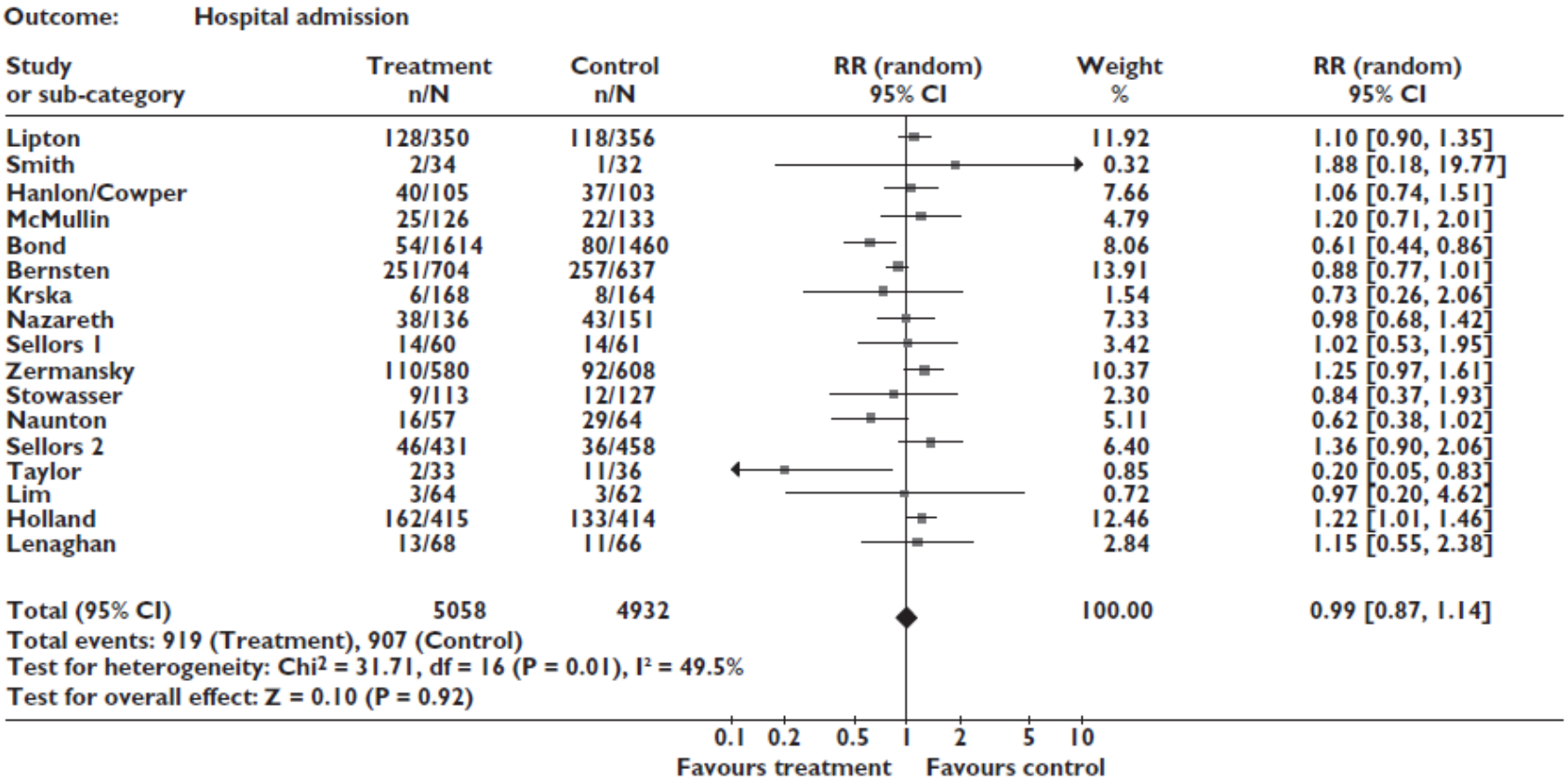

Figure 2

Meta-analysis showing relative risk for all-cause admission

Holland 2007

Medication review and mortality

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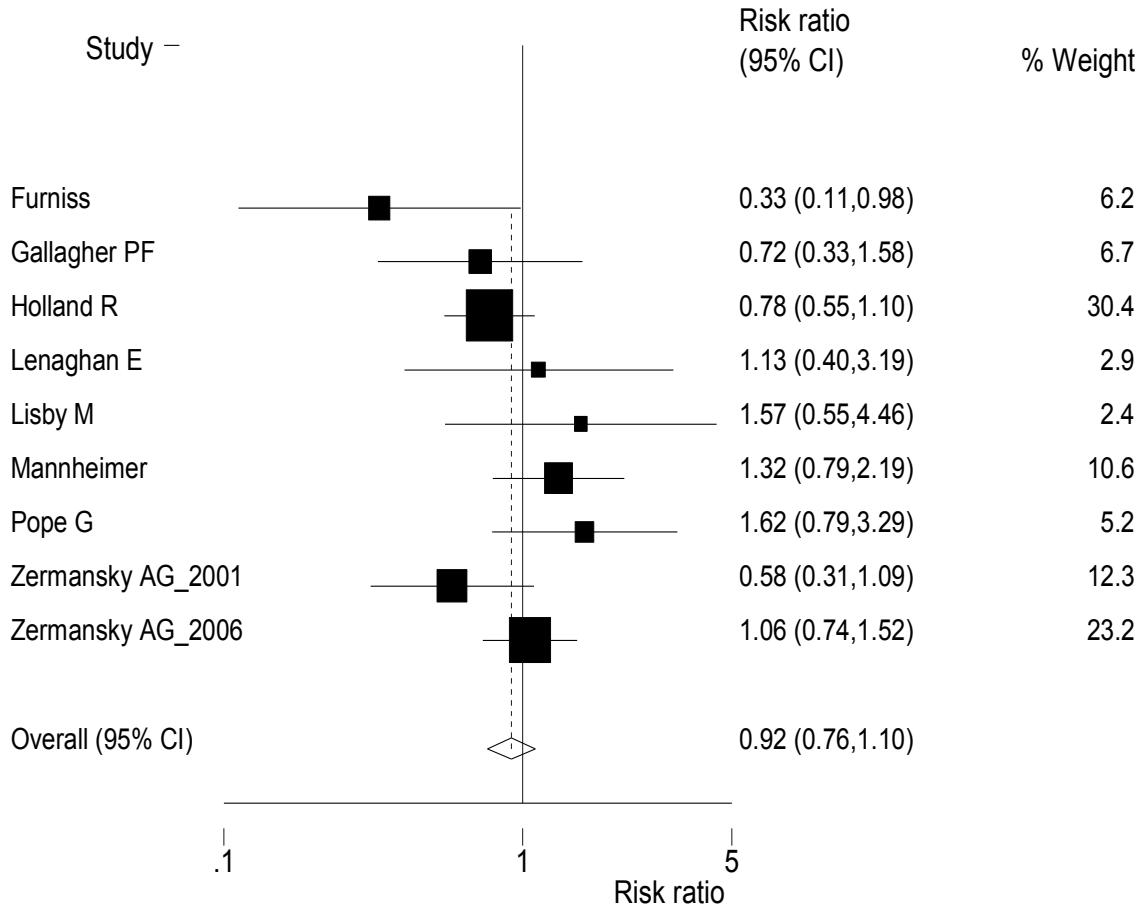

