Complex medication challenges : Where to start

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Conflict of interest

- I have no conflict of interest to declare

Objectives

1. Understand what is a complex patient;

2. Deprescribe drugs safely in elderly patients;

3. Apply a systematic approach in reviewing medications including: preference of the patient frailty scale, therapeutic objectives, life expectancy, time to have an effect and evaluation of the medications.

« This is a complex patient »

- What is a complex patient?

- Your definition

Complex care needs

- Multiple chronic conditions

- Medication-related problems

- Mental health issues

- Social vulnerability
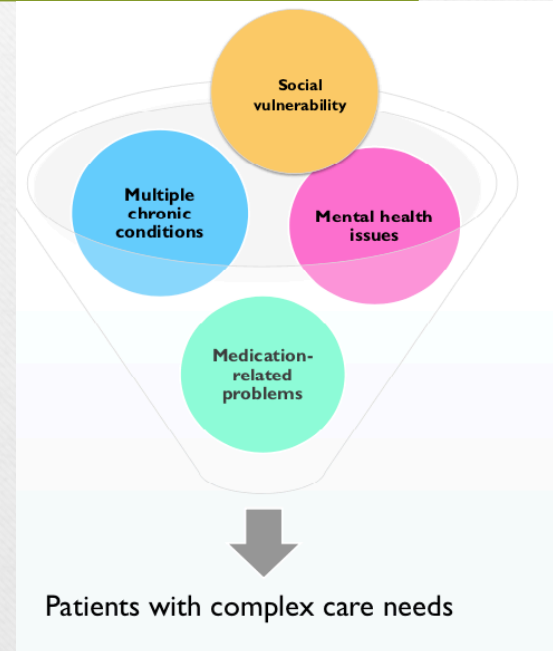
Pluye P et al. Characteristics of complex care needs and interventions suited for patients with such needs: A participatory scoping review.
http://reseau1quebec.ca/wpcontent/uploads/2014/06/McGill_PBRN_Reseau-1_posters.pdf

Table 1. The GERIATRIC 5Ms

GERIATRIC 5Ms*	DESCRIPTION
Mind	• Mentation • Dementia • Delirium • Depression
Mobility	• Impaired gait and balance • Fall injury prevention
Medications	• Polypharmacy, deprescribing • Optimal prescribing • Adverse medication effects and medication burden
Multicomplexity	• Multimorbidity • Complex biopsychosocial situations
Matters most	• Each individual's own meaningful health outcome goals and care preferences

*A French version was also developed by José Morais from McGill University in Montreal, Que: *mental, mobilité, médication, multi-pathologie, mes motivations.*
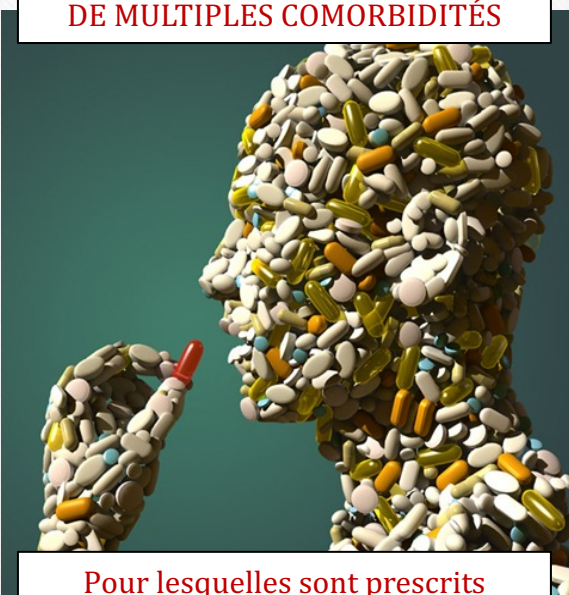Adapted from Molnar et al.[1]

PATIENTS ÂGÉS ET POLYPHARMACIE

DE MULTIPLES COMORBIDITÉS

Pour lesquelles sont prescrits
DE MULTIPLE MÉDICAMENTS

Boyd CM et al. JAMA 2005
Payne RA et al. Neur J Clin Pharmacol 2014
St Sauver JL et al. BMJ Open 2015
Steinman MA. JAMA 2016

LES CONSÉQUENCES

Interactions médicament-médicament
Interactions médicament-comorbidités

Syndromes gériatriques-médicament

Effets indésirables | Erreurs Médicamenteuses

ADHÉSION AUX MÉDICAMENTS ???

