CONOSCERE i FARMACI per una CORRETTA APPROPRIATEZZA D'USO

Quale aiuto dalla farmacoepidemiologia?

Maria Cecilia Giron, PharmD, PhD

Pharmacology Section

Department of Pharmaceutical and Pharmacological Sciences

School of Medicine

University of Padova, Italy

RAPPORTO OsMED

https://www.aifa.gov.it/web/guest/-/l-uso-dei-farmaci-in-italia-rapporto-osmed-2019

RAPPORTO OsMED

L'uso dei farmaci in Italia - Rapporto OsMed 2012

Numero pagine: 393
Data: Settembre 2013

Il Rapporto OsMed 2012, realizzato per la prima volta interamente dall'AIFA, contribuisce all'analisi di ***appropriatezza*** prescrittiva ed economica nell'impiego dei farmaci in Italia, con l'obiettivo di rispondere alle esigenze di trasparenza e informazione sul mondo del farmaco, a beneficio dei cittadini e degli operatori sanitari, e di fornire uno strumento prezioso di supporto alle strategie e alle decisioni in materia di politica sanitaria.
Lo scenario offerto deriva dalla lettura delle informazioni raccolte attraverso diversi flussi informativi, consentendo la ricomposizione dei consumi e dell'assistenza farmaceutica in Italia e a livello regionale. In particolare, il nuovo Rapporto, oltre all'analisi dei dati relativi ai farmaci erogati in regime di assistenza convenzionata, presenta i dati relativi ai medicinali erogati in distribuzione diretta e per conto e nell'ambito dell'assistenza ospedaliera.
Contiene inoltre un'arricchita sezione sulla regolamentazione dell'assistenza farmaceutica in Italia, una sezione dedicata agli strumenti di governo dell'appropriatezza prescrittiva, nuove analisi sull'appropriatezza d'uso e sulle evidenze epidemiologiche e una sezione che riporta e analizza i dati delle reazioni avverse ai farmaci pervenute e registrate dalla Rete Nazionale di ***Farmacovigilanza***.

Allegati

Rapporto Os

Argomenti co

- Osservatorio

Data aggiornamento: settembre 2013

L'uso dei Farmaci in Italia

Rapporto Nazionale Anno 2012

OSSERVATORIO NAZIONALE SULL'IMPIEGO DEI MEDICINALI

Agenzia Italiana del Farmaco

AIFA

Introduzione

Il Rapporto su "L'uso dei farmaci in Italia" negli ultimi dodici anni ha rappresentato una delle principali fonti di riferimento per l'informazione e la formazione degli operatori sanitari sull'utilizzazione dei medicinali in Italia. La nuova edizione del 2012 del Rapporto dell'Osservatorio Nazionale sull'impiego dei Medicinali (OsMed) introduce importanti novità, ampliando gli obiettivi di descrizione dell'assistenza farmaceutica. Tale esigenza deriva dall'evoluzione del mondo farmaceutico che ha ormai raggiunto livelli di complessità tecnico-scientifica, regolatoria e dell'organizzazione assistenziale che sono adeguatamente inquadrabili solo attraverso una visione organica, multidisciplinare e trasversale della materia.

L'Agenzia, negli ultimi anni, pur nella complessità dei processi, ha posto particolare attenzione, e raggiunto importanti risultati riconosciuti anche in ambito internazionale, in termini di trasparenza dei percorsi valutativi e monitoraggio dell'appropriatezza d'uso dei farmaci nella realtà clinica. In questo senso è stata arricchita la sezione dedicata alla descrizione della regolamentazione dell'assistenza farmaceutica, al fine di tentare una sintesi dell'attività dell'AIFA su alcuni snodi rilevanti nella tutela della salute, come: l'autorizzazione di un medicinale, la sua rimborsabilità, la sua innovatività, ecc.; ma anche per rendere chiaro il razionale di alcuni percorsi decisionali/organizzativi ed i loro fondamenti all'interno della cornice normativa. Pertanto la descrizione dell'uso del farmaco non termina con il suo inquadramento in termini farmacoepidemiologici e di farmacoutilizzazione, ma si inserisce in un più ampio contesto dell'organizzazione dell'assistenza farmaceutica. In tal senso, il Rapporto parte da una sintetica descrizione dei nuovi farmaci recentemente autorizzati a livello europeo che si apprestano a diventare disponibili in Italia, arrivando a presentare un quadro riassuntivo dei dati sulle reazioni avverse ai farmaci nel nostro Paese.

In questo iter descrittivo hanno trovato spazio, grazie anche all'apertura dell'Agenzia ai contributi di altri osservatori esperti in assistenza farmaceutica, diverse analisi sull'appropriatezza d'uso dei medicinali. Questo è un tema molto dibattuto negli ultimi anni in Italia, legato all'individuazione di percorsi di cura e scelte terapeutiche efficaci nel singolo paziente ed efficienti in termini di sistema. In questa prospettiva, il nuovo Rapporto OsMed sintetizza un patrimonio di dati provenienti dal SSN che pongono in luce alcune delle principali aree di inappropriatezza, individuando indicatori idonei al loro monitoraggio e fornendo le basi di calcolo per valutare i potenziali benefici economici per il SSN nel caso di una loro modificazione.

RAPPORTO OsMED 2012 – AIFA: introduzione

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RAPPORTO OsMED 2012 – AIFA: introduzione

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OsMED 2012 - Consumi per l'assistenza farmaceutica territoriale pubblica e privata: confronto 2008-12

Tabella 5.1.4. Consumi per l'assistenza farmaceutica territoriale pubblica e privata: confronto 2008-2012

		2008	2009	2010	2011	2012	Δ% 09/08	Δ % 10/09	Δ % 11/10	Δ % 12/11
		*(milioni)^*	*(milioni)^*	*(milioni)^*	*(milioni)^*	*(milioni)^*				
	Ricette #	553	572	587	590	593	3,5	2,6	0,5	0,5
	N° confezioni									
1	Convenzionata	1.022	1.054	1.080	1.089	1.095	3,1	2,5	0,8	0,6
2	Classe A privato*	135	112	123	146	170	-17,1	10,1	18,7	16,4
3	Distrib. diretta e per conto di fascia A	ND	ND	ND	ND	ND				
1+2+3	Totale classe A	1.157	1.166	1.203	1.235	1.265	0,8	3,2	2,7	2,4
4	Classe C con ricetta	296	288	283	284	267	-2,7	-1,7	0,3	-6,0
5	Automedicazione (SOP e OTC)	311	325	308	300	280	4,3	-5,3	-2,6	-6,7
4+5	Totale classe C	607	613	591	584	547	1,0	-3,6	-1,2	-6,3
1+2+3+4+5	Totale confezioni	1.765	1.779	1.794	1.819	1.812	0,8	0,9	1,4	-0,4
	DDD/1000 ab die #	896	934	956	963	985	4,2	2,4	0,7	2,3

ND: dato non disponibile

relative al consumo di medicinali di fascia A erogati in regime di assistenza convenzionale.

* Il dato relativo alla spesa privata di farmaci rimborsabili dal SSN è ricavato per differenza tra la spesa totale (stimata da IMS) e la spesa a carico SSN (ottenuta dai dati OsMed).

^ solo il numero delle ricette e delle confezioni è espresso in milioni di unità.

Fonte: elaborazione OsMed su dati IMS Health (per i dati di spesa privata).

OsMED 2012 - Consumi per l'assistenza farmaceutica territoriale pubblica e privata: confronto 2008-12

lla 3.3.2

Regione	Popolazione residente 2011 (a Ottobre 2011)	Popolazione pesata 2011	Popolazione residente 2012 (al 1-1-2012)	Popolazione pesata 2012
Piemonte	4.363.916	4.691.145	4.357.663	4.687.850
Valle d'Aosta	126.806	129.381	126.620	129.170
Lombardia	9.704.151	9.678.915	9.700.881	9.673.063
P.A. Bolzano	504.643	464.934	504.708	464.561
P.A. Trento	524.832	510.584	524.877	510.401
Veneto	4.857.210	4.830.230	4.853.657	4.825.132
Friuli V.G.	1.218.985	1.322.496	1.217.780	1.322.070
Liguria	1.570.694	1.850.905	1.567.339	1.850.654
Emilia R.	4.342.135	4.580.884	4.341.240	4.584.189
Toscana	3.672.202	3.978.526	3.667.780	3.977.994
Umbria	884.268	950.546	883.215	950.687
Marche	1.541.319	1.625.305	1.540.688	1.626.579
Lazio	5.502.886	5.431.929	5.500.022	5.426.986
Abruzzo	1.307.309	1.347.461	1.306.416	1.347.604
Molise	313.660	328.480	313.145	328.342
Campania	5.766.810	5.062.800	5.764.424	5.052.703
Puglia	4.052.566	3.840.780	4.050.072	3.836.207
Basilicata	578.036	577.802	577.562	577.640
Calabria	1.959.050	1.875.845	1.958.418	1.875.071
Sicilia	5.002.904	4.722.427	4.999.854	4.717.735
Sardegna	1.639.362	1.632.369	1.637.846	1.629.570
Italia	**59.433.744**	**59.433.744**	**59.394.207**	**59.394.207**

Tabella 5.1.4. Consumi per l'assistenza farmaceutica territoriale pubblica e privata: confronto 2008-2012

		2008 (milioni)^	2009 (milioni)^	2010 (milioni)^	2011 (milioni)^	2012 (milioni)^	Δ% 09/08	Δ % 10/09	Δ % 11/10	Δ % 12/11
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4+5	Totale classe C	607	613	591	584	547	1,0	-3,6	-1,2	-6,3
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relative al consumo di medicinali di fascia A erogati in regime di assistenza convenzionale.

ili dal SSN è ricavato per differenza tra la spesa totale (stimata da IMS) e la spesa a carico

in milioni di unità.

di spesa privata).

Tavola A.1

Dati generali di consumo 2000 e 2003

	2000	2003	Δ% 03/00
Popolazione di riferimento (dati Istat)	57.679.895	56.995.744	
N. confezioni SSN (milioni)	745	843	13,1
N. ricette SSN (milioni)	351	439	25,1
DDD/1000 ab die SSN	581	719	23,8
N. confezioni classe C (milioni)	319	316	-0,9
N. confezioni automedicazione (milioni)	327	317	-3,1
Spesa totale: pubblica e privata (milioni)	15.725	18.203	15,7
Spesa pubblica lorda (%)	63,8	67,8	
Spesa pro capite a carico SSN	174,1	216,8	24,5

Dati 2000:
DDD/1000/ab die: 581

Dal 2000 al 2012
Incremento di esposizione del 70%...!!!

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Abruzzo	1.307.309	1.347.461	1.306.416	1.347.604
Molise	313.660	328.480	313.145	328.342
Campania	5.766.810	5.062.800	5.764.424	5.052.703
Puglia	4.052.566	3.840.780	4.050.072	3.836.207
Basilicata	578.036	577.802	577.562	577.640
Calabria	1.959.050	1.875.845	1.958.418	1.875.071
Sicilia	5.002.904	4.722.427	4.999.854	4.717.735
Sardegna	1.639.362	1.632.369	1.637.846	1.629.570
Italia	**59.433.744**	**59.433.744**	**59.394.207**	**59.394.207**

Anni	Spesa convenzionata lorda* (milioni)	Diretta e per conto di fascia A (milioni)	Spesa territoriale pubblica^ (milioni)	Spesa privata (milioni)	Spesa ospedaliera^^ (milioni)
1994	6.539		6.539	3.625	
1995	6.087		6.087	3.785	
1996	6.638		6.638	4.216	
1997	7.321		7.321	4.919	
1998	8.113		8.113	5.332	
1999	8.760		8.760	5.640	
2000	10.041		10.041	5.684	
2001	12.154		12.154	5.232	
2002	12.644		12.644	5.204	
2003	12.354		12.354	5.849	
2004	13.491		13.491	5.694	
2005	13.408		13.408	6.046	
2006	13.440		13.440	5.814	
2007	12.712		12.712	6.046	
2008	12.724	1.651	14.375	6.088	
2009	12.928	1.767	14.695	6.122	
2010	12.985	2.144	15.129	6.046	
2011	12.387	2.832	15.219	6.346	4.774
2012	11.488	2.837	14.325	6.152	5.055
2013	11.226	3.003	14.229	6.732	5.421
2014	10.988	3.250	14.238	6.648	5.744
2015	10.863	4.921	15.784	6.859	6.282
2016	10.638	5.556	16.194	6.681	6.587
2017	10.499	4.792	15.291	6.526	7.332
2018	10.141	4.620	14.761	6.771	7.594
2019	10.089	4.481	14.570	7.261	8.980

^ comprensiva della spesa farmaceutica convenzionata (a lordo del payback e sconto) e della distribuzione diretta e per conto di

Tavola A.1

Dati generali di consumo 2000 e 20

	2000	2003	Δ% 03/00
Popolazione di riferimento (dati Istat)	57.679.895	56.995.744	
N. confezioni SSN (milioni)	745	843	13,1
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Incremento di esposizione del 70%...!!!

OsMED 2012 - Consumi per l'assistenza farmaceutica territoriale pubblica e privata: confronto 2008-12

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Regione	Popolazione residente 2011 (a Ottobre 2011)	Popolazione pesata 2011	Popolazione residente 2012 (al 1-1-2012)	Popolazione pesata 2012
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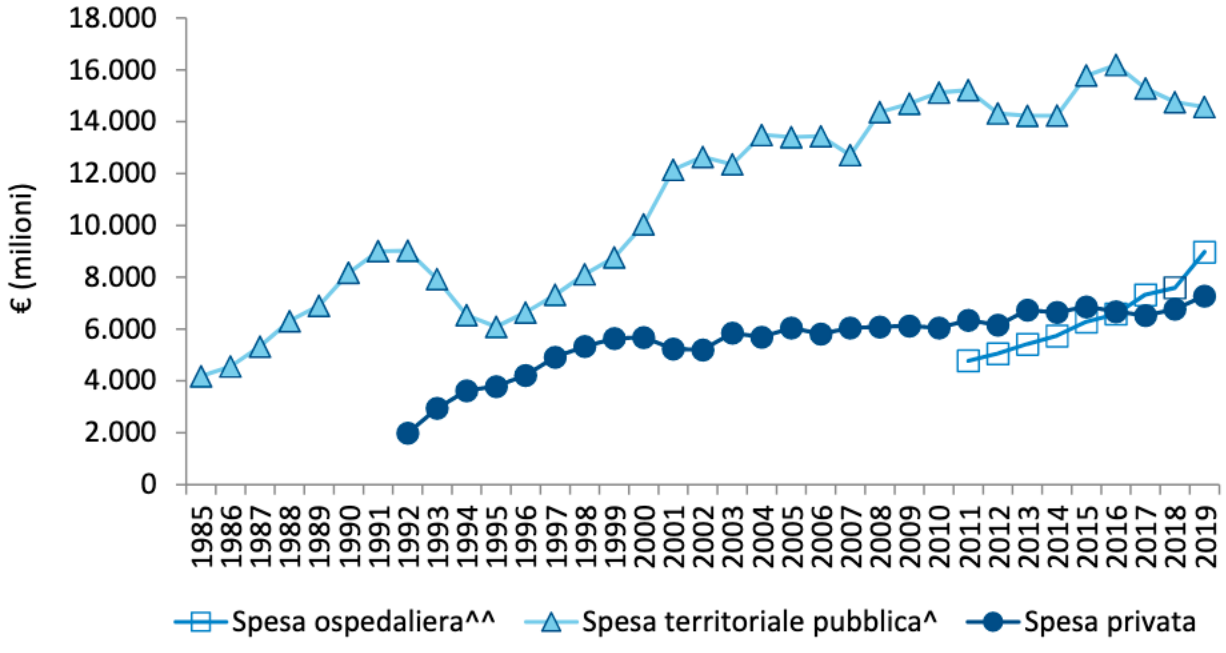
Friuli V.G.				
Liguria				
Emilia R.				
Toscana				
Umbria				
Marche				
Lazio				
Abruzzo				
Molise				
Campania				
Puglia				
Basilicata				
Calabria				
Sicilia				
Sardegna				
Italia				