Huiskes 2015

Despite this, medication is a problem for many patients

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Average patient with rheumatoid arthritis

- 5.5 drug/patient
- 1 adverse event (median)
- 33% non-adherent
- > 90% concerns about medication
- 38% problems with medication package
- 93% does not store their medication adequate

Vd Bemt 2009

Other outcome measures?

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	No. of trials reporting outcome compared with control	No. reporting a significant positive effect (%)	No. reporting a nonsignificant positive effect (%)	No. reporting no effect (%)	No. reporting either a nonsignificant or a significant negative effect (%)
Quality of life	12	0	4 (33)	8 (66)	0
Patient satisfaction	4	2 (50)	1 (25)	0	1 (25)
Drug-related problems	4	4 (100)	0	0	0
Knowledge	11	6 (55)	2 (18)	3 (27)	0
Adherence	14	7 (50)	4 (29)	3 (21)	0
Adverse drug reactions	9	1 (11)	3 (33)	3 (33)	2 (22)
Storage problems	3	2 (66)	0	1 (33)	0
Unnecessary drugs	7	5 (71)	2 (29)	0	0
Cost analysis*	14	4 (29)	6 (43)	2 (14)	2 (14)

*Three studies reported some form of cost-effectiveness analysis.

Holland 2007

What is in fact our goal?

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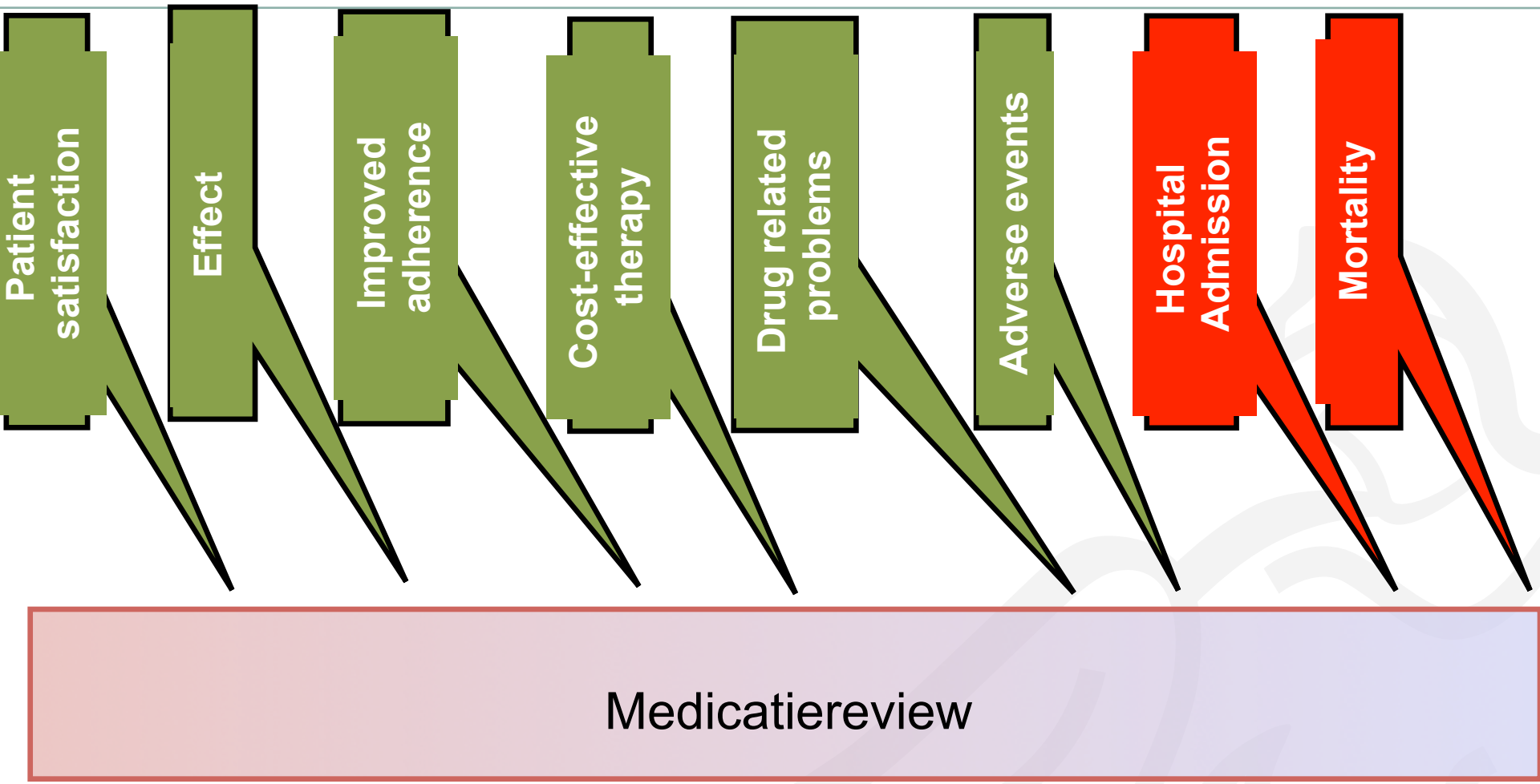

Main focus: DRPs, number of drugs, cost-effectiveness

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Which patients (1)?