PRESCRIPTIONS POTENTIELLEMENT INAPPROPRIÉES

CASCADE MÉDICAMENTEUSE

CHARGE ANTICHOLINERGIQUE

DOSE NON AJUSTÉE SELON LA FONCTION RÉNALE OU LE POIDS

Confusion-delirium

Chutes

Hémorragies

Insuffisance rénale
Hypotension orthostatique

Décès | Visite urgence

Hospitalisations

Effets indésirables des médicaments

Adapté de: https://slideplayer.fr/slide/12363028/Lang

PRISE EN CHARGE D'UN PATIENT ÂGÉ (polymorbidité + polypharmacie)
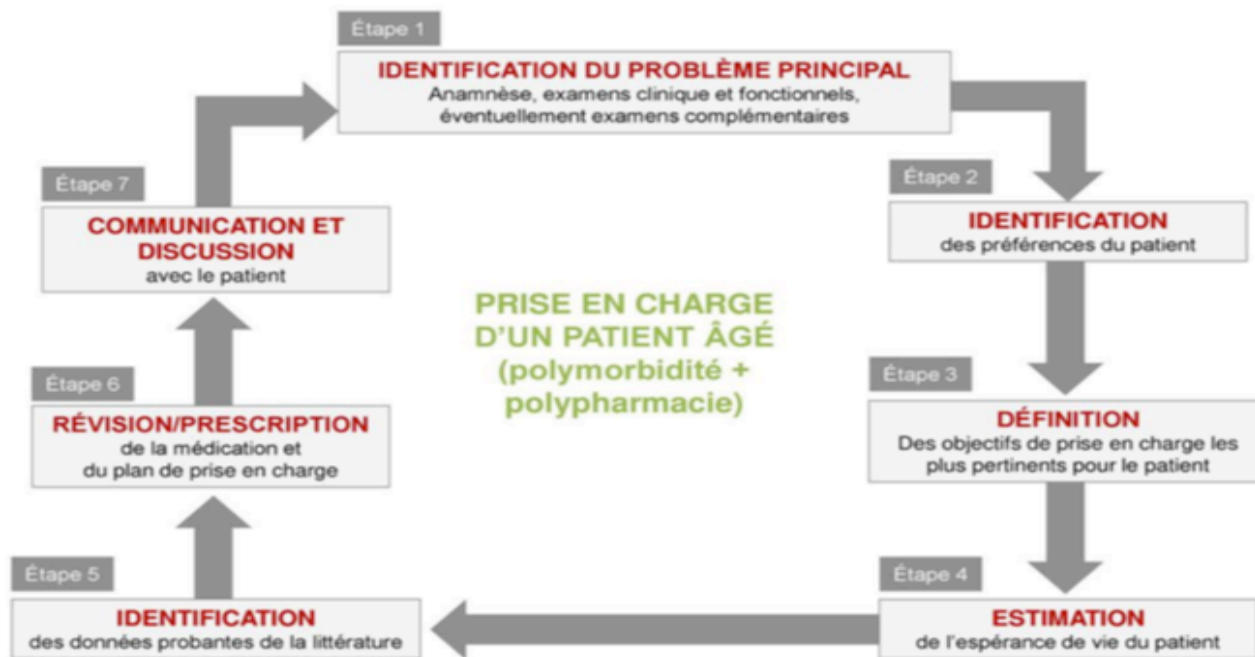
MODÈLE : *patient – évènements fonctionnels*

M. Giroux

M. Giroux, 90 years old, lives alone in his apartment . Today he presents with confusion and falls . His daughter says that he had 2 falls in the past 2 weeks and she notices that he is more confused today.