Tabella 5.1.4. Consumi per l'assistenza farmaceutica territoriale pubblica e privata: confronto 2008-2012

	2008 (milioni)^	2009 (milioni)^	2010 (milioni)^	2011 (milioni)^	2012 (milioni)^	Δ% 09/08	Δ % 10/09	Δ % 11/10	Δ % 12/11
Ricette #	553	572	587	590	593	3,5	2,6	0,5	0,5
							2,5	0,8	0,6
							10,1	18,7	16,4
							3,2	2,7	2,4
							-1,7	0,3	-6,0
							-5,3	-2,6	-6,7
							-3,6	-1,2	-6,3
							0,9	1,4	-0,4
							2,4	0,7	2,3

Figura 1.1.b Spesa farmaceutica nel periodo 1985 – 2019 (Figura e Tabella)



/S) e la spesa a carico

Popolazione			
N. confezioni			
N. ricette SSN (milioni)	351	439	25,1
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OsMED 2012 - Consumi per l'assistenza farmaceutica territoriale pubblica e privata: confronto 2008-12

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Regione	Popolazione residente 2011	Popolazione pesata	Popolazione residente 2012	Popolazione pesata

Tabella 1.1.3. Consumi per assistenza farmaceutica territoriale pubblica e privata: 2015-2019

		2015	2016	2017	2018	2019	Δ %	Δ %	Δ %	Δ %
		*milioni^*	*milioni^*	*milioni^*	*milioni^*	*milioni^*	16/15	17/16	18/17	19/18
	Ricette #	596	587	581	576	570	-1,5	-1,1	-0,8	-1,0
1	Convenzionata	1.131	1.117	1.110	1.102	1.084	-1,2	-0,7	-0,7	-1,6
2	Classe A privato*	225	210	216	162	190	-6,7	2,8	-24,9	17,3
3	Distrib. diretta e per conto di fascia A	ND	86	105	105	112		21,5	0,2	6,7
1+2+3	**Totale classe A**	**1.356**	**1.414**	**1.430**	**1.369**	**1.386**	**4,2**	**1,2**	**-4,3**	**1,2**
4	Classe C con ricetta	248	209	222	229	234	-15,6	6,1	3	2,2
5	Automedicazione (SOP e OTC)	280	259	231	241	242	-7,3	-10,8	4,1	0,4
6	**Esercizi commerciali**		**32**	**30**	**29**	**28**		**-6,2**	**-3,3**	**-3,4**
4+5+6	**Totale classe C**	**528**	**501**	**484**	**498**	**506**	**-5,1**	**-3,4**	**3**	**1,6**
1+2+3 +4+5	Totale confezioni	1.884	1.915	1.914	1.867	1.862	1,6	-0,1	-2,5	-0,3
	DDD/1000 ab die#	980	971,4	969,7	978,8	987,7	-0,9	-0,2	0,9	0,9

^ solo il numero delle ricette e delle confezioni è espresso in milioni di unità.
# relative al consumo di medicinali di fascia A erogati in regime di assistenza convenzionata.
* Il dato relativo alla spesa privata di farmaci rimborsabili dal SSN è ricavato per differenza tra la spesa totale (stimata attraverso i dati della Tracciabilità del Farmaco) e la spesa a carico SSN (ottenuta dai dati OsMed).
Fonte: elaborazione OsMed su dati Tracciabilità del Farmaco (per i dati di spesa privata). Elaborazione sui dati IMS Health per la stima della spesa privata per gli anni precedenti al 2016.

Tabella 5.1.4. Consumi per l'assistenza farmaceutica territoriale pubblica e privata: confronto 2008-2012

	2008	2009	2010	2011	2012	Δ%	Δ %	Δ %	Δ %
	*(milioni)^*	*(milioni)^*	*(milioni)^*	*(milioni)^*	*(milioni)^*	09/08	10/09	11/10	12/11
Ricette #	553	572	587	590	593	3,5	2,6	0,5	0,5
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Distrib. diretta e per conto di fascia A	ND	ND	ND	ND	ND				
Totale classe A	1.157	1.166	1.203	1.235	1.265	0,8	3,2	2,7	2,4
Classe C con ricetta	296	288	283	284	267	-2,7	-1,7	0,3	-6,0
Automedicazione (SOP e OTC)	311	325	308	300	280	4,3	-5,3	-2,6	-6,7
Totale classe C	607	613	591	584	547	1,0	-3,6	-1,2	-6,3
Totale confezioni	1.765	1.779	1.794	1.819	1.812	0,8	0,9	1,4	-0,4
DDD/1000 ab die #	896	934	956	963	985	4,2	2,4	0,7	2,3

isponibile
sumo di medicinali di fascia A erogati in regime di assistenza convenzionale.
bili dal SSN è ricavato per differenza tra la spesa totale (stimata da IMS) e la spesa a carico
in milioni di unità.
di spesa privata).

Dati generali di consumo 2000 e 2003

	2000	2003	Δ% 03/00
Popolazione di riferimento (dati Istat)	57.679.895	56.995.744	
N. confezioni SSN (milioni)	745	843	13,1
N. ricette SSN (milioni)	351	439	25,1
DDD/1000 ab die SSN	581	719	23,8
N. confezioni classe C (milioni)	319	316	-0,9
N. confezioni automedicazione (milioni)	327	317	-3,1
Spesa totale: pubblica e privata (milioni)	15.725	18.203	15,7
Spesa pubblica lorda (%)	63,8	67,8	
Spesa pro capite a carico SSN	174,1	216,8	24,5

Dati 2000:
DDD/1000/ab die: 581

Dal 2000 al 2012
Incremento di esposizione del 70%...!!!

…forse è un segnale di bisogno di essere curati?

…o di aumento della popolazione anziana?

OsMed 2009

Tavola A.2

Dati generali di consumo farmaceutico territoriale^ 2000 e 2009

	2000	2009	Δ% 09/00
Popolazione di riferimento (dati Istat)	57.679.895	60.045.068	
N. confezioni (milioni)			
Classe A-SSN	745	1.054	41,5
Acquisto privato (A, C, SOP e OTC)	784	727	-7,2
Totale	1.529	1.781	16,5
Spesa farmaceutica (milioni)			
Classe A-SSN (lorda)	10.041	12.929	28,7
Acquisto privato (A, C, SOP e OTC)	5.684	6.153	8,3
Totale	15.725	19.083	21,3
N. ricette classe A-SSN (milioni)	351	572	63,1
DDD/1000 ab die classe A-SSN	580	926	59,7
% copertura SSN farmaci classe A-SSN	88	94	

OsMed 2008

Tavola A.4

Distribuzione per età della spesa e dei consumi territoriali^ di classe A-SSN

	Spesa lorda pro capite			Spesa totale		DDD/1000 ab die			DDD totali	
Fascia d'età	uomini	donne	totale	%	% cum	uomini	donne	totale	%	% cum
0-4	41,6	35,2	38,5	0,8	0,8	134,6	114,2	124,7	0,4	0,4
5-14	36,1	29,1	32,7	1,6	2,3	97,0	79,5	88,5	0,7	1,1
15-24	34,0	33,9	34,0	1,7	4,0	101,4	156,0	128,0	1,1	2,3
25-34	42,2	53,1	47,6	3,3	7,4	145,4	270,7	207,4	2,5	4,8
35-44	68,0	82,2	75,0	6,7	14,0	284,7	394,6	339,1	5,2	10,0
45-54	137,6	140,7	139,1	10,5	24,5	716,2	733,5	724,9	9,5	19,5
55-64	287,9	270,8	279,2	18,4	42,9	1687,2	1471,2	1576,5	18,2	37,7
65-74	477,3	436,0	455,2	26,3	69,3	2919,1	2507,4	2698,7	27,5	65,2
≥75	607,7	512,7	547,7	30,7	100,0	3696,4	3173,2	3368,9	34,8	100,0

^ *Esclusa la distribuzione diretta e per conto*

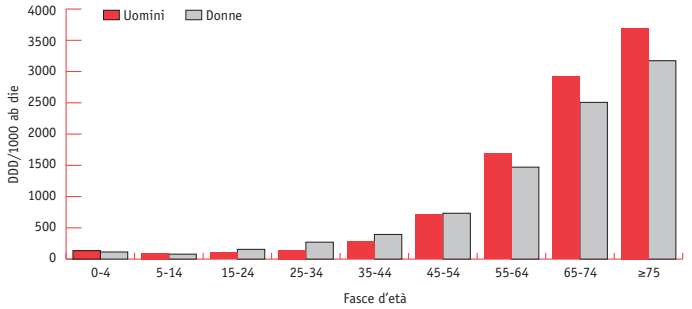
57,0% **62,3%**

...l'età avanza e la medicalizzazione aumenta...

OsMed 2008

Figura A.1

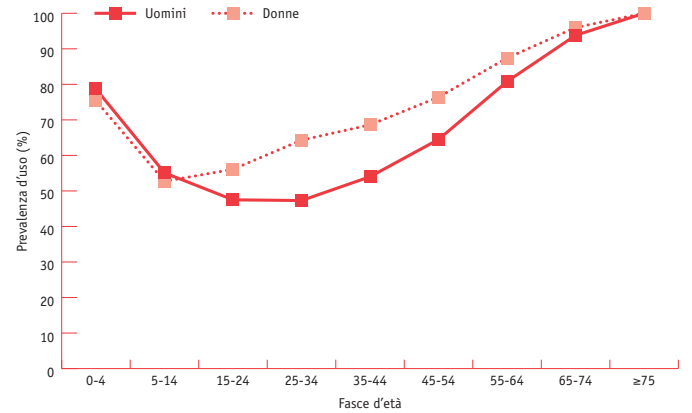
Andamento delle DDD/1000 ab die territoriali^ di classe A-SSN per età e sesso



^ *Esclusa la distribuzione diretta e per conto*

Figura A.2

Andamento della prevalenza d'uso per età e sesso dei farmaci territoriali^ di classe A-SSN



^ *Esclusa la distribuzione diretta e per conto*

…a relatively common scenario

- An elderly patient with coronary artery disease usually needs:
  1. a β-blocker,
  2. aspirin,
  3. a statin,
  4. nitroglycerin
- If he also has hypertension (uncontrolled with the β-blocker alone), the standard of care is to add
  5. a thiazide
  6. and…, perhaps, another agent
- An elderly patient with congestive heart failure or diabetes, should be treated with 3 or 4 more drugs.
- If both disease are present, possibly 5 or 6 more drugs may be prescribed.
- but… it would be convenient also to add:
  - a bisphosphonate to prevent fractures from osteoporosis…
  - NSAID for osteoarthritis
  - …a SSRI for depression

❖ **Therefore, it would be considered medically appropriate for an elderly patient to be taking as many as 9 or more medicines**

ORIGINAL INVESTIGATION

A Drug Burden Index to Define the Functional Burden of Medications in Older People

Sarah N. Hilmer, MD, PhD; Donald E. Mager, PharmD, PhD; Eleanor M. Simonsick, PhD; Ying Cao, MB; Shari M. Ling, MD; B. Gwen Windham, MD; Tamara B. Harris, MD, MS; Joseph T. Hanlon, PharmD, MS; Susan M. Rubin, MPH; Ronald I. Shorr, MD, MS; Douglas C. Bauer, MD, MPH; Darrell R. Abernethy, MD, PhD

Background: Older people carry a high burden of illness for which medications are indicated, along with increased risk of adverse drug reactions. We developed an index to determine drug burden based on pharmacologic principles. We evaluated the relationship of this index to physical and cognitive performance apart from disease indication.

Methods: Data from the Health, Aging, and Body Composition Study on 3075 well-functioning community-dwelling persons aged 70 to 79 years were analyzed by multiple linear regression to assess the cross-sectional association of drug burden index with a validated composite continuous measure for physical function, and with the Digit Symbol Substitution Test for cognitive performance.

Results: Use of anticholinergic and sedative medications was associated with poorer physical performance score (anticholinergic exposure, 2.08 vs 2.21, $P<.001$; sedative exposure, 2.09 vs 2.19, $P<.001$) and cognitive performance on the Digit Symbol Substitution Test (anticholinergic exposure, 34.5 vs 35.5, $P=.045$; sedative exposure, 34.0 vs 35.5, $P=.01$). Associations were strengthened when exposure was calculated by principles of dose response. An increase of 1 U in drug burden index was associated with a deficit of 0.15 point ($P<.001$) on the physical function scale and 1.5 points ($P=.01$) on the Digit Symbol Substitution Test. These values were more than 3 times those associated with a single comorbid illness.

Conclusions: The drug burden index demonstrates that anticholinergic and sedative drug exposure is associated with poorer function in community-dwelling older people. This pharmacologic approach provides a useful evidence-based tool for assessing the functional effect of exposure to medications in this population.

Arch Intern Med. 2007;167:781-787

Polypharmacy

ORIGINAL INVESTIGATION

A Drug Burden Index to Define the Functional Burden of Medications in Older People

Sarah N. Hilmer, MD, PhD; Donald E. Mager, PharmD, PhD; Eleanor M. Simonsick, PhD; Ying Cao, MB; Shari M. Ling, MD; B. Gwen Windham, MD; Tamara B. Harris, MD, MS; Joseph T. Hanlon, PharmD, MS;

- ✧ is usually defined as the use of 5 or + drugs, including prescribed, OTC, and complementary medicines.
- ✧ may be a useful prompt for medication review, as it is associated with **problems of medication management and suboptimal prescribing**
- ✧ is not a clinically useful independent marker of the quality use of medicines.

The type and dose of medications rather than the number of medications determine meaningful clinical outcomes.

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Arch Intern Med. 2007;167:781-787

Polypharmacy

A drug burden index to define the functional burden of medications in older people.
Hilmer SN, et al. Arch Intern Med 2007;167:781-7

- ✧ is usually defined as the use of 5 or more drugs, including prescribed, OTC, and complementary medicines.
- ✧ may be a useful prompt for medication review, as it is associated with problems of medication management and **suboptimal** prescribing
- ✧ is not a clinically useful independent marker of the quality use of medicines

- ❑ **The type and dose of medications rather than the number of medications determine meaningful clinical outcomes**.

Polypharmacy

… As older patients move through time, often from physicians to physicians, they are at increasing risk of accumulating layer upon layer of drug therapy, as a reef of accumulates layer upon layer of coral… *(Gurwitz & Avorn, Ann Intern Med. 1991)*

Ann Intern Med. 1991 Jun 1;114(11):956-66.

The ambiguous relation between aging and adverse drug reactions.

Gurwitz JH, Avorn J.

Program for the Analysis of Clinical Strategies, Beth Israel Hospital, Boston, Massachusetts.

Abstract

PURPOSE: To examine the evidence for a relation between advancing patient age and the risk for adverse drug reactions.

DATA SOURCE: A computer-assisted search of the English-language literature (MEDLINE, 1966 to 1990) followed by selective review of all pertinent articles.

STUDY SELECTION: Studies that stratified data on adverse drug reactions by patient age were screened for review. Article selection was not limited by study design; the relation between age and the occurrence of adverse drug reactions did not have to be a primary focus of the study.

DATA EXTRACTION: Pertinent data were abstracted from the results of case-control and cohort studies and from clinical trials. The methodologic strengths and weaknesses of these studies are discussed with particular reference to gerontologic issues.

RESULTS OF DATA SYNTHESIS: Most studies have neglected the issue of whether the increased frequency of adverse drug reactions in the elderly is attributable to age alone or to the fact that older patients are more likely to have coexisting illnesses and to be taking several medications. Studies that combine all drug exposures for each patient and report the risk for any adverse effect provide little useful information about the risks associated with specific drug therapies in the elderly. The association between age and the risk for adverse drug reactions is best examined for individual pharmacologic agents. However, the exclusion of elderly subjects from clinical trials makes the determination of age effects impossible in many studies. Where subjects do represent an adequate age range, most studies fail to control for important clinical differences among subjects of different ages to distinguish the independent effects of chronologic age.

CONCLUSION: Conventional clinical wisdom suggests that the risk for adverse drug reactions increases with advancing age, but available data do not confirm this "truism" of geriatric medicine. The inter-individual variability of the aging process, including the non-uniform nature of the pharmacokinetic and pharmacodynamic changes that occur with aging, indicates that clinical reality is far more complex. Patient-specific physiologic and functional characteristics are probably more important than any chronologic measure in predicting both adverse and beneficial outcomes associated with specific drug therapies.