Original article

Drug-related problems in a clinical setting: a literature review and cross-sectional study evaluating factors to identify patients at risk

Carli Michèle Wilmer,[1,2] Victor Johan Bernard Huiskes,[3] Stephanie Natsch,[2] Alexander Johannes Maria Rennings,[4,5] Bartholomeus Johannnes Frederikus van den Bemt,[2,3] Jacqueline Maria Bos[6]

ABSTRACT

Objectives This study aims to summarise existing evidence on risk factors for drug-related problems (DRPs) in hospitals as well as ambulatory care or nursing homes and adds additional empirical evidence on risk factors for DRPs in non-elective hospitalised patients.

reaching agreement with the patient about drug therapy, optimising the impact of medicines and minimising the number of DRPs.[2] The effectiveness of medication review is assessed in several randomised controlled trials, indicating that medication review reduces both the number of DRPs and the

Epub 2015

Which patients (2)?

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- 328 studies
- 21 associations clinical/pharmacological factors hospital admission, DRPs, adverse events
  - 11 (52%) First line
  - 8 (38%) Hospital
  - 2 (10%) Nursing homes

- 21 different factors associated with occurance DRPS

Wilmer 2015

Which patients (3)?

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Table 1 Overview of literature results of the comprehensive review, which shows associations of patient characteristics with DRPs and the setting it applies to (ambulatory, nursing homes or hospital)

	Study population (n)										
Setting	Alkema *et al*[20] (n=615)	Bourgeois *et al*[21] (n=4 335 990)	Buck *et al*[22] (n=61 250)	George *et al*[23] (n=645)	Goulding[24] (n=13 003)	Hu *et al*[25] (n=82)	Leendertse *et al*[26] (n=29 852)	Olivier *et al*[27] (n=789)	Onder *et al*[28] (n=28 411)	O'Neil and Poirer[29] (n=78)	Ruiter *et al*[30] (n=2 127 133)
Factor	A	A	A	A	A	A	A	A	A	A	A
Polypharmacy	+	+	+	+	+	+	+	+	+	0	
Comorbidity				0			+		+	+	
Female gender	0	+	+	0	+	0	0		+	+	+
Age	+	+		0	+	+	0		+	0	+
Renal impairment							+	0			
Alcohol use									+		
Antibacterial drug use								+			
Antidiabetic drug use							+				+
Antirheumatic drug use											+
Antithrombotic drug use							+	+			+
Anxiolytic drug use							+	0			
Better patient perception on drugs										–	
Dependent living situation							+				
Depression											
Drug use of narrow therapeutic index				+						0	
Impaired cognition							+		0		
Living alone	0					0				0	
Long hospital stay						+					
Non-adherence							+			0	
Poor economic situation											
Self-medication								+			

Continued

+ positive association; - negative association; 0 no association

Wilmer 2015

Which patients (4)?

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Polypharmacy: 16/18 positive associations DRPs…

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Factor	A	A	A	A	A	A	A	A	A	A	A
Polypharmacy	+	+	+	+	+	+	+	+	+	0	

Setting	Ben-Yehuda *et al*[31] (n=137)	Claydon-Platt *et al*[32] (n=9530)	Hanlon *et al*[33] (n=397)	Laroche *et al*[34] (n=2 018)	NIVEL-EMGO[35] (n=4 023)	Onder *et al*[36] (n=5 743)	Passarelli *et al*[37] (n=186)	Schuler *et al*[38] (n=543)	Fialova *et al*[39] (n=2707)	Ruggiero *et al*[40] (n=1716)
Factor	H	H	H	H	H	H	H	H	N	N
Polypharmacy	+		+	+		+	+	0	+	+

Co-morbidity: 11/13 positive associations DRPs..

Table 1 Overview of literature results of the comprehensive review, which shows associations of patient characteristics with DRPs and the setting it applies to (ambulatory, nursing homes or hospital)

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Factor	A	A	A	A	A	A	A	A	A	A	A
Comorbidity				0			+		+	+	

Setting	Ben-Yehuda *et al*[31] (n=137)	Claydon-Platt *et al*[32] (n=9530)	Hanlon *et al*[33] (n=397)	Laroche *et al*[34] (n=2 018)	NIVEL-EMGO[35] (n=4 023)	Onder *et al*[36] (n=5 743)	Passarelli *et al*[37] (n=186)	Schuler *et al*[38] (n=543)	Fialova *et al*[39] (n=2707)	Ruggiero *et al*[40] (n=1716)
Factor	H	H	H	H	H	H	H	H	N	N
Comorbidity	+	+	+	0	+	+	+	+		+

Wilmer 2015

Which patients (5)?

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Age: 8/18 positive associations; 3/18 negative associations

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	Study population (n)										
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Factor	A	A	A	A	A	A	A	A	A	A	A
Age	+	+		0	+	+	0		+	0	+
	Ben-Yehuda *et al*[31] (n=137)	Claydon-Platt *et al*[32] (n=9530)	Hanlon *et al*[33] (n=397)	Laroche *et al*[34] (n=2 018)	NIVEL-EMGO[35] (n=4 023)	Onder *et al*[36] (n=5 743)	Passarelli *et al*[37] (n=186)	Schuler *et al*[38] (n=543)	Fialova *et al*[39] (n=2707)	Ruggiero *et al*[40] (n=1716)	
Setting	H	H	H	H	H	H	H	H	N	N	
Factor											
Age		–	0	+	+	–	0	0	–	0	

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Which patients (6)?