Daughter visits 3 times a week and helps with meals. His wife died 5 years ago.

Has a cane, CLSC 1 x/week for shower, decrease appetite as per daughter

PMH: Diabetes, hypertension, hypothyroidism, leg pain, depression, constipation, insomnia

NKDA, one glass of wine a week, ex-smoker

Medications

Delivered in vials

Take his own medications.

Does not know the name of his medications but knows the reasons. He says he takes too many medications.

His daughter sayts that she often finds some medications on the floor when she visits.

Name	Posologie	Reason
ECASA 80 mg	1 tab po 1 x/day	??
Sitagliptine 50 mg /Metformin 1 gm	1 tab po 2 x/day	Diabetes
Glyburide 5 mg	1 tab po daily prn	Diabetes
Telmisartan 80 mg + HCTZ 12,5 mg	1 tab po 1 x/day	Hypertension
Atorvastatin 40 mg	1 tab po 1 x/day	Cholesterol
Levothyroxine 0.075 mg	1 tab po 1 x/day	Hypothyroidism
Pantoprazole 40 mg	1 tab po 1 x/day	?? GI protection on ASA
Citalopram 20 mg	1 tab po 1x/day	Dépression
Acetaminophen 500 mg	1 tab po 4 x/day	Leg pain
Acetaminophen 500 mg /Methocarbamol 500 mg	1 tab po q 4-6 hrs prn	Leg pain : took 4 tabs/day for past 4 days
Lorazepam 1 mg	1 tab po q hs regular	Insomnia
Colace 100 mg	1 cap po 2 x/d	Constipation
Lax-a-day 17 gm	17 gm po daily	Constipation

Time	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
8h00	ECASA Sitagliptin Metformin Glyburide prn Telmisartan HCTZ Colace Acetaminophen Acetaminophen +Methocarbamol	ECASA Sitagliptin Metformin Glyburide prn Telmisartan HCTZ Colace Acetaminophen Acetaminophen +Methocarbamol	ECASA Sitagliptin Metformin Glyburide prn Telmisartan HCTZ Colace Acetaminophen Acetaminophen +Methocarbamol	ECASA Sitagliptin Metformin Glyburide prn Telmisartan HCTZ Colace Acetaminophen Acetaminophen +Methocarbamol	ECASA Sitagliptin Metformin Glyburide prn Telmisartan HCTZ Colace Acetaminophen Acetaminophen +Methocarbamol	ECASA Sitagliptin Metformin Glyburide prn Telmisartan HCTZ Colace Acetaminophen Acetaminophen +Methocarbamol	ECASA Sitagliptin Metformin Glyburide prn Telmisartan HCTZ Colace Acetaminophen Acetaminophen +Methocarbamol
12h00	Levothyroxine Acetaminophen Acetaminophen +Methocarbamol	Levothyroxine Acetaminophen Acetaminophen +Methocarbamol	Levothyroxine Acetaminophen Acetaminophen +Methocarbamol	Levothyroxine Acetaminophen Acetaminophen +Methocarbamol	Levothyroxine Acetaminophen Acetaminophen +Methocarbamol	Levothyroxine Acetaminophen Acetaminophen +Methocarbamol	Levothyroxine Acetaminophen Acetaminophen +Methocarbamol
17h00	Sitagliptin Metformin Acetaminophen Pantoprazole Atorvastatin Colace Lax-a-day Acetaminophen +Methocarbamol	Sitagliptin Metformin Acetaminophen Pantoprazole Atorvastatin Colace Lax-a-day Acetaminophen +Methocarbamol	Sitagliptin Metformin Acetaminophen Pantoprazole Atorvastatin Colace Lax-a-day Acetaminophen +Methocarbamol	Sitagliptin Metformin Acetaminophen Pantoprazole Atorvastatin Colace Lax-a-day Acetaminophen +Methocarbamol	Sitagliptin Metformin Acetaminophen Pantoprazole Atorvastatin Colace Lax-a-day Acetaminophen +Methocarbamol	Sitagliptin Metformin Acetaminophen Pantoprazole Atorvastatin Colace Lax-a-day Acetaminophen +Methocarbamol	Sitagliptin Metformin Acetaminophen Pantoprazole Atorvastatin Colace Lax-a-day Acetaminophen +Methocarbamol
22h00	Acetaminophen Citalopram Lorazapem Acetaminophen +Methocarbamol	Acetaminophen Citalopram Lorazapem Acetaminophen +Methocarbamol	Acetaminophen Citalopram Lorazapem Acetaminophen +Methocarbamol	Acetaminophen Citalopram Lorazapem Acetaminophen +Methocarbamol	Acetaminophen Citalopram Lorazapem Acetaminophen +Methocarbamol	Acetaminophen Citalopram Lorazapem Acetaminophen +Methocarbamol	Acetaminophen Citalopram Lorazapem Acetaminophen +Methocarbamol