Polypharmacy

Mayo Clin Proc. 2004 Jan;79(1):122-39.

Inappropriate medications for elderly patients.

Chutka DS, Takahashi PY, Hoel RW.

Division of Preventive and Occupational Medicine and Internal Medicine, Mayo Clinic College of Medicine, Rochester, Minn 55905, USA.

Abstract

The use of medications is common in elderly persons, and this population has the highest risk of medication-related problems. Elderly persons are more susceptible to the effects of various medications for a number of reasons. It is well known that polypharmacy is one of the most serious problems in caring for elderly persons; however, many of these patients continue to receive medications that have an increased risk of causing harm. In 1991, an important article was published about inappropriate medication use in the elderly population. This article raised awareness of the problem and presented explicit criteria for determining which medications were inappropriate for elderly patients residing in long-term care facilities. This list of drugs is still used for evaluating medications taken by elderly persons and for determining whether satisfactory prescribing practices are being used. We reviewed the medications described as inappropriate for elderly persons and searched the scientific literature to determine whether evidence exists to defend or refute the labeling of particular drugs. At times, evidence was difficult to find, and many of the original studies were dated. For most medications listed as inappropriate, we found evidence to support these designations.

Polypharmacy

J Gerontol A Biol Sci Med Sci. 2013 Aug 2. [Epub ahead of print]

High Prevalence of Poor Quality Drug Prescribing in Older Individuals: A Nationwide Report From the Italian Medicines Agency (AIFA).

Onder G, Bonassi S, Abbatecola AM, Folino-Gallo P, Lapi F, Marchionni N, Pani L, Pecorelli S, Sancarlo D, Scuteri A, Trifirò G, Vitale C, Zuccaro SM, Bernabei R, Fini M; the Geriatrics Working Group of the Italian Medicines Agency (AIFA).

Centro Medicina dell'Invecchiamento, Dipartimento di Scienze Gerontologiche, Geriatriche e Fisiatriche, Università Cattolica del Sacro Cuore, Largo F. Vito 1, 00168 Roma, Italy. graziano_onder@rm.unicatt.it.

Abstract

BACKGROUND: Poor quality of drug prescribing in older persons is often associated with increased drug-related adverse events, hospitalization, and mortality. The present study describes a set of prescribing quality indicators developed by the Geriatrics Working Group of the Italian Medicines Agency (AIFA) and estimates their prevalence in the entire elderly (≥65 years) population in Italy.

METHODS: We performed a cross-sectional study using 2011 data from the OsMed (Osservatorio dei Medicinali) database, which comprises all prescribed drugs that are reimbursed by the Italian National Healthcare System. Yearly prevalence of drug prescribing quality indicators in the Italian older population (n = 12,301,537) was determined.

RESULTS: Overall, 13 quality indicators addressing polypharmacy, adherence to treatment of chronic diseases, prescribing cascade, undertreatment, drug-drug interactions, and drugs to be avoided were identified. Polypharmacy was common, with more than 1.3 million individuals taking greater than or equal to 10 drugs (11.3% of the study population). The prevalence of low adherence and undertreatment was also elevated and increased with advancing age, with highest prevalence occurring in individuals aged 85 years and older. Prevalence was less than 3% for quality indicators assessing the prescribing cascade, drug-drug interactions, and drugs to be avoided.

CONCLUSIONS: These results confirm the high frequency of suboptimal drug prescribing in older adults, using a database that covers the whole Italian population. In general, this descriptive study may help in prioritizing strategies aimed at improving the quality of prescribing in elderly population.

High Prevalence of Poor Quality Drug Prescribing in Older Individuals: A Nationwide Report From the Italian Medicines Agency (AIFA).

Onder G et al. J Gerontol A Biol Sci Med Sci. 2013 Aug 2

Tabella II. Prevalenza degli indicatori di qualità nella popolazione anziana italiana

Indicatori di qualità	Tutti i gruppi di età (≥ 65 anni) n=12,301,537 (%)	65-74 anni n=6,154,421 (%)	75-84 anni n=4,474,887 (%)	≥85 anni n=1,672,229 (%)
1. Politerapia • 5-9 farmaci • ≥10 farmaci	 6,024,383 (49.0) 1,389,591 (11.3)	 2,681,639 (43.6) 529,506 (8.6)	 2,462,378 (55.0) 629,043 (14.1)	 880,366 (52.6) 231,042 (13.8)
2. Bassa aderenza al trattamento con farmaci antidepressivi	201,290 (63.9)	83,110 (62.6)	82,623 (63.0)	35,557 (69.6)
3. Bassa aderenza al trattamento con farmaci anti-ipertensivi*	179,975 (46.4)	84,983 (43.2)	65,450 (47.2)	29,542 (56.1)
4. Bassa aderenza al trattamento con farmaci antidiabetici*	92,017 (63.0)	44,227 (63.0)	35,497 (64.7)	12,293 (70.1)
5. Bassa aderenza al trattamento con farmaci antiosteoporotici*	56,621 (52.4)	24,424 (48.7)	24,351 (53.4)	7,846 (64.0)
6. Uso di farmaci anti-Parkinson e antispicotici	25,949 (0.2)	10,200 (0.2)	10,625 (0.2)	5,124 (0.3)
7. Sotto-utilizzo di statine nei pazienti diabetici (% dell'intera popolazione anziana) - % della popolazione anziana in trattamento con ipoglicemici†	918,662 (7.5) 53.4	418,257 (6.8) 48.3	366,813 (8.2) 54.4	133,592 (8.0) 73.1
8. Uso concomitante di farmaci che aumentano il rischio di sanguinamento a. warfarina + tradizionali FANS/ inibitori COX-2 b. warfarina + aspirina/antipiastricini c. warfarina + FANS/inibitori COX-2 + aspirina/antipiastricini	 178,458 (1.5) 100,236 (0.8) 22,174 (0.2)	 64,939 (1.1) 38,953 (0.6) 8,574 (0.1)	 90,580 (2.0) 49,736 (1.1) 11,135 (0.2)	 22,939 (1.4) 11,547 (0.7) 2,465 (0.1)
9. Uso concomitante di farmaci che aumentano il rischio di insufficienza renale e/o iperkaliemia (ACE inibitori/ARB + antagonisti dell'aldosterone + FANS/ inibitori COX-2)	85,412 (0.7)	28,860 (0.5)	40,665 (0.9)	15,887 (1.0)
10. Uso concomitante di ≥ 2 farmaci che prolungano l'intervallo Q-T ‡	36,359 (0.3)	13,580 (0.2)	15,903 (0.4)	6,876 (0.4)
11. Uso di farmaci anti-ipertensivi con profilo rischio-beneficio sfavorevole (doxazosina, clonidina o metildopa in monoterapia o uso di qualsiasi calcio-antagonista di breve durata d'azione) (% di tutta la popolazione anziana) - % della popolazione anziana in trattamento con farmaci	196,690 (1.6) 2.5	88,069 (1.4) 2.3	78,826 (1.8) 2.5	29,795 (1.8) 2.8

High Prevalence of Poor Quality Drug Prescribing in Older Individuals: A Nationwide Report From the Italian Medicines Agency (AIFA).

Onder G et al. J Gerontol A Biol Sci Med Sci. 2013 Aug 2

Tabella II. Prevalenza degli indicatori di qualità nella popolazione anziana italiana

Indicatori di qualità	Tutti i gruppi di età (≥ 65 anni) n=12,301,537 (%)	65-74 anni n=6,154,421 (%)	75-84 anni n=4,474,887 (%)	≥85 anni n=1,672,229 (%)
1. Politerapia				
• 5-9 farmaci	6,024,383 (49.0)	2,681,639 (43.6)	2,462,378 (55.0)	880,366 (52.6)
• ≥10 farmaci	1,389,591 (11.3)	529,506 (8.6)	629,043 (14.1)	231,042 (13.8)

Popolazione

Pazienti ≥ 65 a = 12.301.537
Pazienti 65-74 a = 6.154.421
Pazienti 75-84 a = 4.474.887
Pazienti ≥ 85 a = 1.672.229

Dispensazione concomitante: **5-9 farmaci/die**

Pazienti ≥ 65 a = 49,0%
Pazienti 65-74 a = 43,6%
Pazienti 75-84 a = 55,0%
Pazienti ≥ 85 a = 52,6%

Dispensazione concomitante: **>10 farmaci/die**

Pazienti ≥ 65 a = 11,3%
Pazienti 65-74 a = 8,6%
Pazienti 75-84 a = 14,1%
Pazienti ≥ 85 a = 13,8%

Polifarmacoterapia nell'anziano

Bajcar *et al. BMC Family Practice* 2010, **11**:75
http://www.biomedcentral.com/1471-2296/11/75

BMC
Family Practice

RESEARCH ARTICLE Open Access

From pharmaco-therapy to pharmaco-prevention: trends in prescribing to older adults in Ontario, Canada, 1997-2006

Jana M Bajcar[1,2,3,4,5], Li Wang[3], Rahim Moineddin[5,6], Jason X Nie[3,7], C Shawn Tracy[3,8], Ross EG Upshur[3,5,6,8,9*]

Abstract

Background: The developed world is undergoing a demographic transition with greater numbers of older adults and higher rates of chronic disease. Most elder care is now provided by primary care physicians, who prescribe the majority of medications taken by these patients. Despite these significant trends, little is known about population-level prescribing patterns to primary care patients aged 65+.

Methods: We conducted a population-based retrospective cohort study to examine 10-year prescribing trends among family physicians providing care to patients aged 65+ in Ontario, Canada.

Results: Both crude number of prescription claims and prescription rates (i.e., claims per person) increased dramatically over the 10-year study period. The greatest change was in prescribing patterns for females aged 85+. Dramatic increases were observed in the prescribing of preventive medications, such as those to prevent osteoporosis (+2,347%) and lipid-lowering agents (+697%). And lastly, the number of unique classes of medications prescribed to older persons has increased, with the proportion of older patients prescribed more than 10 classes of medications almost tripling during the study period.

Conclusions: Prescribing to older adults by family physicians increased substantially during the study period. This raises important concerns regarding quality of care, patient safety, and cost sustainability. It is evident that further research is urgently needed on the health outcomes (both beneficial and harmful) associated with these dramatic increases in prescribing rates.

Polifarmacoterapia nell'anziano

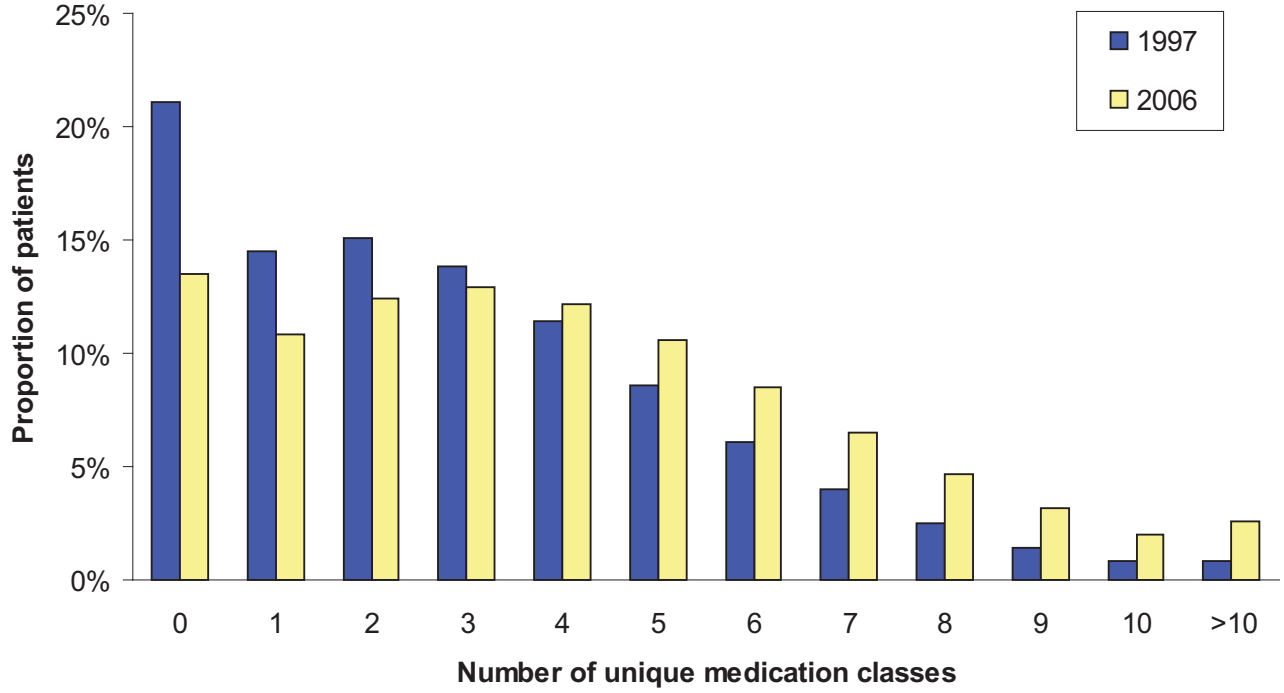

Figure 1 Frequency distribution of number of unique medication classes for older adults aged 65+ in Ontario, Canada, 1997-2006.

Bajcar er al. From pharmaco-therapy to pharmaco-prevention: trends in prescribing to older adults in Ontario, Canada, 1997-2006. BMC Family Practice 2010;11: 75

Polifarmacoterapia nell'anziano

The increase in prescription claims cannot be explained entirely by increase in population, as the prescription claims per person is **almost threefold higher** than population increases.

The prescription increases may be partially explained by greater reliance on **clinical practice guidelines**, particularly more aggressive identification and management of risk factors for chronic conditions such as cardiovascular disease and osteoporosis.

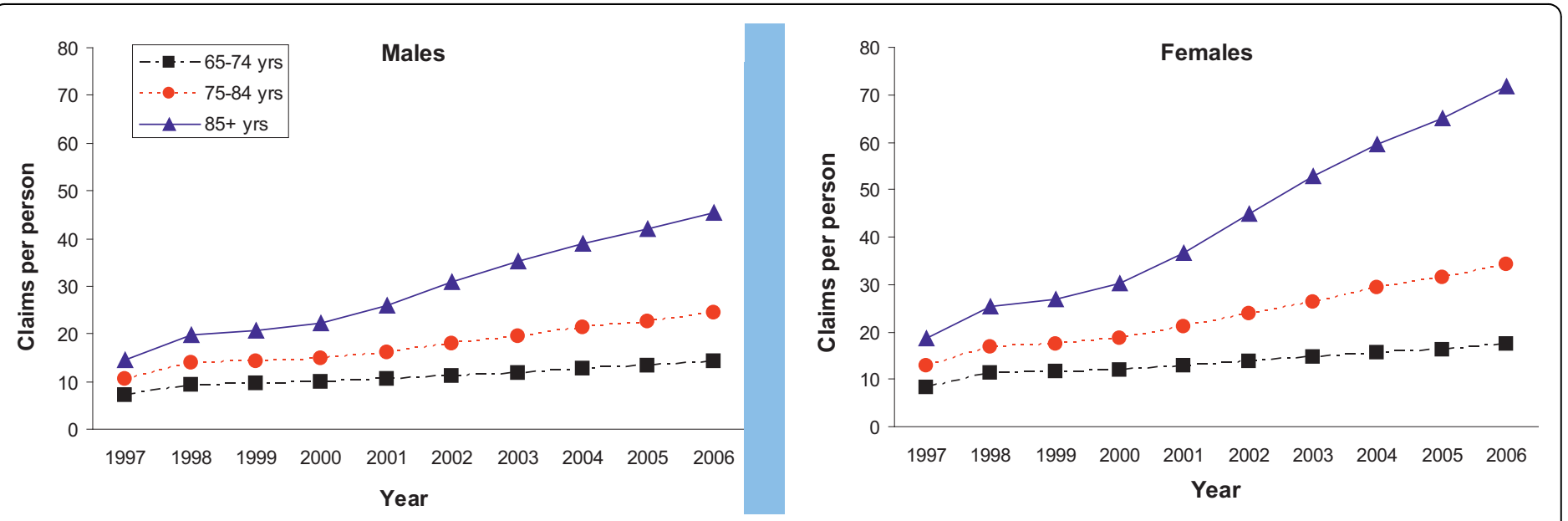

Figure 3 Age differences in prescription claims per person for older adults aged 65+ in Ontario, Canada, 1997-2006.