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Gender: 8/17 positive associations

Table 1 Overview of literature results of the comprehensive review, which shows associations of patient characteristics with DRPs and the setting it applies to (ambulatory, nursing homes or hospital)

	Study population (n)										
Setting	Alkema *et al*[20] (n=615)	Bourgeois *et al*[21] (n=4 335 990)	Buck *et al*[22] (n=61 250)	George *et al*[23] (n=645)	Goulding[24] (n=13 003)	Hu *et al*[25] (n=82)	Leendertse *et al*[26] (n=29 852)	Olivier *et al*[27] (n=789)	Onder *et al*[28] (n=28 411)	O'Neil and Poirer[29] (n=78)	Ruiter *et al*[30] (n=2 127 133)
Factor	A	A	A	A	A	A	A	A	A	A	A
Female gender	0	+	+	0	+	0	0		+	+	+

	Ben-Yehuda *et al*[31] (n=137)	Claydon-Platt *et al*[32] (n=9530)	Hanlon *et al*[33] (n=397)	Laroche *et al*[34] (n=2 018)	NIVEL-EMGO[35] (n=4 023)	Onder *et al*[36] (n=5 743)	Passarelli *et al*[37] (n=186)	Schuler *et al*[38] (n=543)	Fialova *et al*[39] (n=2707)	Ruggiero *et al*[40] (n=1716)
Setting										
Factor	H	H	H	H	H	H	H	H	N	N
Female gender		+	0	0		0	0	+	0	

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Which patients (7)?

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Decreased renal function: 3/6 positive associations

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Factor	A	A	A	A	A	A	A	A	A	A	A
Renal impairment							+	0			

	Ben-Yehuda *et al*[31] (n=137)	Claydon-Platt *et al*[32] (n=9530)	Hanlon *et al*[33] (n=397)	Laroche *et al*[34] (n=2 018)	NIVEL-EMGO[35] (n=4 023)	Onder *et al*[36] (n=5 743)	Passarelli *et al*[37] (n=186)	Schuler *et al*[38] (n=543)	Fialova *et al*[39] (n=2707)	Ruggiero *et al*[40] (n=1716)
Setting										
Factor	H	H	H	H	H	H	H	H	N	N
Renal impairment				0	+		0	+		

Wilmer 2015

Which patients (8)?

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Antithrombotic use: 3/3 positive associations

Table 1 Overview of literature results of the comprehensive review, which shows associations of patient characteristics with DRPs and the setting it applies to (ambulatory, nursing homes or hospital)

	Study population (n)										
Setting	Alkema *et al*[20] (n=615)	Bourgeois *et al*[21] (n=4 335 990)	Buck *et al*[22] (n=61 250)	George *et al*[23] (n=645)	Goulding[24] (n=13 003)	Hu *et al*[25] (n=82)	Leendertse *et al*[26] (n=29 852)	Olivier *et al*[27] (n=789)	Onder *et al*[28] (n=28 411)	O'Neil and Poirer[29] (n=78)	Ruiter *et al*[30] (n=2 127 133)
Factor	A	A	A	A	A	A	A	A	A	A	A
Antithrombotic drug use							+	+			+

Setting	Ben-Yehuda *et al*[31] (n=137)	Claydon-Platt *et al*[32] (n=9530)	Hanlon *et al*[33] (n=397)	Laroche *et al*[34] (n=2 018)	NIVEL-EMGO[35] (n=4 023)	Onder *et al*[36] (n=5 743)	Passarelli *et al*[37] (n=186)	Schuler *et al*[38] (n=543)	Fialova *et al*[39] (n=2707)	Ruggiero *et al*[40] (n=1716)
Factor	H	H	H	H	H	H	H	H	N	N
Antithrombotic drug use										

Wilmer 2015

Number of risk factors

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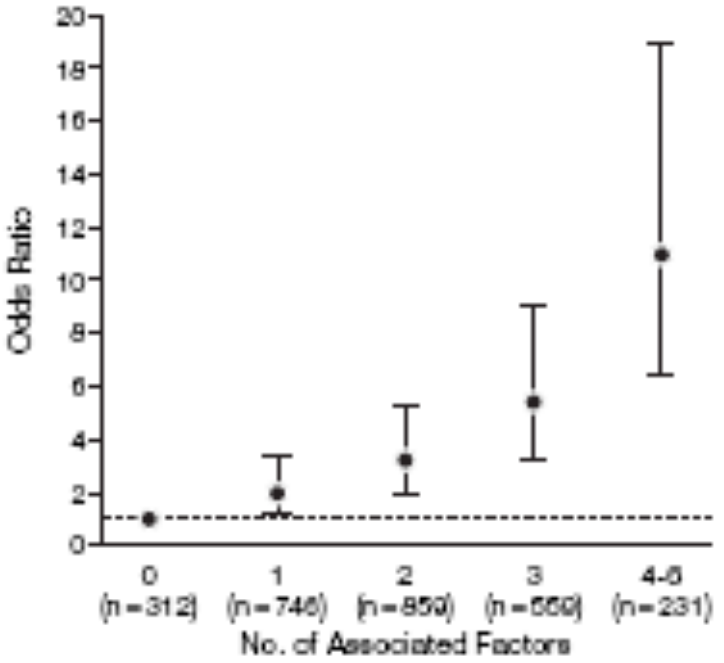
Figure 3. Odds of Potentially Inappropriate Medication Use According to the Number of Patient-Related Predictive Factors



Factors are listed in Table 5. No associated factor is the referent group. Error bars indicate 95% confidence intervals.

Fialova 2005

Validated patient screening

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1. How many prescription medications do you take regularly? (Fill in reported number)
2. During the past month, have you forgotten to take your medication(s) for any reason? (Yes/no)
3. In the past year, have you not filled a new prescription or stopped taking a prescription medication because of the cost? (Yes/no)
4. In a typical month, from how many pharmacies do you get prescriptions, including mail order? (Fill in reported number)
5. Have you been admitted into a hospital in the past 6 months? (Yes/no)
6. How many physicians have prescribed medications for you in the past year? (Fill in reported number)
7. Please tell me the number of medical conditions for which you are receiving treatment. (Fill in reported number)

Doucette 2013

Selection of patients (9)

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- Dependent on goal medication review
- Real selection criteria are missing
- Combination of:
  - Age, number of drugs, co-morbidity, high risk drugs
  - Indicated by health care professional
  - Patient Reported Outcome Measures (PROMs)
    - Adverse events, adherence, knowledge, quality of life?
  - Clinical outcomes