Total # of medications/day : 16
Total # of doses/day : 28

Table 2
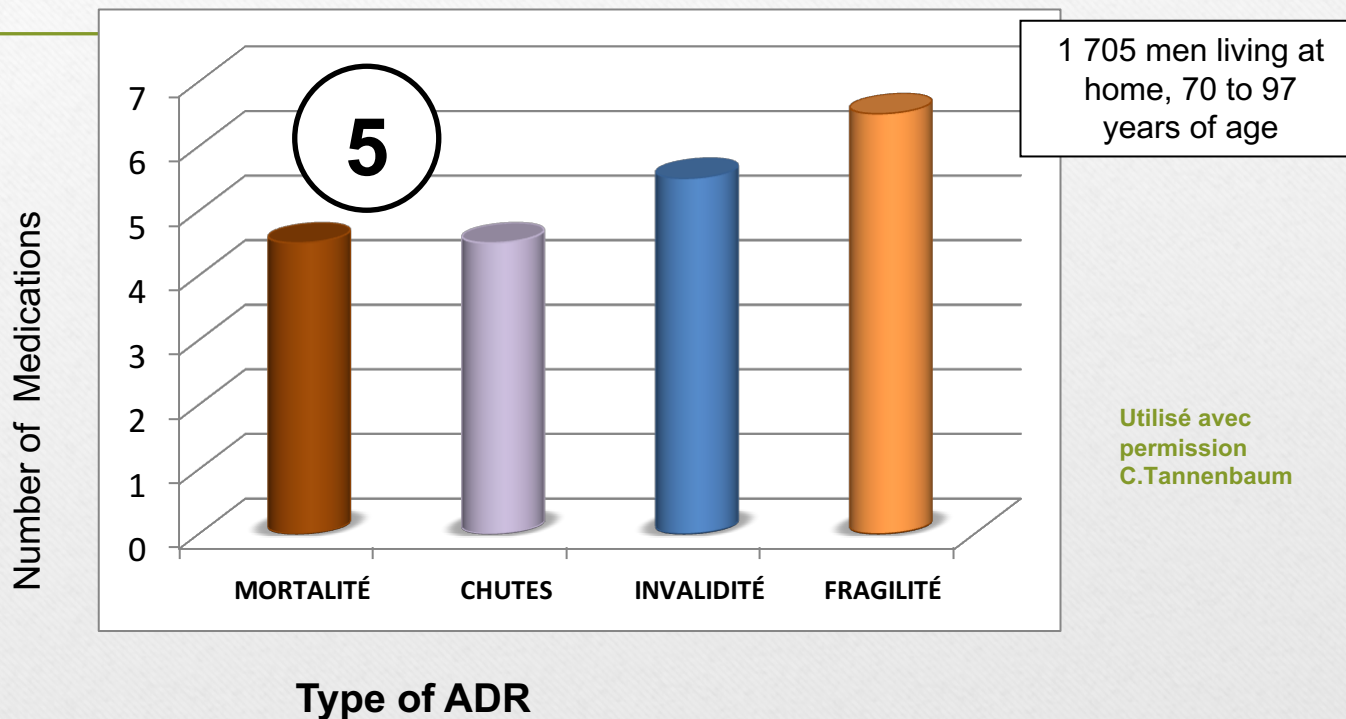**Risk factors of adverse drug events in the elderly**