Bajcar er al. From pharmaco-therapy to pharmaco-prevention: trends in prescribing to older adults in Ontario, Canada, 1997-2006. BMC Family Practice 2010;11: 75

Polifarmacoterapia nell'anziano

Clinical Practice Guidelines and Quality of Care for Older Patients With Multiple Comorbid Diseases

Implications for Pay for Performance

Scopo: valutare l'applicabilità di linee guida per la pratica clinica (prodotte da società internazionali fino a marzo del 2005)nella cura di pazienti anziani affetti da gravi co-morbilità.

Patologie considerate:

- ✧ Ipertensione
- ✧ Insufficienza cardiaca
- ✧ Angina stabile,
- ✧ Fibrillazione atriale
- ✧ Ipercolesterolemia
- ✧ Diabete mellito
- ✧ Osteoartrosi
- ✧ BPCO (broncopneumopatia cronica ostruttiva)
- ✧ osteoporosi

Boyd CM et al. JAMA 2005;294:716-24

Context Clinical practice guidelines (CPGs) have been developed to improve the quality of health care for many chronic conditions. Pay-for-performance initiatives assess physician adherence to interventions that may reflect CPG recommendations.

Objective To evaluate the applicability of CPGs to the care of older individuals with several comorbid diseases.

Data Sources The National Health Interview Survey and a nationally representative sample of Medicare beneficiaries (to identify the most prevalent chronic diseases in this population); the National Guideline Clearinghouse (for locating evidence-based CPGs for each chronic disease).

Study Selection Of the 15 most common chronic diseases, we selected hypertension, chronic heart failure, stable angina, atrial fibrillation, hypercholesterolemia, diabetes mellitus, osteoarthritis, chronic obstructive pulmonary disease, and osteoporosis, which are usually managed in primary care, choosing CPGs promulgated by national and international medical organizations for each.

Data Extraction Two investigators independently assessed whether each CPG addressed older patients with multiple comorbid diseases, goals of treatment, interactions between recommendations, burden to patients and caregivers, patient preferences, life expectancy, and quality of life. Differences were resolved by consensus. For a hypothetical 79-year-old woman with chronic obstructive pulmonary disease, type 2 diabetes, osteoporosis, hypertension, and osteoarthritis, we aggregated the recommendations from the relevant CPGs.

Data Synthesis Most CPGs did not modify or discuss the applicability of their recommendations for older patients with multiple comorbidities. Most also did not comment on burden, short- and long-term goals, and the quality of the underlying scientific evidence, nor give guidance for incorporating patient preferences into treatment plans. If the relevant CPGs were followed, the hypothetical patient would be prescribed 12 medications (costing her $406 per month) and a complicated nonpharmacological regimen. Adverse interactions between drugs and diseases could result.

Conclusions This review suggests that adhering to current CPGs in caring for an older person with several comorbidities may have undesirable effects. Basing standards for quality of care and pay for performance on existing CPGs could lead to inappropriate judgment of the care provided to older individuals with complex comorbidities and could create perverse incentives that emphasize the wrong aspects of care for this population and diminish the quality of their care. Developing measures of the quality of the care needed by older patients with complex comorbidities is critical to improving their care.

JAMA. 2005;294:716-724 www.jama.com

Table 3. Treatment Regimen Based on Clinical Practice Guidelines for a Hypothetical 79-Year-Old Woman With Hypertension, Diabetes Mellitus, Osteoporosis, Osteoarthritis, and COPD*

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	

Abbreviations: ADA, American Diabetes Association; COPD, chronic obstructive pulmonary disease; DASH, Dietary Approaches to Stop Hypertension.

*Clinical practice guidelines used: (1) Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure VII.[39] (2) ADA[19-32]; glycemic control is recommended; however, specific medicines are not described. (3) American College of Rheumatology[33-36]; recent evidence about the safety and appropriateness of cyclooxygenase inhibitors, particularly in individuals with comorbid cardiovascular disease, led us to omit them from the list of medication options, although they are discussed in the reviewed clinical practice guidelines. (4) National Osteoporosis Foundation[40]; this regimen assumes dietary intake of 200 IU of vitamin D. (5) National Heart, Lung, and Blood Institute and World Health Organization.[37,38]

†Taken orally unless otherwise indicated. The medication complexity score of the regimen for this hypothetical woman is 14, with 19 doses of medications per day, assuming 2 as needed doses of albuterol metered dose inhaler plus 70

DASH (Dietary Approaches to Stop Hypertension) guidelines

Boyd CM et al. JAMA 2005;294:716-24

Table 4. Potential Treatment Interactions for a Hypothetical 79-Year-Old Woman with 5 Chronic Diseases

		Type of Interaction		
Type of Disease	Medications With Potential Interactions	Medication and Other Disease	Medications for Different Diseases	Medication and Food
Hypertension	Hydrochlorothiazide, lisinopril	Diabetes: diuretics increase serum glucose and lipids*	Diabetes medications: hydrochlorothiazide may decrease effectiveness of glyburide	NA
Diabetes	Glyburide, metformin, aspirin, and atorvastatin	NA	Osteoarthritis medications: NSAIDs plus aspirin increase risk of bleeding Diabetes medications: glyburide plus aspirin may increase the risk of hypoglycemia; aspirin may decrease effectiveness of lisinopril	Aspirin plus alcohol: increased risk of gastrointestinal tract bleeding Atorvastatin plus grapefruit juice: muscle pain, weakness Glyburide plus alcohol: low blood sugar, flushing, rapid breathing, tachycardia Metformin plus alcohol: extreme weakness and heavy breathing Metformin plus any type of food: medication absorption decreased
Osteoarthritis	NSAIDs	Hypertension: NSAIDs: raise blood pressure†; NSAIDs plus hypertension increase risk of renal failure	Diabetes medications: NSAIDs in combination with aspirin increase risk of bleeding Hypertension medications: NSAIDs decrease efficacy of diuretics	NA
Osteoporosis	Calcium, alendronate	NA	Diabetes medications: calcium may decrease efficacy of aspirin; asprin plus alendronate can cause upset stomach Osteoporosis medications: calcium may lower serum alendronate level	Alendronate plus calcium: take on empty stomach (>2 h from last meal) Alendronate: avoid orange juice Calcium plus oxalic acid (spinach and rhubarb) or phytic (bran and whole cereals): eating these foods may decrease amount of calcium absorbed (>2 h from last meal)
Chronic obstructive pulmonary disease	Short-acting β-agonists	NA	NA	NA

Abbreviations: NA, no interaction is known; NSAIDs, nonsteroidal anti-inflammatory drugs.
*Thiazide-type diuretics may worsen hyperglycemia, but effect thought to be small and not associated with increased incidence of cardiovascular events.
†This interaction is noted to be particularly relevant for individuals with diabetes; no recommendation for treatment is given.

Boyd CM et al. JAMA 2005;294:716-24

Eligibility Criteria of Randomized Controlled Trials Published in High-Impact General Medical Journals

JAMA, March 21, 2007—Vol 297, No. 11

A Systematic Sampling Review

Table 2. Categories of Exclusion Criteria

Exclusion Criteria	No. (%) of Trials*
Inability to give informed consent	242 (85.5)
Age, y	204 (72.1)
<16	170 (60.1)
>65	109 (38.5)
Sex	133 (47.0)
Related to female sex	111 (39.2)
Female sex	19 (6.7)
Pregnancy	90 (31.9)
Lactation	41 (14.5)
Lack of contraception use	25 (8.8)
Menopausal status	11 (3.9)
Related to male sex	22 (7.8)
Medical comorbidities	230 (81.3)
Unspecified medical condition	87 (30.9)
Nephrological	74 (26.1)
Infectious	69 (24.4)
Cardiac	69 (24.4)
Hepatic	63 (22.3)
Hematological	59 (20.8)
Malignancy	46 (16.3)
Neurological	43 (15.2)
Endocrine	43 (15.2)
Psychiatric	42 (14.8)
Substance abuse	37 (13.1)
Cerebrovascular	35 (12.4)
Decreased life expectancy	34 (12.1)
Poorly controlled hypertension	28 (9.9)
Physical disability or functional status	31 (11.0)
Pulmonary	29 (10.2)
HIV or AIDS	25 (8.9)
Rheumatological	22 (7.8)
Cognitive impairment	22 (7.8)
Musculoskeletal	13 (4.6)
Peripheral vascular	12 (4.2)
Dermatological	11 (3.9)
Medication-related	153 (54.1)
Socioeconomic status	39 (13.8)
Communication or language barrier	30 (10.6)
Participation in other trials	20 (7.1)
Ethnicity	6 (2.1)

Abbreviation: HIV, human immunodeficiency virus.
*Denominator is category-specific.

Criteri di esclusione dei pazienti nei 283 RCT considerati

- **Età** nel 72,1%
- **Bambini (<16 anni) nel 60,1%**
- **Anziani (>65 anni) nel 38,5%**
- **Sesso fermminile nel 39,2%** *(sesso maschile come criterio di esclusione nel 7.8%)*
- **Patologie concomitanti nell'81,3%** *(nel 30,9% non è stato chiarito né il tipo di patologia né le ragioni).*

Table 3. Justification of Exclusion Criteria

	No. (%) of Trials*
Grading of individual exclusion criteria	
Total number of exclusions	2709 (100.0)
Strongly justified	1275 (47.2)
Potentially justified	430 (15.9)
Poorly justified	1004 (37.1)
At least 1 poorly justified exclusion criterion	238 (84.1)
Category with poor justification	
Age	160 (78.4)
Medical comorbidity	149 (64.8)
Sex	70 (52.6)
Females	69 (62.2)
Males	1 (4.5)
Medication-related	56 (36.6)
Socioeconomic status	31 (79.5)
Percentage of poorly justified exclusion criteria	
≥10	228 (80.6)
≥25	174 (61.5)
≥50	83 (29.3)
≥75	24 (8.5)
Exclusions per trial, mean (SD)	9.5 (6.1)

*Unless otherwise indicated.

Van Spall et al. JAMA. 2007;297:1233-40.

The dilemma of polypharmacy

Sarah N Hilmer, Departments of Clinical Pharmacology and Aged Care, Royal North Shore Hospital and University of Sydney

The prevalence of chronic diseases, for which one or more medicines may be indicated, increases with age. Polypharmacy is usually defined as the use of five or more drugs, including prescribed, over-the-counter, and complementary medicines. It may be a useful prompt for medication review, as it is associated with problems of medication management and suboptimal prescribing. However, polypharmacy is not a clinically useful independent marker of the quality use of medicines. The type and dose of medications rather than the number of medications determine meaningful clinical outcomes.[1]

The more drugs a patient takes, the harder it may be to obtain an accurate medication history, which impedes informed medication review and prescribing. The incidence of adverse drug reactions increases with the number of medications used. Polypharmacy is a barrier to adherence because of the associated complex medication regimens, increased risk of adverse drug events and high medication costs. Poor adherence contributes to the increased risk of medication errors seen with polypharmacy.

- Polypharmacy = ≥ 5 medicines
- The **type and dose** of medications rather than the number of medications **determine meaningful clinical outcomes**
- **More drugs = less accurate medication history**
- **Incidence of ADRs increases with number of drugs used**
- **Polypharmacy is a barrier to adherence**
- **Poor adherence contributes to higher risk of medication errors**
- **Suboptimal precriptions**
- **Innapropriate prescription** (i.e. unnecessary drugs, drugs to avoid)
- **Drug interactions**
- **The "PRESCRIPTION CASCADE"**

Polypharmacy: unnecessary drugs

Wien Klin Wochenschr (2008) 120: 733–741
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Wiener klinische Wochenschrift
The Middle European Journal of Medicine

Polypharmacy and inappropriate prescribing in elderly internal-medicine patients in Austria

Jochen Schuler[1], Christina Dückelmann[2], Wolfgang Beindl[2], Erika Prinz[1], Thomas Michalski[1], Max Pichler[1]

- accurate medication history
- unnecessary drugs
- drugs to avoid
- duplication
- wrong dosage
- drug interactions
- adverse drug events
- the "prescription cascade"

Polypharmacy: unnecessary drugs

Use of Prescription and Over-the-counter Medications and Dietary Supplements Among Older Adults in the United States

Context Despite concerns about drug safety, current information on older adults' use of prescription and over-the-counter medications and dietary supplements is limited.

Objective To estimate the prevalence and patterns of medication use among older adults (including concurrent use), and potential major drug-drug interactions.

Design, Setting, and Participants Three thousand five community-residing individuals, aged 57 through 85 years, were drawn from a cross-sectional, nationally representative probability sample of the United States. In-home interviews, including medication logs, were administered between June 2005 and March 2006. Medication use was defined as prescription, over-the-counter, and dietary supplements used "on a regular schedule, like every day or every week." Concurrent use was defined as the regular use of at least 2 medications.

Main Outcome Measure Population estimates of the prevalence of medication use, concurrent use, and potential major drug-drug interactions, stratified by age group and gender.

Results The unweighted survey response rate was 74.8% (weighted response rate, 75.5%). Eighty-one percent (95% confidence interval [CI], 79.4%-83.5%) used at least 1 prescription medication, 42% (95% CI, 39.7%-44.8%) used at least 1 over-the-counter medication, and 49% (95% CI, 46.2%-52.7%) used a dietary supplement. Twenty-nine percent (95% CI, 26.6%-30.6%) used at least 5 prescription medications concurrently; this was highest among men (37.1%; 95% CI, 31.7%-42.4%) and women (36.0%; 95% CI, 30.2%-41.9%) aged 75 to 85 years. Among prescription medication users, concurrent use of over-the-counter medications was 46% (95% CI, 43.4%-49.1%) and concurrent use of dietary supplements was 52% (95% CI, 48.8%-55.5%). Overall, 4% of individuals were potentially at risk of having a major drug-drug interaction; half of these involved the use of nonprescription medications. These regimens were most prevalent among men in the oldest age group (10%; 95% CI, 6.4%-13.7%) and nearly half involved anticoagulants. No contraindicated concurrent drug use was identified.

Conclusions In this sample of community-dwelling older adults, prescription and nonprescription medications were commonly used together, with nearly 1 in 25 individuals potentially at risk for a major drug-drug interaction.

JAMA. 2008;300(24):2867-2878 www.jama.com

Table 6. Potential Major Medication Interactions by Age and Gender[a]

	Interactions, Weighted No.							
	Age 57-64 y (n = 1016)		Age 65-74 y (n = 1082)		Age 75-85 y (n = 878)			
Medication Interaction[b]	Men (n = 525)	Women (n = 491)	Men (n = 543)	Women (n = 539)	Men (n = 377)	Women (n = 501)	Total (N = 2976)	Potential Interaction Effect
Prescription-prescription								
Albuterol-atenolol	0	1	1	0	1	1	5	Decreased effectiveness
Albuterol-metoprolol	0	1	1	1	2	1	6	Decreased effectiveness
Warfarin-simvastatin	5	2	4	3	7	5	25	Increased risk of bleeding/ rhabdomyolysis
Clopidogrel-warfarin	0	0	0	1	1	1	3	Increased risk of bleeding
Lisinopril-potassium	0	8	5	5	9	6	33	Increased risk of hyperkalemia
Nonprescription-prescription								
Aspirin-warfarin[c]	7	0	7	1	11	2	27	Increased risk of bleeding
Niacin-atorvastatin[d]	7	0	5	0	3	3	18	Increased risk of myopathy or rhabdomyolysis
Garlic-warfarin	0	0	0	0	1	0	1	Increased risk of bleeding
Niacin-simvastatin	1	1	4	2	1	0	10	Increased risk of myopathy or rhabdomyolysis
Nonprescription-nonprescription								
Ginkgo-aspirin	0	0	1	3	4	3	10	Increased risk of bleeding
Any interaction, No. (% [95% CI])[e]	18 (2.9 [0.9-4.8])	13 (2.1 [0.2-4.0])	24 (4.7 [2.9-6.4])	14 (2.6 [1.2-3.9])	31 (10.1 [6.4-13.7])	19 (4.8 [2.7-6.9])	118 (4.0 [3.1-4.8])	

[a] Percentages and numbers are weighted estimates to account for differential probabilities of selection and differential nonresponse.
[b] Potential major medication interactions for the 20 most common prescription and over-the-counter medications and 20 most common dietary supplements.
[c] Statistically significant ($P < .001$) difference between men and women.
[d] Statistically significant ($P = .03$) difference between men and women.
[e] Statistically significant ($P = .01$) difference between men and women.