Content

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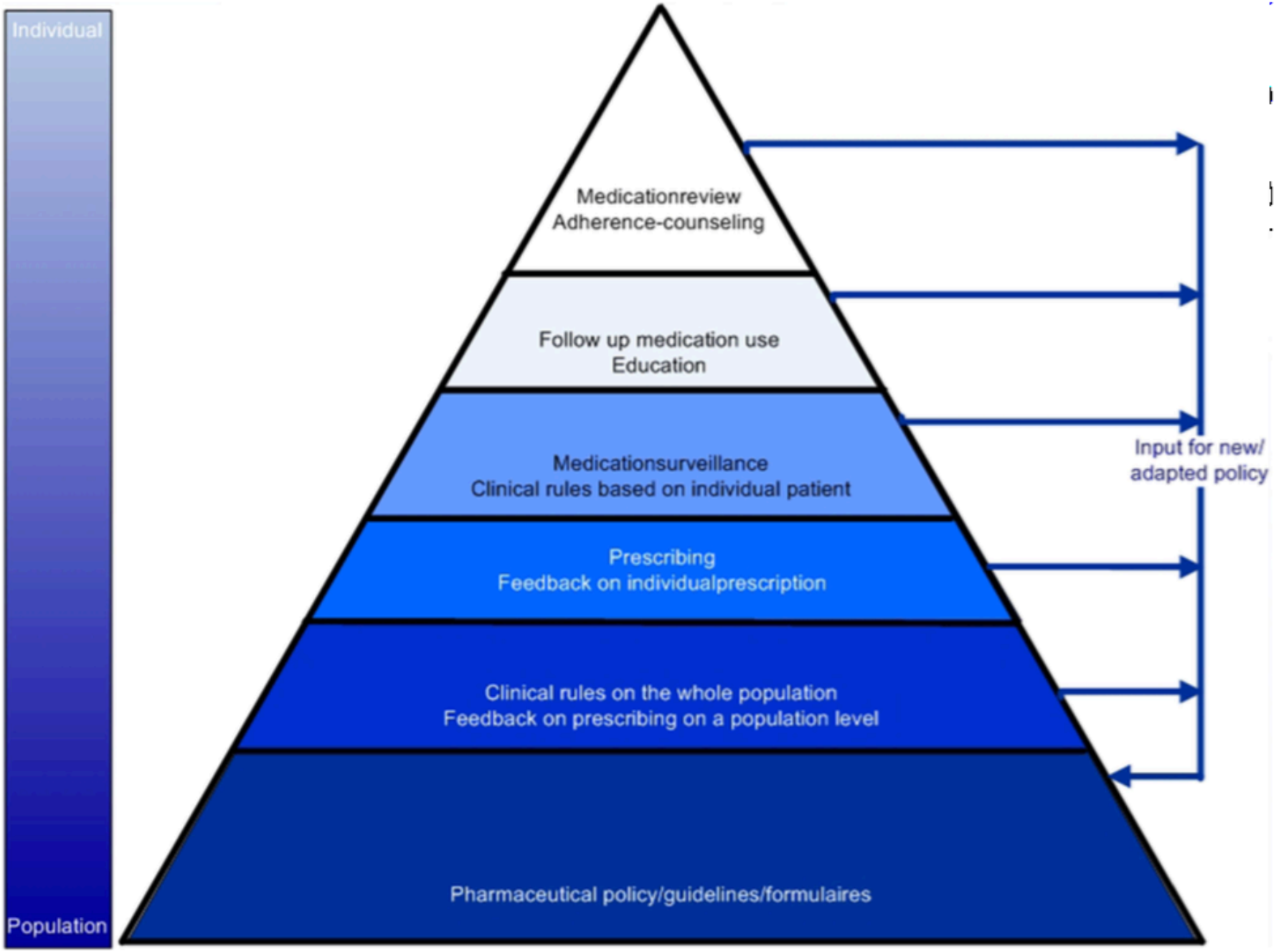
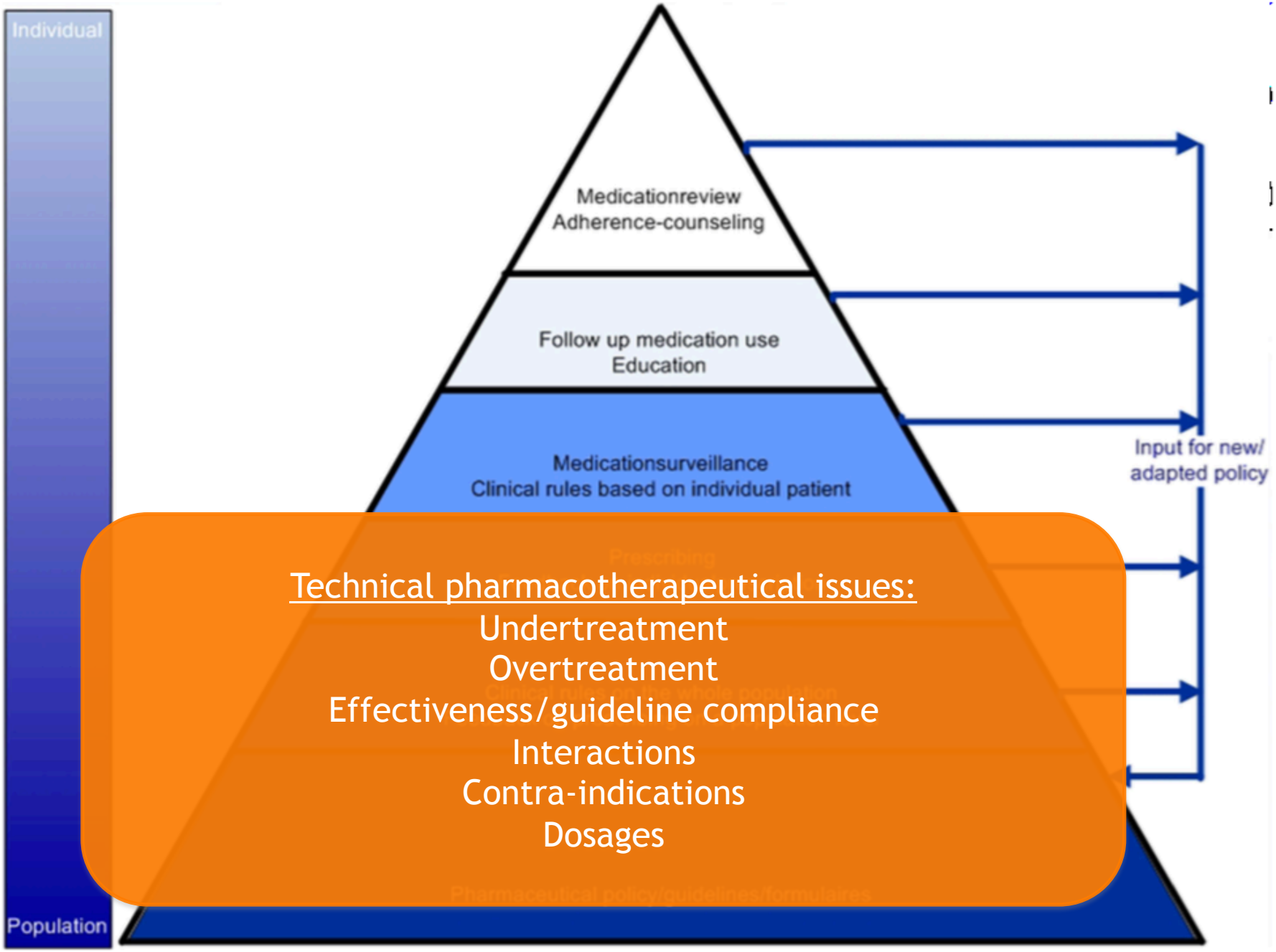