Qato DM et al. JAMA. 2008;300:2867-78.

Polypharmacy: unnecessary drugs

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The Middle European Journal of Medicine

Polypharmacy and inappropriate prescribing in elderly internal-medicine patients in Austria

Jochen Schuler[1], Christina Dückelmann[2], Wolfgang Beindl[2], Erika Prinz[1], Thomas Michalski[1], Max Pichler[1]

3-month screening period
543 patients ≥75 years of age admitted to selected internal wards of a university hospital (33.7% of all admissions).

Unnecessary drugs:
36.3% of patients (197/543)
6.8% of prescriptions (277/4061).
✓pentoxiphylline (n = 52)
✓ginkgo biloba (n = 40)
✓allopurinol (n = 28)
✓magnesium salts (n = 26)

Unnecessary drugs

These were identified in 36.3% of patients (197/543) and in 6.8% of prescriptions (277/4061). The most common unnecessary drugs were pentoxiphylline (n = 52) and ginkgo biloba (n = 40), followed by allopurinol (n = 28), magnesium salts (n = 26), laxatives (n = 18), bladder spasmolytics (n = 16), prokinetics (n = 14), β-adrenergic drugs for low blood pressure (n = 11), herbal sedatives (n = 10), venous therapeutics (n = 9), herbal liver and cardiac therapeutics (n = 9) and herbal prostate therapeutics (n = 5).

The prescription of unnecessary drugs was significantly correlated with polypharmacy: prevalence among patients with >6 drugs was 48.1% and among patients with ≤6 drugs 19.9% ($P < 0.0005$, OR 3.73).

Potentially Inappropriate Medication Use Among Elderly Home Care Patients in Europe

Daniela Fialová, PharmD
Eva Topinková, MD, PhD
Giovanni Gambassi, MD
Harriet Finne-Soveri, MD, PhD
Pálmi V. Jónsson, MD
Iain Carpenter, MD, FRCP
Marianne Schroll, DrScM
Graziano Onder, MD, PhD
Liv Wergeland Sørbye, RN
Cordula Wagner, MD, PhD
Jindra Reissigová, RNDr
Roberto Bernabei, MD
for the AdHOC Project Research Group

Context Criteria for potentially inappropriate medication use among elderly patients have been used in the past decade in large US epidemiological surveys to identify populations at risk and specifically target risk-management strategies. In contrast, in Europe little information is available about potentially inappropriate medication use and is based on small studies with uncertain generalizability.

Objective To estimate the prevalence and associated factors of potentially inappropriate medication use among elderly home care patients in European countries.

Design, Setting, and Participants Retrospective cross-sectional study of 2707 elderly patients receiving home care (mean [SD] age, 82.2 [7.2] years) representatively enrolled in metropolitan areas of the Czech Republic, Denmark, Finland, Iceland, Italy, the Netherlands, Norway, and the United Kingdom. Patients were prospectively assessed between September 2001 and January 2002 using the Minimum Data Set in Home Care instrument.

Main Outcome Measures Prevalence of potentially inappropriate medication use was documented using all expert panels criteria for community-living elderly persons (Beers and McLeod). Patient-related characteristics independently associated with inappropriate medication use were identified with a multiple logistic regression model.

Results Combining all 3 sets of criteria, we found that 19.8% of patients in the total sample used at least 1 inappropriate medication; using older 1997 criteria it was 9.8% to 10.9%. Substantial differences were documented between Eastern Europe (41.1% in the Czech Republic) and Western Europe (mean 15.8%, ranging from 5.8% in Denmark to 26.5% in Italy). Potentially inappropriate medication use was associated with patient's poor economic situation (adjusted relative risk [RR], 1.96; 95% confidence interval [CI], 1.58-2.36), polypharmacy (RR, 1.91; 95% CI, 1.62- 2.22), anxiolytic drug use (RR, 1.82; 95% CI, 1.51-2.15), and depression (RR, 1.29; 95% CI, 1.06-1.55). Negatively associated factors were age 85 years and older (RR, 0.78; 95% CI, 0.65-0.92) and living alone (RR, 0.76; 95% CI, 0.64-0.89). The odds of potentially inappropriate medication use significantly increased with the number of associated factors ($P<.001$).

Conclusions Substantial differences in potentially inappropriate medication use exist between European countries and might be a consequence of different regulatory measures, clinical practices, or inequalities in socioeconomic background. Since financial resources and selected patient-related characteristics are associated with such prescribing, specific educational strategies and regulations should reflect these factors to improve prescribing quality in elderly individuals in Europe.

JAMA. 2005;293:1348-1358 www.jama.com

USE OF POTENTIALLY INAPPROpriate medications in elderly patients is a major health care concern. It is likely to increase the risk of adverse drug events, which are estimated to be the fifth most common cause of death among hospitalized patients[1] and which account for a large number of hospital admissions and a substantial increase in health care costs.[2]

In the United States and Canada, epidemiological studies have documented widespread use of potentially inappropriate medications among nursing home residents (up to 40%) and

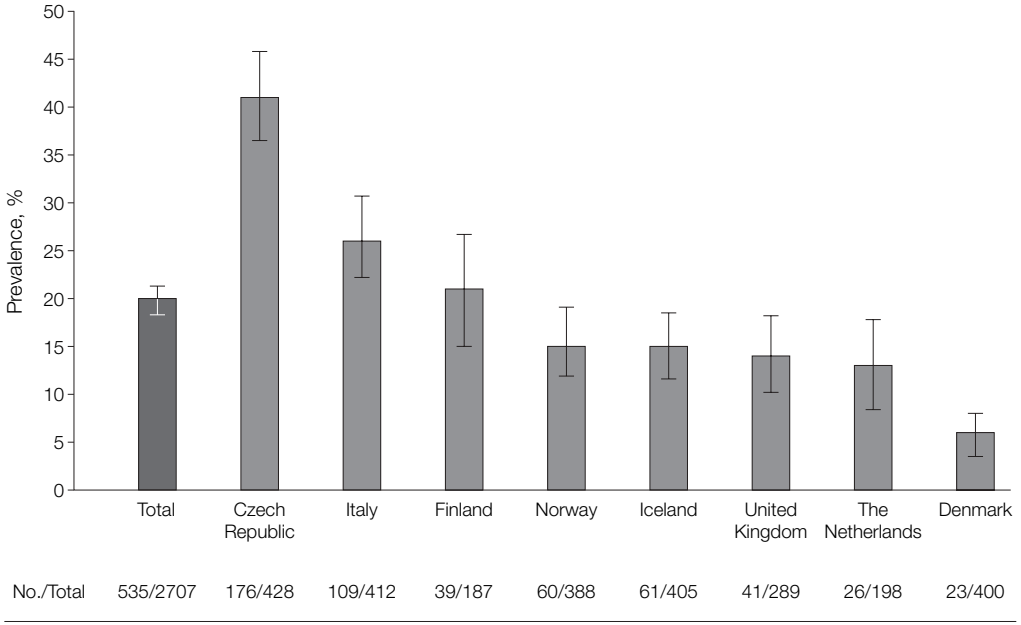
Polypharmacy: inappropriate drugs

Table 1. Inappropriate Medications and Classes to Avoid in Elderly Patients, as Defined by Expert Panel Criteria (cont)

Inappropriate Medication by Class	Expert Panel Criteria: Beers 1997[15]	McLeod 1997[16]	Beers 2003[17]
All barbiturates except phenobarbital	✓	✓	
All barbiturates except phenobarbital and except seizure control			✓
Diuretic			
Ethacrynic acid			✓
Ergot mesyloid	✓		✓
H_2 antagonist			
Cimetidine			✓
Hormonal			
Dessicated thyroid			✓
Estrogens only (oral)			✓
Methyltestosterone			✓
Hypoglycemic			
Chlorpropamide	✓		
Laxative			
Long-term use of stimulant laxative: bisacodyl, cascara sagrada			✓
Mineral oil			✓
Muscle relaxants and antispasmodics: methocarbamol, carisoprodol, chlorzoxazone, metaxalone, cyclobenzaprine, orphenadrine	✓	✓	✓
Niacin		✓	
Sedative			
Chlordiazepoxide	✓	✓	✓
Chlordiazepoxide-amitriptyline			✓
Diazepam	✓	✓	✓
Flurazepam	✓	✓	✓
Meprobamate	✓		✓
Quazepam, halazepam, chlorazepat			✓
Triazolam		✓	
Triazolam >0.25 mg/d			✓
Short-acting benzodiazepines: lorazepam >3 mg/d, oxazepam >60 mg/d, alprazolam >2 mg/d, temazepam >15 mg/d			✓
Stimulant			
Amphetamines (excluding methylphenidate) and anorexics			✓
Methylphenidate		✓	
Vasodilator			
Cyclandelate	✓		✓
Isoxsuprine			✓
Nylidrin		✓	
Pentoxifylline		✓	

Fialovà et al. Potentially inappropriate medication use among elderly home care patients in Europe. JAMA 2005; 293: 1348-58

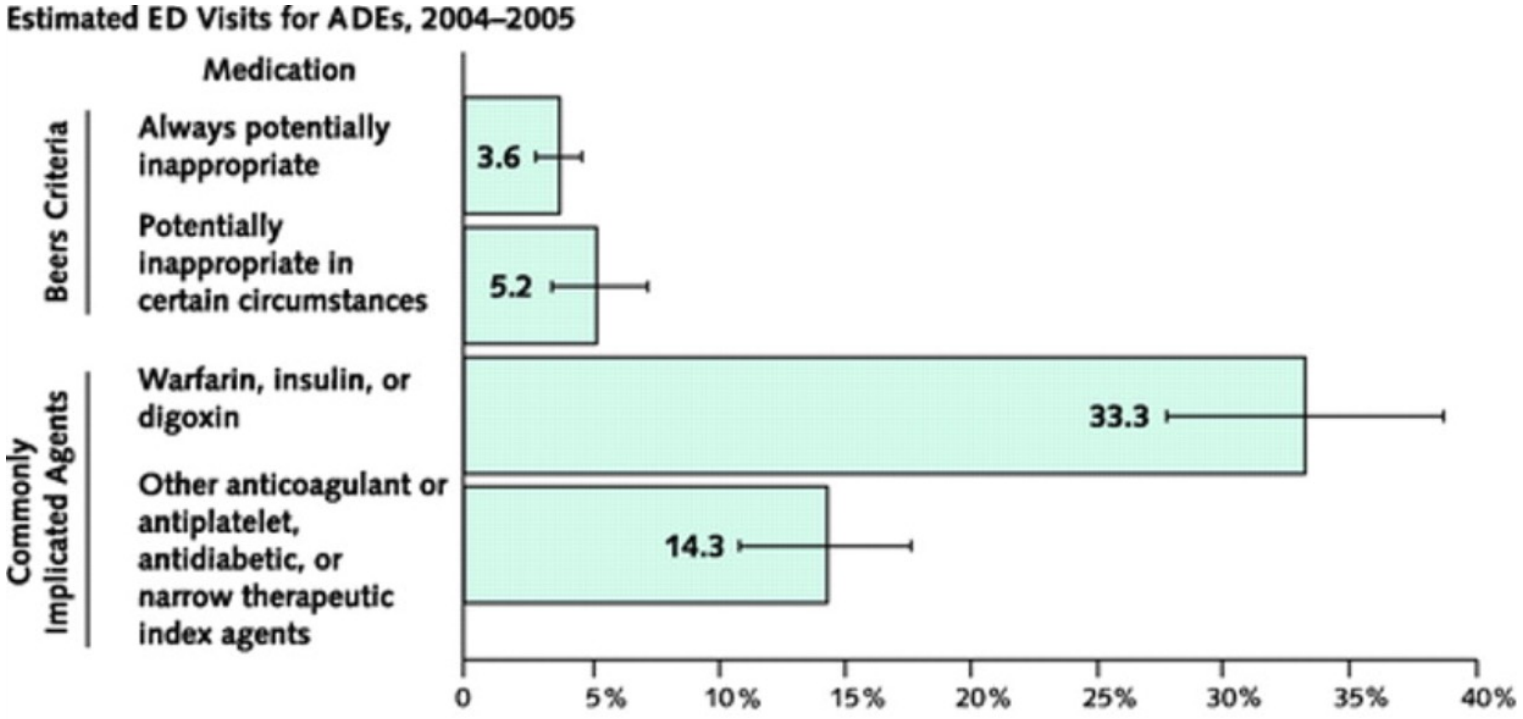
Figure 1. Prevalence of Potentially Inappropriate Medication Use Considering All Explicit Criteria Combined (Beers 1997,[15] Beers 2003,[17] and McLeod 1997[16])



Annals of Internal Medicine
Established in 1927 by the American College of Physicians

Medication Use Leading to Emergency Department Visits for Adverse Drug Events in Older Adults

Ann Intern Med. 2007;147(11):755-765. doi:10.7326/0003-4819-147-11-200712040-00006



Polypharmacy: unnecessary drugs

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Drugs to avoid:

30.1% of patients (163/543)
4.6% of prescriptions (187/4061)
F vs M: 38.0% vs 18.1%
✓benzodiazepines (n = 110)
✓nifedipine(n = 23)
✓amitriptyline (n = 10)
✓ergotamine(n = 8)
✓fluoxetine (n = 6)
✓NSAIDs (n = 6)
✓oxybutynin (n = 5)

Drugs to avoid

Inadequate drugs, following the modified Beers criteria, were found in 30.1% of the patients (163/543) and 4.6% of prescriptions (187/4061). Women were found to have a much higher rate of inadequate drugs than men (38.0% vs. 18.1%). The most important inadequate drugs identified were benzodiazepines (n = 110), nifedipine (n = 23), amitriptyline (n = 10), ergotamine (n = 8), daily fluoxetine (n = 6), long-acting NSAIDs (n = 6) and oxybutynin (n = 5). Inadequate drug use was significantly correlated with polypharmacy: prevalence among patients with >6 drugs was 38.6% and among patients with ≤6 drugs 18.1% ($P < 0.0005$, OR 2.84).

Inadequate drug use was significantly correlated with polypharmacy: prevalence among patients with >6 drugs was 38.6% and among patients with ≤6 drugs 18.1% ($P < 0.0005$, OR 2.84).

Polypharmacy: unnecessary drugs

High Prevalence of Poor Quality Drug Prescribing in Older Individuals: A Nationwide Report From the Italian Medicines Agency (AIFA).

Onder G et al. J Gerontol A Biol Sci Med Sci. 2013 Aug 2

8. Uso concomitante di farmaci che aumentano il rischio di sanguinamento a. warfarina + tradizionali FANS/ inibitori COX-2 b. warfarina + aspirina/antipiastricini c. warfarina + FANS/inibitori COX-2 + aspirina/antipiastricini	178,458 (1.5) 100,236 (0.8) 22,174 (0.2)	64,939 (1.1) 38,953 (0.6) 8,574 (0.1)	90,580 (2.0) 49,736 (1.1) 11,135 (0.2)	22,939 (1.4) 11,547 (0.7) 2,465 (0.1)
9. Uso concomitante di farmaci che aumentano il rischio di insufficienza renale e/o iperkaliemia (ACE inibitori/ARB + antagonisti dell'aldosterone + FANS/ inibitori COX-2)	85,412 (0.7)	28,860 (0.5)	40,665 (0.9)	15,887 (1.0)
10. Uso concomitante di ≥ 2 farmaci che prolungano l'intervallo Q-T ‡	36,359 (0.3)	13,580 (0.2)	15,903 (0.4)	6,876 (0.4)
11. Uso di farmaci anti-ipertensivi con profilo rischio-beneficio sfavorevole (doxazosina, clonidina o metildopa in monoterapia o uso di qualsiasi calcio-antagonista di breve durata d'azione) (% di tutta la popolazione anziana) - % della popolazione anziana in trattamento con farmaci	196,690 (1.6) 2.5	88,069 (1.4) 2.3	78,826 (1.8) 2.5	29,795 (1.8) 2.8

Polypharmacy: prescription duplication

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Prescription duplication:

7,6% of patients (41/543)

1.2% of prescriptions (49/4061)

✓benzodiazepines

✓diuretics

Duplication

Double prescriptions were found in 7.6% of the patients (41/543) and 1.2% of the prescriptions (49/4061). Patients with polypharmacy had a significantly higher risk for duplication (12.6% vs. 0.4%, $P < 0.0005$, OR 32.6). The most common duplicated drugs were benzodiazepines and diuretics.