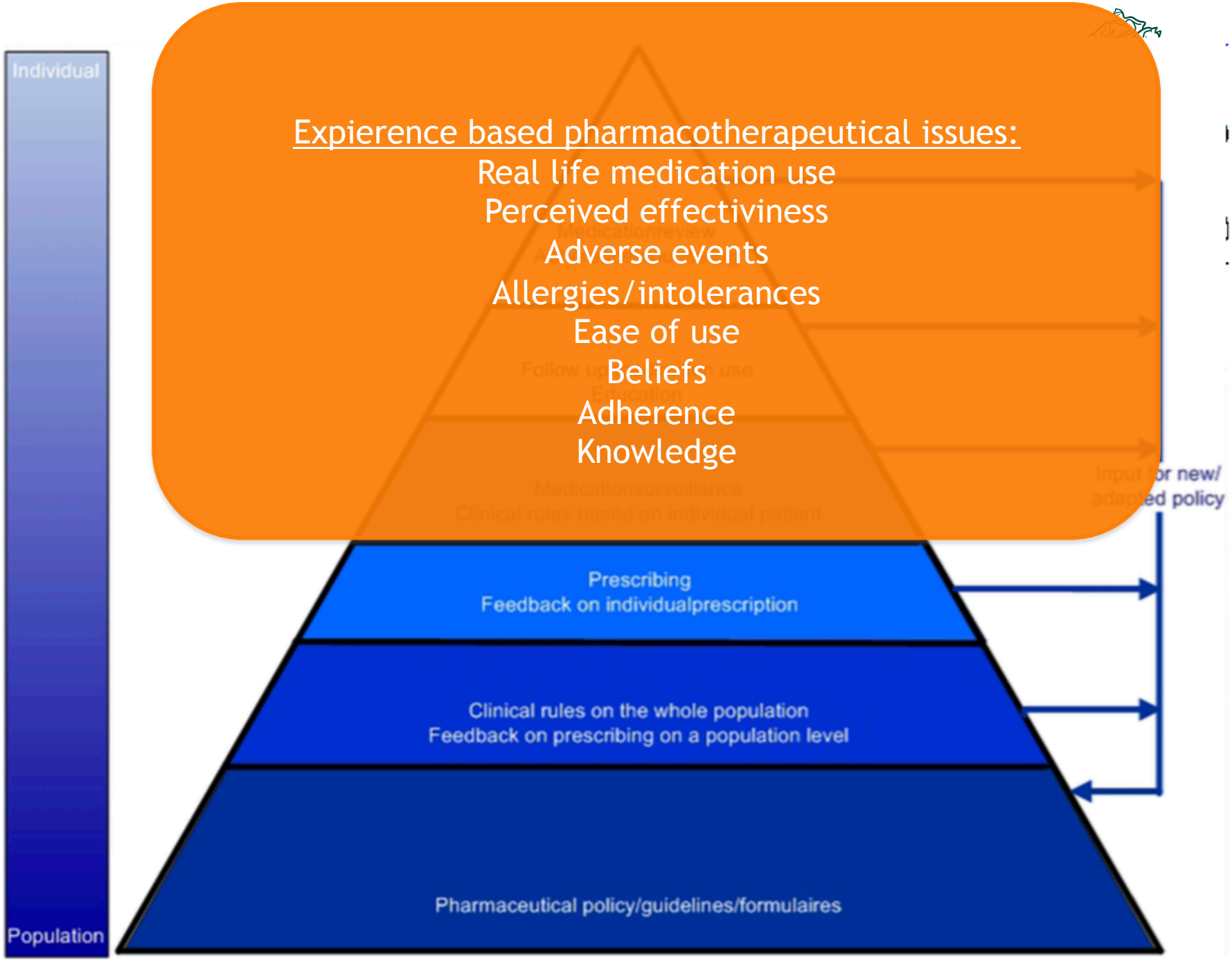
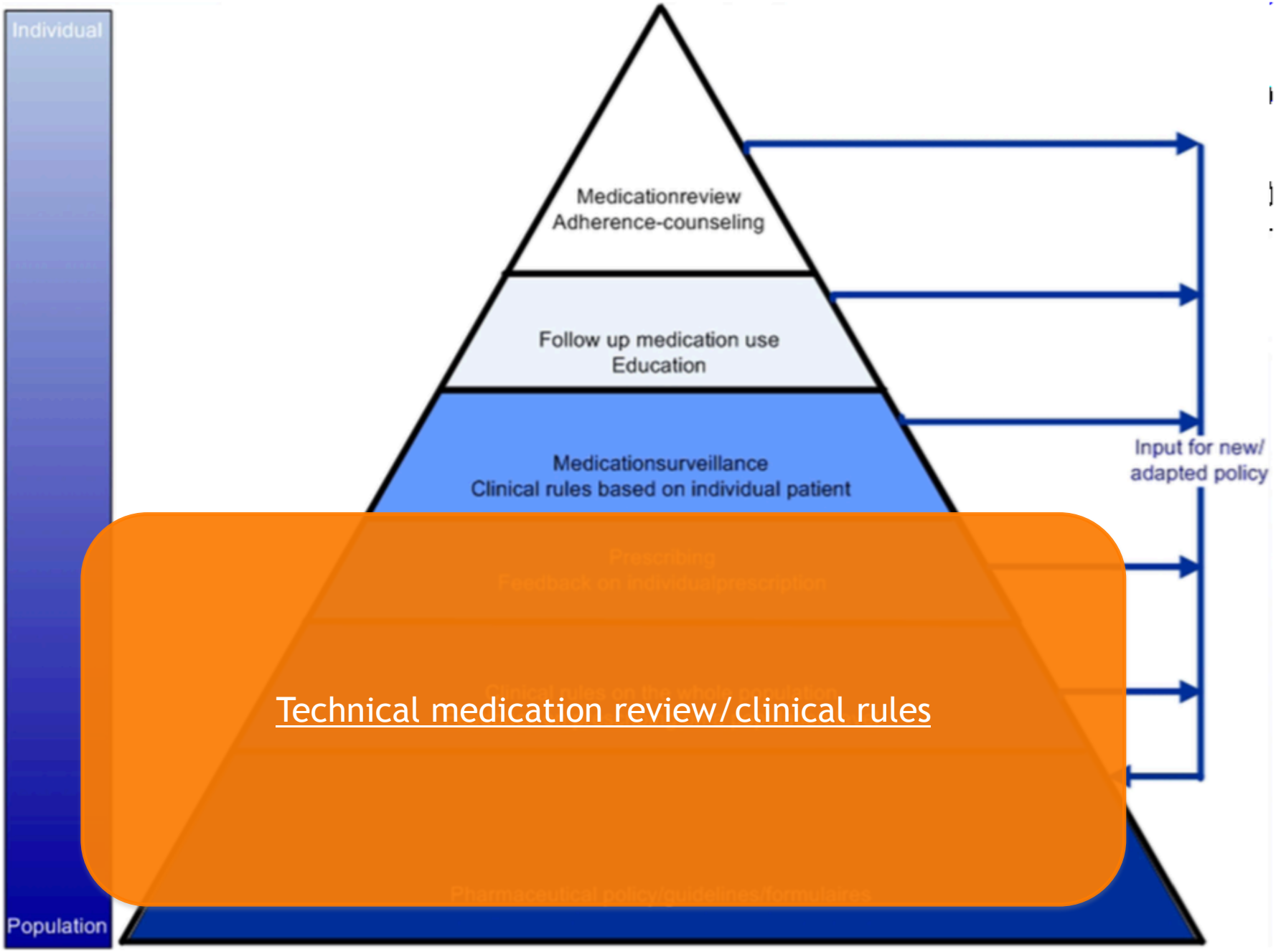
- Review on the effectiveness of medication review
- Outcome measures
- Selection of patients
- Interventions based on
  Medication management pyramid
- Time to follow up:
  From horizontal to longitudinal medication management