Polypharmacy: wrong dosage

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Wrong dosage:
23,4% of patients (127/543)
3,8% of prescriptions (156/4061)
✓Diuretics
✓PPI
✓NSAIDs
✓Cardiac glycosides
✓Opiate

Wrong dosage

Incorrect drug dosage, namely overdosing, was found in 23.4% of the patients (127/543) and 3.8% of prescriptions (156/4061). Patients with polypharmacy had a significantly higher risk for wrong dosage (31.0% vs. 12.8%, $P < 0.0005$, OR 3.05). In many cases, the overdosage occurred in patients with renal failure (300 mg allopurinol: n = 19, >50 mg spironolactone: n = 21) or low body weight (200 mg amiodarone: n = 16). Other common errors were overdoses of proton-pump inhibitors (n = 59), NSAIDs (n = 18), intoxication with cardiac glycosides (n = 3) and symptomatic opiate overdoses (n = 4).

Polypharmacy: drug interactions

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Drug interaction:

65.8% of patients (356/543)

22.6% of prescriptions (919/4061)

✓Majority Pharmacodynamic interactions

✓Less Pharmacokinetics interactions

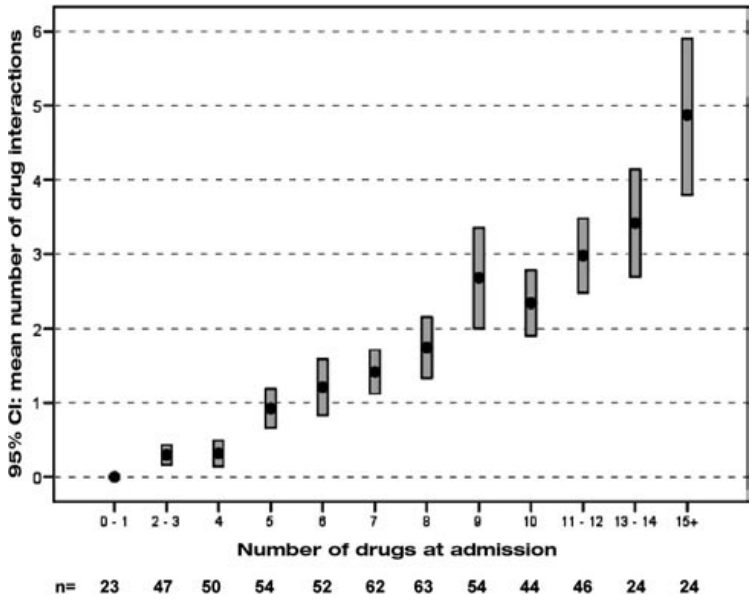


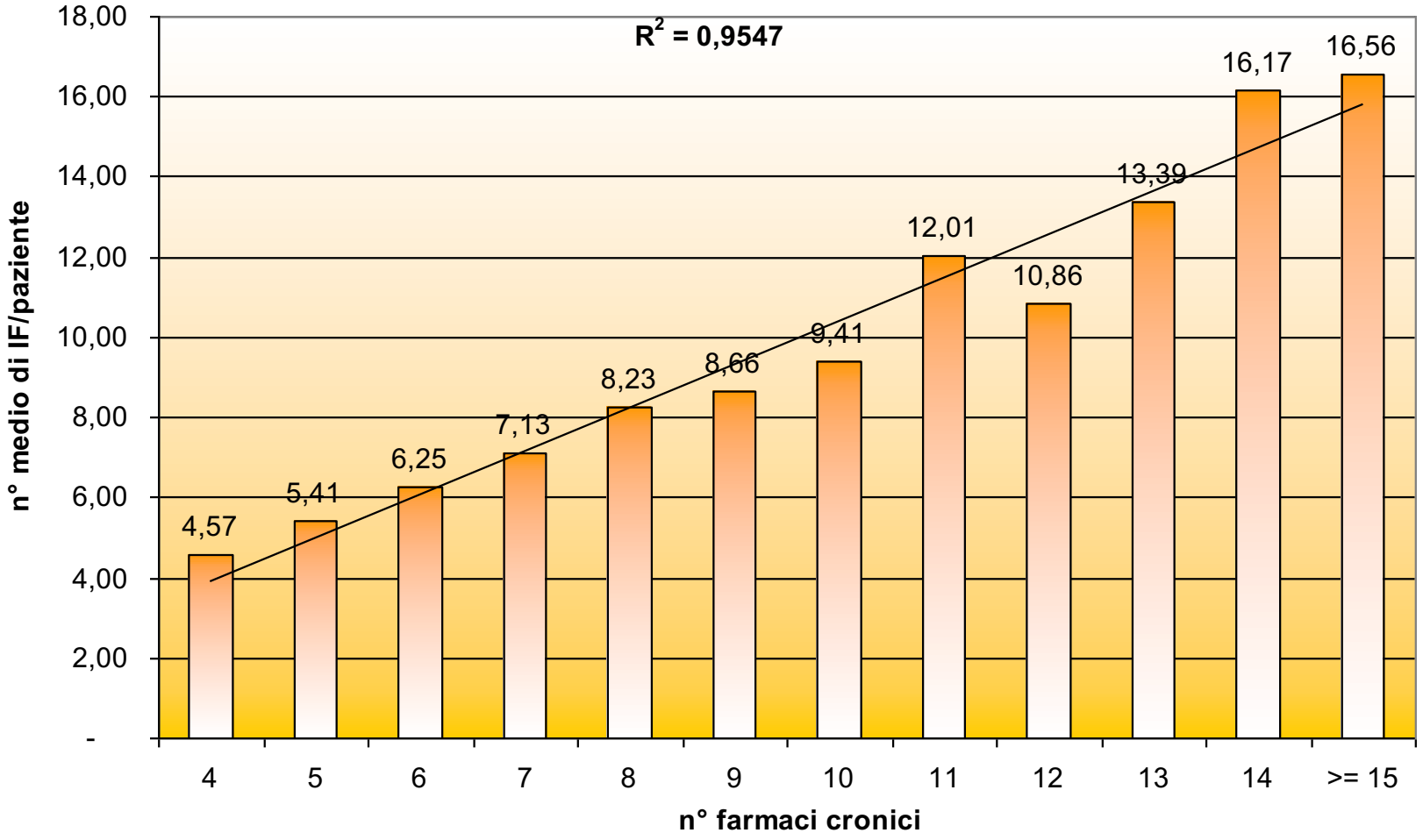
Fig. 1. Relationship between the number of prescribed drugs and the mean number of potential drug interactions

Drug interactions

Potential drug-drug interactions were identified in 65.8% of patients (356/541) and in 22.6% of all drugs (919/4061). We found an almost linear association between the number of drugs prescribed and the mean number of potential drug interactions (Fig. 1). The majority of drug interactions were pharmacodynamic ones such as synergistic actions of benzodiazepines and opiates, amiodarone and beta-blockers, tramadol and serotonin reuptake inhibitors. Potential pharmacokinetic drug interactions such as acenocoumarol and celecoxib (protein-binding competition) or simvastatin and clarithromycin (inhibition of cytochrome p450 metabolism) were less prominent.

Politerapia e potenziali Interazioni Farmacologiche: controindicate e maggiori

(dic 08- nov 09 – AUSL Ferrara)



Polypharmacy: ADE

Wien Klin Wochenschr (2008) 120: 733–741
DOI 10.1007/s00508-008-1089-z
Printed in Austria

Wiener klinische Wochenschrift
The Middle European Journal of Medicine

Polypharmacy and inappropriate prescribing in elderly internal-medicine patients in Austria

Jochen Schuler[1], Christina Dückelmann[2], Wolfgang Beindl[2], Erika Prinz[1], Thomas Michalski[1], Max Pichler[1]

Drug interaction:

17.8% of patients (97/543)

197 ADEs:

- ✓ 56.7% (55/107) hospitalization
- ✓ Hemorrhages (n = 16)
- ✓ Hyponatremia (n = 13)
- ✓ Hypokalemia (n = 10)
- ✓ Bradycardia (n = 10)

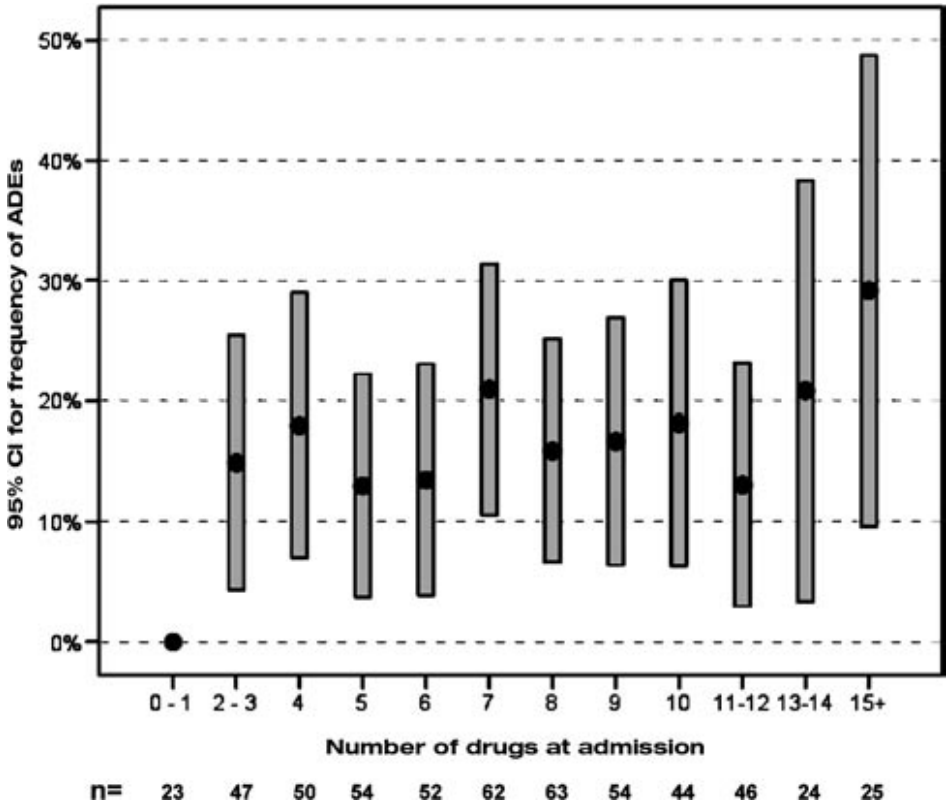


Fig. 2. Frequency of adverse drug events in relation to the number of drugs at admission

Polypharmacy: ADE

British Journal of Clinical Pharmacology DOI:10.1111/j.1365-2125.2005.02543.x

Polypharmacy and falls in the middle age and elderly population

G. Ziere,[1,2] J. P. Dieleman,[3] A. Hofman,[2] H A. P. Pols,[2,4] T. J. M. van der Cammen[1,2] & B. H. CH. Stricker[2,4,5]

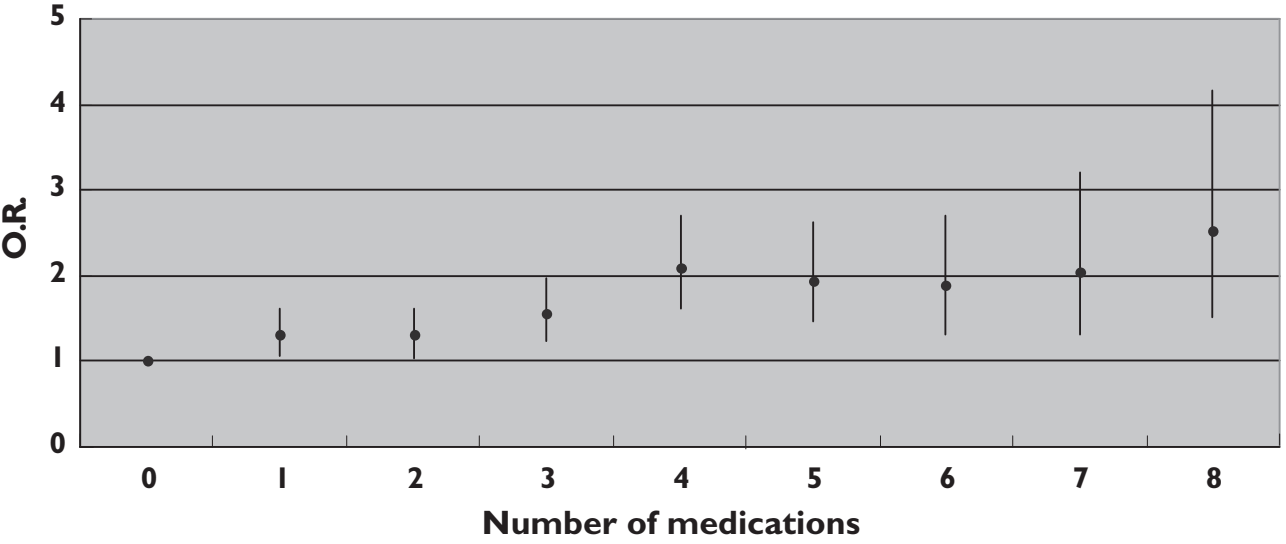


Figure 1

Influence of the number of medications on falling adjusted for age & gender (p for trend <0.001)

Table 2
Drugs associated with falling

ATC code	Description	Cases	Percent cases within users	OR*	(95% CI)	OR† (adj.)	(95% CI)
A	*Alimentary tract and metabolism*						
A06AB	Contact laxatives	26	37.1%	1.8	(1.1, 3.0)	1.3	(0.6, 2.9)
A06AG	Enemas	5	83.3%	23.4	(2.6, 207.8)	0,0	(0.0, ∞)
A08AA	Central acting antiobesity products	7	58.3%	7.7	(2.4, 24.8)	4.9	(1.0, 24.7)
A10BB	Sulphonamides urea derivatives	60	26.2%	1.5	(1.1, 2.0)	1.4	(0.7, 3.1)
A11BA	Multivitamins	19	30.2%	2	(1.1, 3.5)	2.0	(0.9, 4.2)
A11EA	Vitamin b complex	82	26.8%	1.5	(1.1, 2.0)	1.2	(0.8, 1.7)
A12AA	Calcium preparations	36	33.6%	1.9	(1.3, 2.9)	1.9	(1.0, 3.3)
B	*Blood and blood-forming organs*						
B03AA	Oral ferro preparations	24	46.2%	2.8	(1.6, 5.0)	2.3	(0.8, 6.7)
B04AD	Bile acid sequestrants	6	42.9%	3.8	(1.2, 11.8)	2.3	(0.4, 13.5)
C	*Cardiovascular system*						
C03BA	Diuretics—sulphonamides	26	31.0%	2.1	(1.3, 3.4)	1.4	(0.7, 2.9)
C03DB	Diuretics—potassium-sparing agents	18	36.7%	1.9	(1.0, 3.5)	3.6	(1.1, 11.8)
C04AE	Ergot alkaloids	7	50.0%	3.3	(1.1, 9.7)	2.0	(0.4, 9.9)
C05CA	Bioflavonoids	5	50.0%	5	(1.4, 17.9)	3.3	(0.8, 14.6)
G	*Genitourinary system and sex hormones*						
G02CB	Prolactine inhibitors	7	70.0%	10.5	(2.6, 43.4)	NA	(0.0, 0.0)
M	*Musculoskeletal system*						
M01AC	Oxicams	18	40.9%	3.1	(1.6, 5.8)	3.2	(1.3, 7.9)
M09AA	Quinine and derivatives	35	35.0%	1.8	(1.2, 2.8)	2.2	(1.2, 4.2)
N	*Nervous sytem*						
N02BE	Anilides	214	20.7%	1.4	(1.1, 1.6)	1.3	(1.0, 1.6)
N03AB	Hydantoin derivatives	9	33.3%	3	(1.3, 7.0)	1.1	(0.2, 5.8)
N04AA	Anticholinergic agents—tertiary amines	3	60.0%	12	(2.0, 73.6)	4.2	(0.2, 80.2)
N04BA	Dopa and dopa derivatives	17	50.0%	3.5	(1.7, 7.1)	0.8	(0.1, 6.7)
N04BB	Adamantane derivatives	7	43.8%	3.2	(1.1, 9.2)	0.3	(0.0, 4.0)
N04BD	Mao-inhibitors type b	8	50.0%	4.6	(1.7, 12.9)	1.9	(0.2, 20.0)
N05BA	Anxiolytics, benzodiazepine-derivatives	132	26.1%	1.5	(1.2, 1.9)	1.3	(1.0, 1.9)
N05CD	Hypnotics benzodiazepine derivatives	147	27.1%	1.3	(1.0, 1.6)	1.6	(1.1, 2.1)
N07CA	Antivertiginous drugs	59	33.0%	1.7	(1.2, 2.4)	1.0	(0.6, 1.7)
R	*Respiratory system*						
R03BB	Parasympathicolytics	21	29.2%	2.6	(1.5, 4.5)	1.1	(0.4, 2.7)
R05CB	Mucolytics	25	26.9%	1.8	(1.1, 2.9)	1.0	(0.4, 2.3)
S	*Sensory organs*						
S01AA	Ocular antibiotics	4	44.4%	4.7	(1.2, 18.1)	5.9	(0.9, 37.1)

**Corrected for age, gender. †Corrected for age, gender, alcohol use, history of diabetes, history of heart attack, history of hypertension, history of Parkinson's disease, history of stroke, history of thyroid diseases, history of depressive episodes, disability, dizziness, gait disturbance, staying indoors because of poor health, joint complaints, memory complaints, orthostatic hypotension systolic and diastolic after 5 min, postural disturbance and visual acuity.*

G. Ziere et al ,
Polypharmacy and falls in the middle age and elderly population.
BJCP 2005; 61: 218-23

Increased Risk of Achilles Tendon Rupture With Quinolone Antibacterial Use, Especially in Elderly Patients Taking Oral Corticosteroids

Paul D. van der Linden, PharmD; Miriam C. J. M. Sturkenboom, PhD; Ron M. C. Herings, PhD; Hubert M. G. Leufkens, PhD; Sam Rowlands, MD; Bruno H. Ch. Stricker, PhD

Background: In several case reports, the occurrence of Achilles tendon rupture has been attributed to the use of quinolones, but the epidemiologic evidence for this association is scanty.

Methods: We conducted a population-based case-control study in the General Practice Research Database in the United Kingdom during the period 1988 through 1998. Cases were defined as all persons who had a first-time recording of an Achilles tendon rupture, and who had at least 18 months of valid history before the index date. As a control group, we randomly sampled 50 000 patients with at least 18 months of valid history who were assigned a random date as index date.

Results: We identified 1367 cases that met the inclusion criteria. The adjusted odds ratio (OR) for Achilles tendon rupture was 4.3 (95% confidence interval [CI], 2.4-7.8) for current exposure to quinolones, 2.4 (95% CI, 1.5-3.7) for recent exposure, and 1.4 (95% CI, 0.9-2.1) for past exposure. The OR of Achilles tendon rupture was 6.4 (95% CI, 3.0-13.7) in patients aged 60 to 79 years and 20.4 (95% CI, 4.6-90.1) in patients aged 80 years or older. In persons aged 60 years and older, the OR was 28.4 (95% CI, 7.0-115.3) for current exposure to ofloxacin, while the ORs were 3.6 (95% CI, 1.4-9.1) and 14.2 (95% CI, 1.6-128.6) for ciprofloxacin and norfloxacin, respectively. Approximately 2% to 6% of all Achilles tendon ruptures in people older than 60 years can be attributed to quinolones.

Conclusions: Current exposure to quinolones increased the risk of Achilles tendon rupture. The risk is highest among elderly patients who were concomitantly treated with corticosteroids.

Arch Intern Med. 2003;163:1801-1807

Increased risk of Achilles tendon rupture with current use of quinolone in elderly patients (OR e IC95%):

60-79 ys = 6,4 (3,0-13,8)
≥ 80 ys = 20,4 (4,6-90,1)

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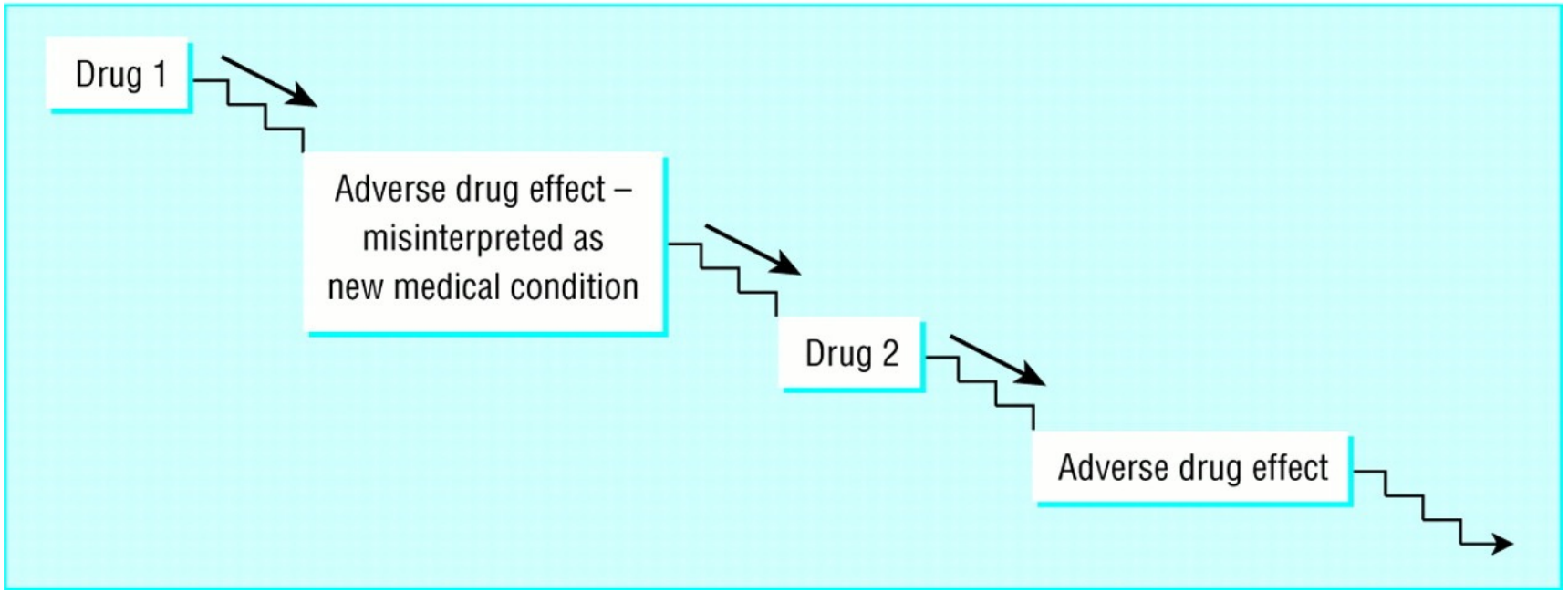
Increased risk of Achilles tendon rupture with quinolone in elderly patients taking oral corticosteroids (OR e IC95%):

No oral corticosteroids = 5,3 (1,8-15,2)
Current exposure to corticosteroids = 17,5 (5,0-60,9)
Recent exposure to corticosteroids = 18,4 (1,42-240,2)

criteria. The adjusted odds ratio (OR) for Achilles tendon rupture was 4.3 (95% confidence interval [CI], 2.4-7.8)

Polypharmacy: the prescription cascade

- The "prescribing cascade" cascade begins an adverse drug reaction is misinterpreted as a new medical condition
- Another drug is then prescribed, and the patient is placed at risk of developing additional adverse effects relating to this potentially unnecessary treatment
- Before any new drug treatment is started, the need for the drug should be re-evaluated and a non-drug treatment should be considered
- If drug treatment is necessary the lowest feasible dose of the drug should be used and alternative drugs with fewer adverse effects considered



Rochon, P. A et al. BMJ 1997;315:1096-1099

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Examples of prescribing cascade

Initial treatment	Adverse effect	Subsequent treatment
Non-steroidal anti-inflammatory drugs[8]	Rise in blood pressure	Antihypertensive treatment
Thiazide diuretics[9]	Hyperuricaemia	Treatment for gout
Metoclopramide treatment[10]	Parkinsonian symptoms	Treatment with levodopa

Rochon, P. A et al. BMJ 1997;315:1096-1099

Polypharmacy: the prescription cascade

Journal of Clinical Pharmacy and Therapeutics (2005) 30, 533–539

ORIGINAL ARTICLE

Measuring the appropriateness of prescribing in primary care: are current measures complete?

N. Barber* PhD, C. Bradley† MD, C. Barry‡ PhD, F. Stevenson§ PhD, N. Britten¶ PhD and L. Jenkins** MSc

*Department of Practice and Policy, The School of Pharmacy, London, UK, †General Practice, University College Cork, Ireland, ‡Centre for the Study of Health and Illness, Brunel University, Uxbridge, UK, §University College, London, UK, ¶Institute of Health and Social Care Research, Peninsula Medical School, Universities of Exeter and Plymouth, Exeter, UK and **Department of General Practice, Kings College, London, UK

SUMMARY

Background and objectives: Appropriateness of prescribing is often assessed by standard instruments. We wished to establish whether judgements of appropriateness that included patients' perspectives and contextual factors could lead to different conclusions when compared with commonly used instruments. To explore the predictive accuracy of these instruments.

Methods: The design was interviews of patients, audio recordings of the consultation and interviews of the doctors, in varied primary care practices in England. Participants were patients who were likely to discuss a medication issue. The outcome measures were judgements of appropriateness made by the researchers and by two instruments: the Prescribing Appropriateness Index and the Medication Appropriateness Index. Implications for the predictive accuracy of the measures was also investigated.

Results: From 35 cases there was agreement between the judges and the instruments in 22 cases, 16 were appropriate and 6 inappropriate. Of 10 cases classified as inappropriate by the instruments the judges thought four were appropriate. Of 18 cases classified as appropriate by the instruments, two were considered inappropriate by the judges. In seven cases the prescribing decisions could not be classified by the instruments because the decision was to not prescribe.

Conclusions: Current measures of appropriateness of prescribing depend predominantly on pharmacological criteria, and so do not represent cases that would be judged appropriate when including the patient's views and contextual factors. If most prescribing is appropriate then use of these measures may lead to more false negatives than real negatives. The instruments should be renamed as measures of 'pharmacological appropriateness' and are useful where the incidence of this type of inappropriate prescribing is relatively high.

Keywords: appropriateness, Medication Appropriateness Index, prescribing, prescribing appropriateness index, primary care

INTRODUCTION

Medicines have enormous capabilities to help and to harm, and form a substantial part of healthcare expenditure. For these reasons it is important that they are prescribed well and, ideally, that this is demonstrable. However there is very little literature that explores the nature of ideal prescribing – most of the literature refers to 'good' or 'appropriate' prescribing. Cribb and Barber (1) have argued that good prescribing is a balance of the technical qual-

Medication Appropriateness Index (MAI). Barber N & al. J Clin Pharm Ther 2005; 30: 533-9

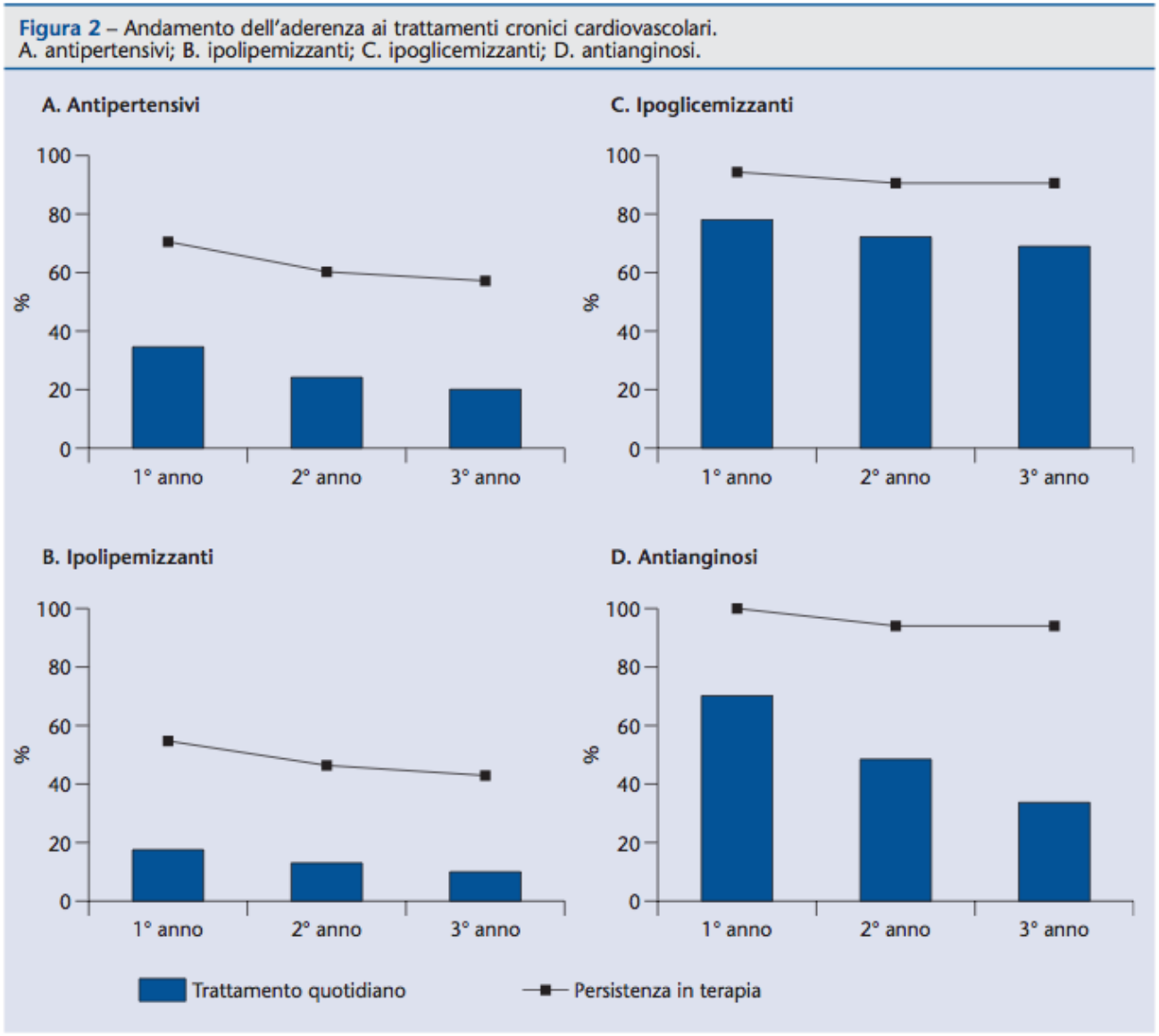
Polypharmacy: the prescription cascade

Table 1. Items in the Medication Appropriateness Index (MAI) and Prescribing Appropriateness Indicators (PAI). BNF refers to the British National Formulary

MAI	PAI
Is there an indication for the drug	The indication for the drug is recorded and upheld in the BNF
Is the medication effective for the condition	The reason for prescribing a drug of limited value is recorded and valid
Is the dosage correct	If the total daily dose is outside the range stated in the BNF, the prescriber gives a valid reason
Are the directions correct	If the dosing frequency is outside the range stated in the BNF, the prescriber gives a valid reason
Are the directions practical	A generic product is prescribed if one is available
Are there clinically significant drug–drug interactions	If a potentially hazardous drug–drug combination is prescribed, the prescriber shows knowledge of the hazard
Are there clinically significant drug–disease/condition interactions	Prescribing for hypertension adheres to the evidence-based guidelines in the BNF
Is the duration of therapy acceptable?	If the duration of therapy is outside the ranges stated in the BNF, the prescriber gives a valid reason
Is this drug the least expensive alternative compared to others of equal utility	Compared with alternative treatments in the same therapeutic class, which are just as safe and effective, the drug prescribed is either one of the cheapest or a valid reason is given for using an alternative
Is there unnecessary duplication with other drug (s)	

Medication Appropriateness Index (MAI). Barber N & al. J Clin Pharm Ther 2005; 30: 533-9

Polypharmacy: the prescription cascade



BIF 1-2005; AIFA: http://www.agenziafarmaco.gov.it/sites/default/files/bif050136.pdf

Aderenza alla terapia

- Basso rischio immediato per la salute del soggetto
- È assente una sintomatologia su cui la prescrizione abbia un effetto positivo rapidamente avvertibile
- Le prescrizioni determinano modifiche dello stile di vita
- Le prescrizioni devono di solito essere seguite a tempo indefinito
- **Vengono assunti più farmaci**

Bassa aderenza alla terapia

High Prevalence of Poor Quality Drug Prescribing in Older Individuals: A Nationwide Report From the Italian Medicines Agency (AIFA).