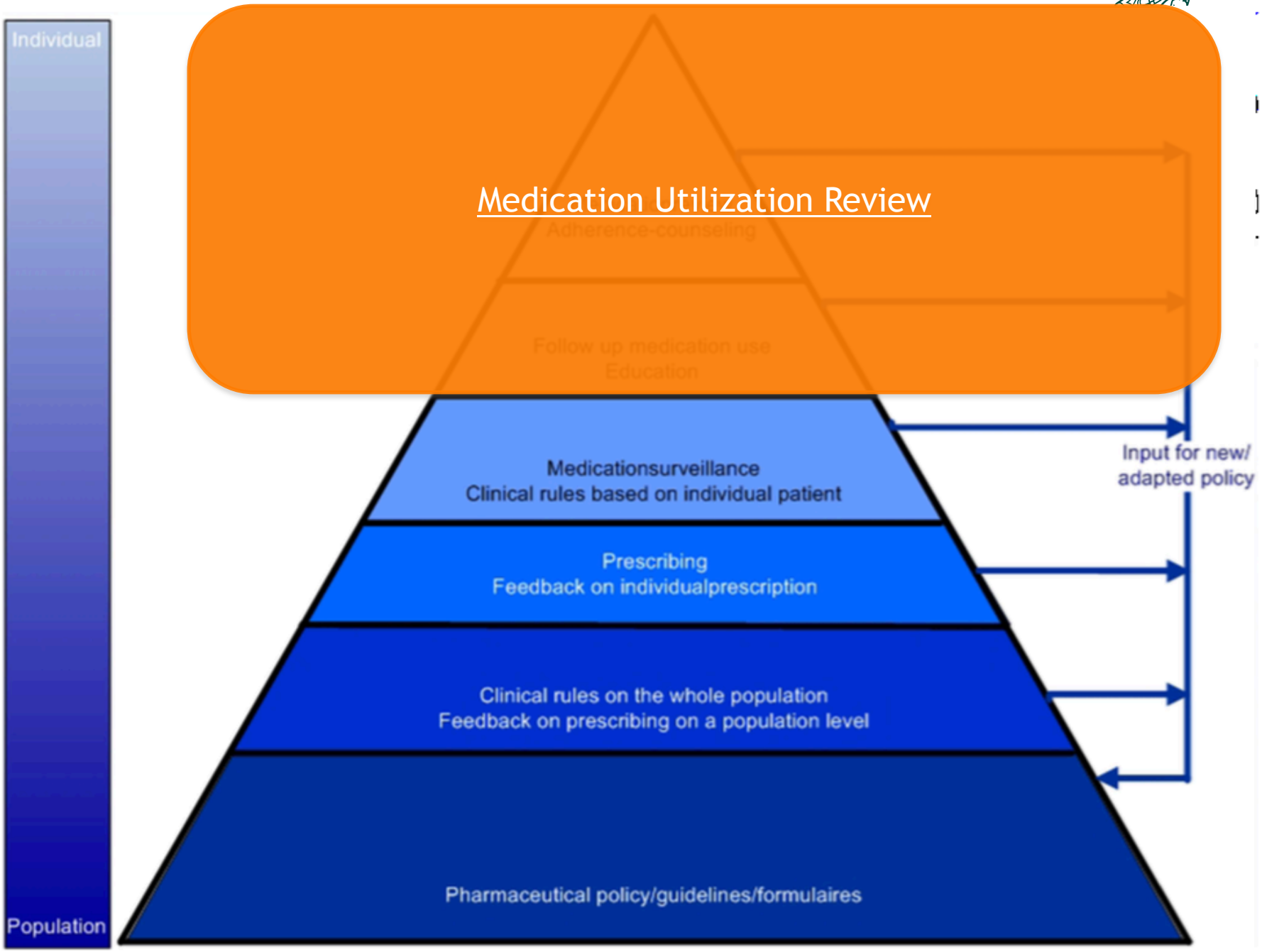


Bemt en Huiskes, PW maart 2014, EJHP 2015


Individual
Population
Medicationreview
Adherence-counseling
Follow up medication use
Education
Medicationsurveillance
Clinical rules based on individual patient
Input for new/
adapted policy
Technical pharmacotherapeutical issues:
Undertreatment
Overtreatment
Effectiveness/guideline compliance
Interactions
Contra-indications
Dosages


Individual
Population
Expierence based pharmacotherapeutical issues:
Real life medication use
Perceived effectiviness
Adverse events
Allergies/intolerances
Ease of use
Beliefs
Adherence
Knowledge
Prescribing
Feedback on individualprescription
Clinical rules on the whole population
Feedback on prescribing on a population level
Pharmaceutical policy/guidelines/formulaires


Individual
Medicationreview
Adherence-counseling
Follow up medication use
Education
Medicationsurveillance
Clinical rules based on individual patient
Input for new/
adapted policy
Technical medication review/clinical rules
Population


Individual
Population
Medication Utilization Review
Adherence-counseling
Follow up medication use
Education
Medicationsurveillance
Clinical rules based on individual patient
Prescribing
Feedback on individualprescription
Clinical rules on the whole population
Feedback on prescribing on a population level
Pharmaceutical policy/guidelines/formulaires
Input for new/
adapted policy

Medicines use review

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- **Medicines Use Review (MUR):** "A structured concordance centred review with the patients receiving medicines for long-term conditions, to establish a picture of their use of the medicines- both prescribed and non-prescribed. The review will help patients understand their therapy and it will identify any problems **they** are experiencing along with possible solutions"

Clyne 2008 (update Room for review 2002 (UK))

Patient involvement(1)

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- 1556 potential DRPs
- 155 patients (10/pat)
- 27% during patient interview
- 74% derived from medical file

Kwint 2012

Patient involvement(2)

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- DRPs derived from patientinterviews:
  - Higher priority (OR1,8 (1,4-2,2)
  - More often change in therapy (OR2,4 (1,9-3,1)
  - More often implemented (OR 2,8 (2,1-3,7)

Kwint 2012

Content

Sint Maartenskliniek

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Longitudinal pharmaceutical care

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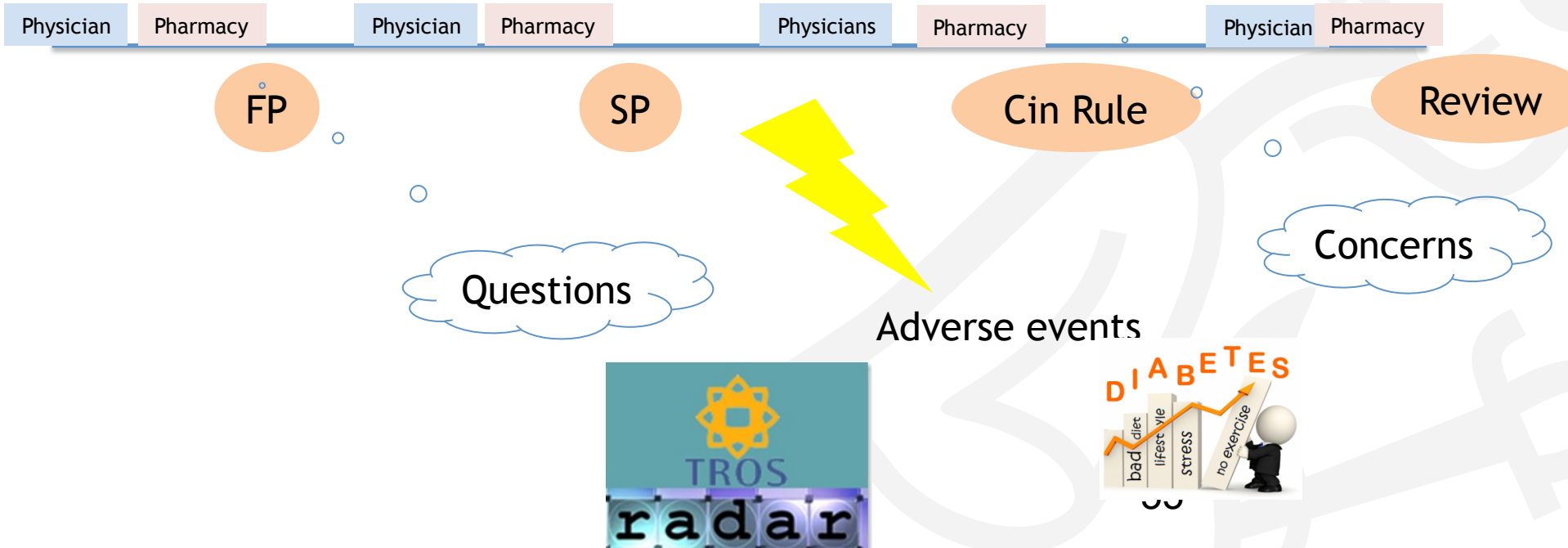
Longitudinale pharmaceutical care
- Based on best possible medication history
- Based on patient's need
- Contact moments
- Pharmaceutical file
- Education
- Exchanging expierences



Conclusion

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- Medication review is one intervention which should be complimentary to other interventions like medication policy (formulary) and clinical rules
- Search for better outcome measures
- Prediction of patients at risk is hard
- From cross sectional to longitudinal