Onder G et al. J Gerontol A Biol Sci Med Sci. 2013 Aug 2

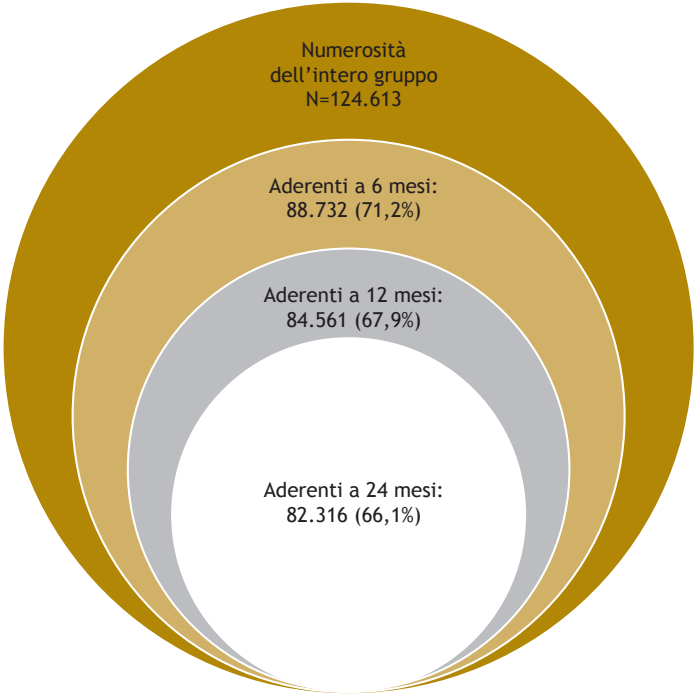
Tabella II. Prevalenza degli indicatori di qualità nella popolazione anziana italiana

Indicatori di qualità	Tutti i gruppi di età (≥ 65 anni) n=12,301,537 (%)	65-74 anni n=6,154,421 (%)	75-84 anni n=4,474,887 (%)	≥85 anni n=1,672,229 (%)
1. Politerapia				
• 5-9 farmaci	6,024,383 (49.0)	2,681,639 (43.6)	2,462,378 (55.0)	880,366 (52.6)
• ≥10 farmaci	1,389,591 (11.3)	529,506 (8.6)	629,043 (14.1)	231,042 (13.8)
2. Bassa aderenza al trattamento con farmaci antidepressivi*	201,290 (63.9)	83,110 (62.6)	82,623 (63.0)	35,557 (69.6)
3. Bassa aderenza al trattamento con farmaci anti-ipertensivi*	179,973 (46.4)	84,983 (45.2)	69,450 (47.2)	25,542 (56.1)
4. Bassa aderenza al trattamento con farmaci antidiabetici*	92,017 (63.0)	44,227 (63.0)	35,497 (64.7)	12,293 (70.1)
5. Bassa aderenza al trattamento con farmaci antiosteoporotici*	56,621 (52.4)	24,424 (48.7)	24,351 (53.4)	7,846 (64.0)

La prevalenza di depressione negli anziani è elevata ma c'è una bassa aderenza dovuta a diversi fattori (deficit sensoriali, cognitivi, funzionali, depressione, politerapie etc.)

Bassa aderenza alla terapia

- Grafico 1.22 -
Aderenza alla terapia nei pazienti in trattamento con farmaci per l'osteoporosi (nota 79)[1]



http://www.agenziafarmaco.gov.it/it/content/nota-79

1. La valutazione dell'aderenza a 24 mesi potrebbe essere sottostimata, essendo in quegli anni il periodo di trattamento massimo raccomandato pari a 18 mesi

Bassa aderenza alla terapia

High Prevalence of Poor Quality Drug Prescribing in Older Individuals: A Nationwide Report From the Italian Medicines Agency (AIFA).

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La scarsa aderenza riduce sostanzialmente l'efficacia del trattamento

Bassa aderenza alla terapia

Osteoporos Int (2013) 24:2639–2647
DOI 10.1007/s00198-013-2365-y

ORIGINAL ARTICLE

Association between refill compliance to oral bisphosphonate treatment, incident fractures, and health care costs—an analysis using national health databases

K. R. Olsen · C. Hansen · B. Abrahamsen

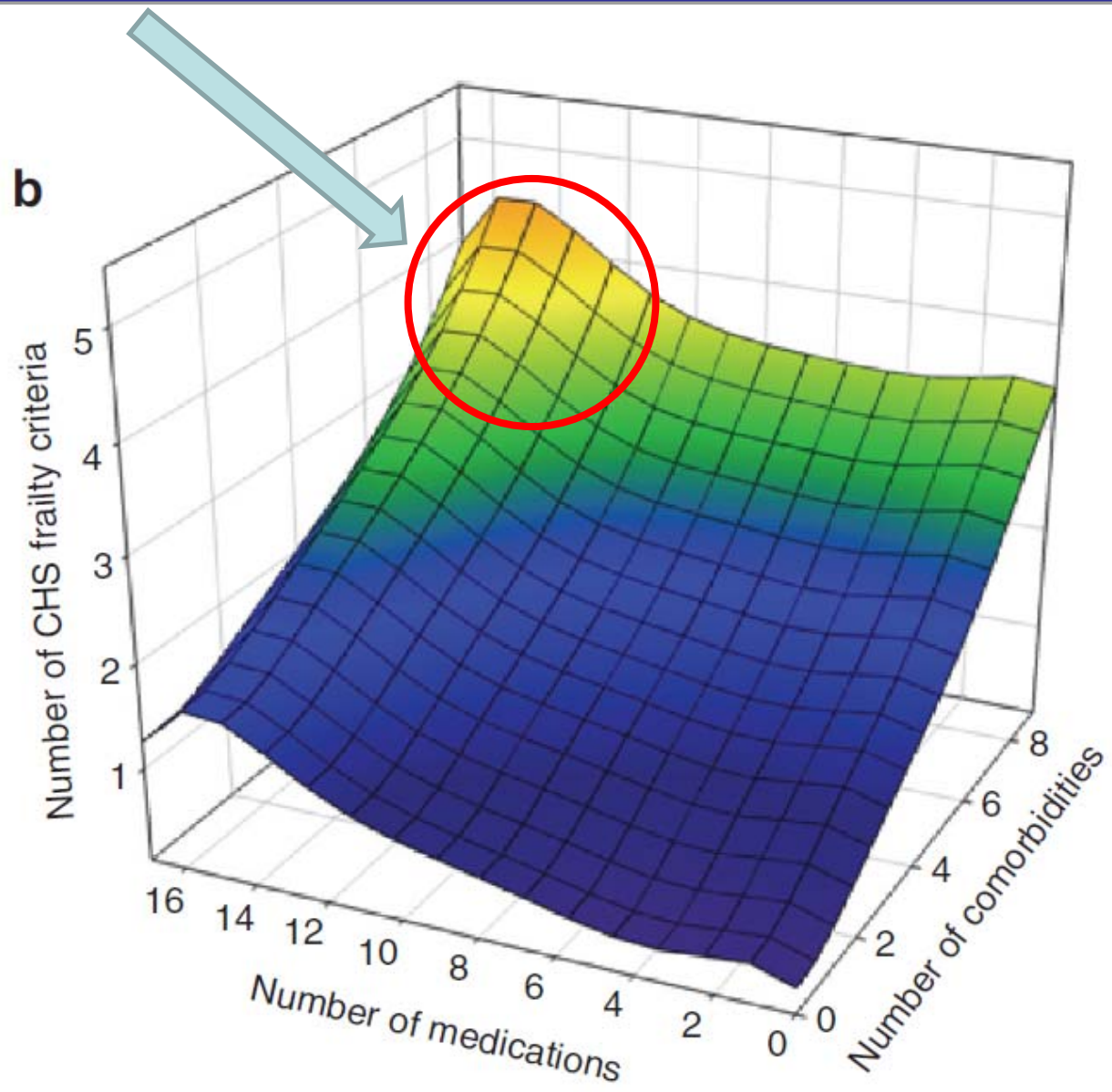
Table 1 Descriptive statistics: confounder variables at baseline, grouped by MPR category

N	MPR<0.5 13,397 (28 %)	0.5≤MPR<0.8 5,581 (12 %)	MPR≥0.8 28,198 (60 %)	*p*
Comorbidity				
Charlson Comorbidity Index	1.20	1.16	1.09	<0.01
Fractures at baseline				
Major	3,654 (27 %)	1,528 (27 %)	7,657 (27 %)	0.93
Hip	1,302(10 %)	521 (9 %)	2,539 (9 %)	0.06
Spine	847 (6 %)	341 (6 %)	1,513 (5 %)	<0.01
Forearm	1,625 (12 %)	697 (13 %)	3,745 (13 %)	<0.01
Humerus	811 (6 %)	331 (6 %)	1,667 (6 %)	0.85
Any	4,984 (37 %)	2,057 (37 %)	10,370 (37 %)	0.70
Socio-demographics				
Age	71	70	70	<0.01
Women	11,391 (85 %)	4,861 (87 %)	24,538 (87 %)	<0.01
Education level				
Only primary school	9,477 (71 %)	3,793 (68 %)	18,360 (65 %)	<0.01
Secondary school	2,409 (18 %)	1,089 (20 %)	5,987 (21 %)	<0.01
Minimum bachelor	1,511 (11 %)	6,999 (13 %)	3,851 (14 %)	<0.01
Income tertile				
Income 1. tertile	4,045 (30 %)	1,721 (31 %)	8,905 (32 %)	<0.05
Income 2. tertile	4,999 (37 %)	1,988 (36 %)	9,623 (34 %)	<0.01
Income 3. tertile	4,248 (32 %)	1,847 (33 %)	9,579 (34 %)	<0.01
Medication history				
Number of co-medications	7.4	7.3	6.9	<0.01

Categorical variables were tested by chi-sq test. The Kruskal–Wallis test was used for comparing Charlson index and age across the categories

La scarsa aderenza riduce l'efficacia del trattamento

The frailest people have BOTH most illnesses and most medicines



Deprescription

Dr. Philippe Pinel
physician & psychiatrist
(1745-1826)

"It is an art of no little importance to administer medicines properly: but, it is an art of much greater and more difficult acquisition to know when to suspend or altogether to omit them."

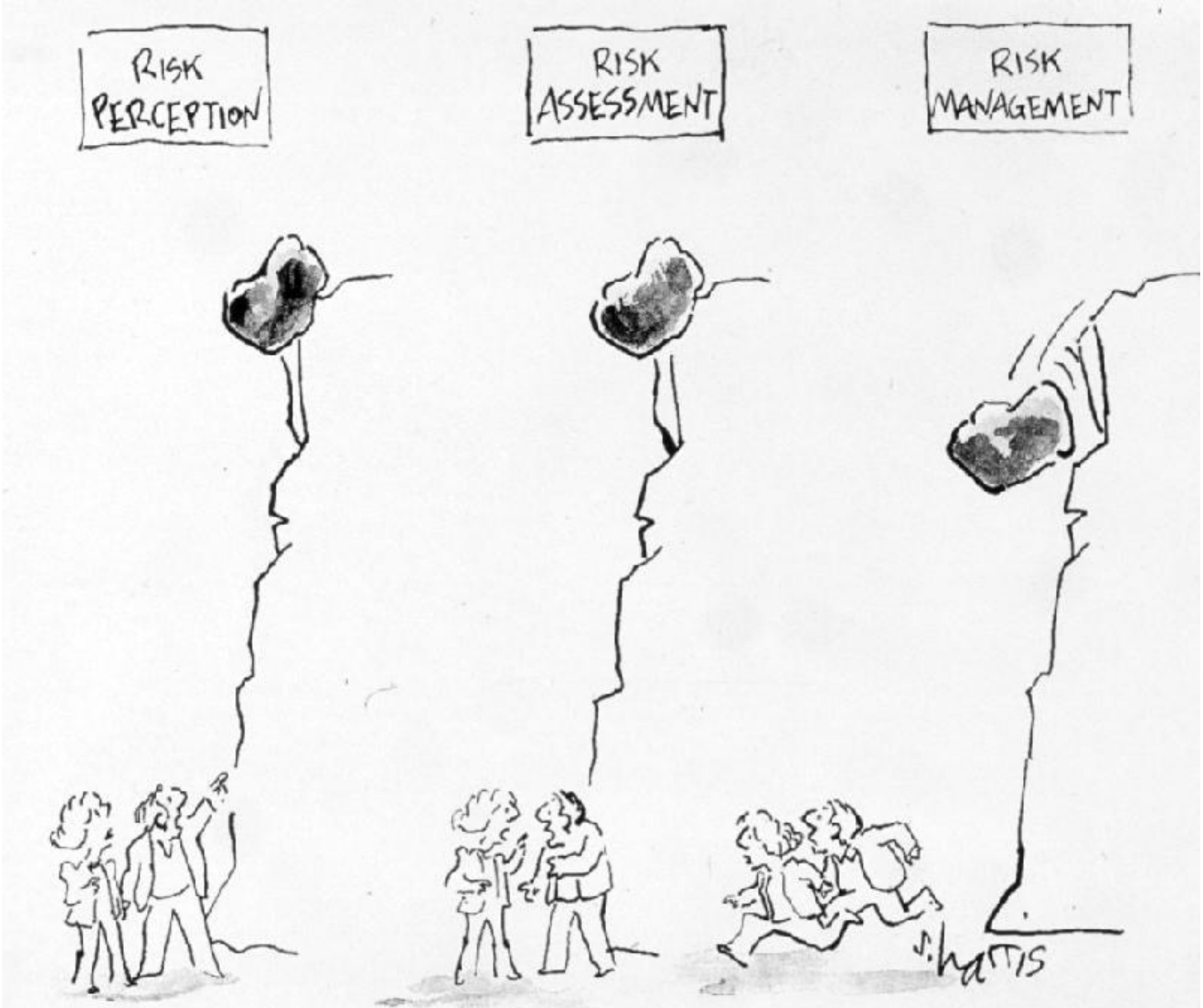
“The young physician starts life with 20 drugs for each disease, and the old physician ends life with one drug for 20 diseases. ”

William Osler,1891

EMA/FDA
evaluates
benefits/risks
for the population

Provider
evaluates
benefits/risks
for a patient

Patient
evaluates
benefits/risks
in terms of
personal values


RISK PERCEPTION
RISK ASSESSMENT
RISK MANAGEMENT
J. HATTIS

A framework for evaluating good prescribing.

Barber N Qual Saf Health Care 2004;13:450-454