Patient Factors	Health Care System Factors
Age >85 y	Multiple prescribers
Frailty	Multiple pharmacies
Low body weight or body mass index	No regular reviews of patient's medication list
Six or more chronic health conditions	Poor communication among providers
Memory problems	Prescription of complex medical regimens
Estimated CrCl <50 mL/min	
9 + medications (prescribed and over the counter)	
12 + doses of medications/d	
Prior ADE	

Number of medications and adverse drug reactions

1 705 men living at home, 70 to 97 years of age

Utilisé avec permission C.Tannenbaum

Type of ADR

2019-12-03

Gnjidic D et al. Polypharmacy cutoff and outcomes. J Clin Epidemiol 2012;65:989-995

Number of medications and risk of hospitalisation associated with medications
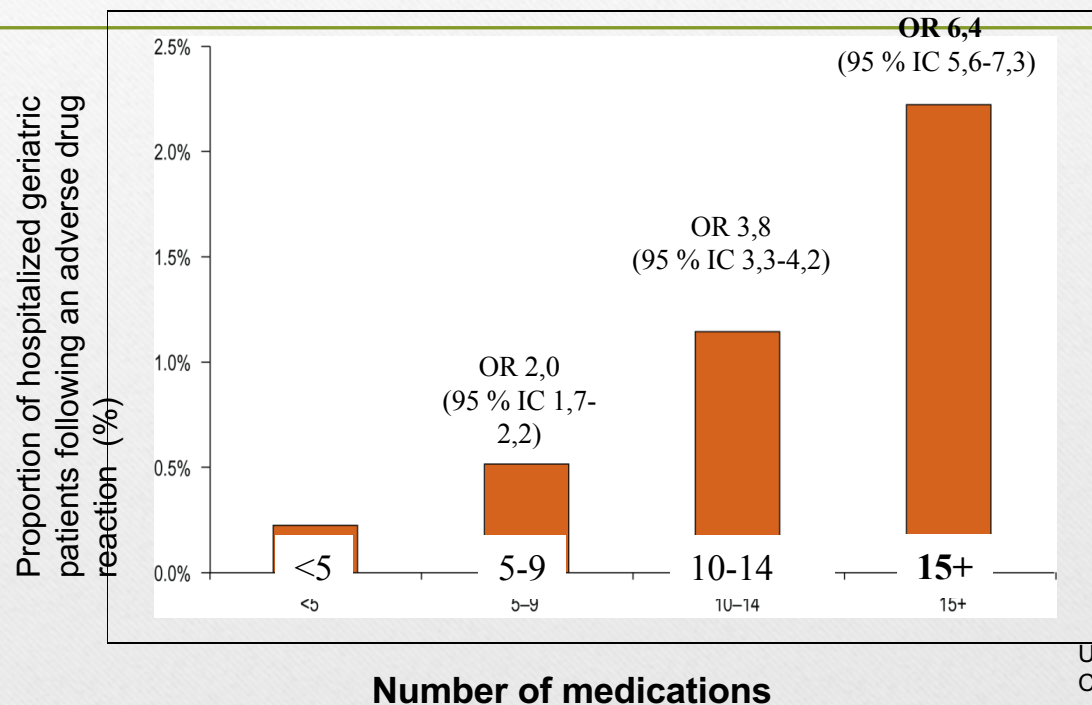
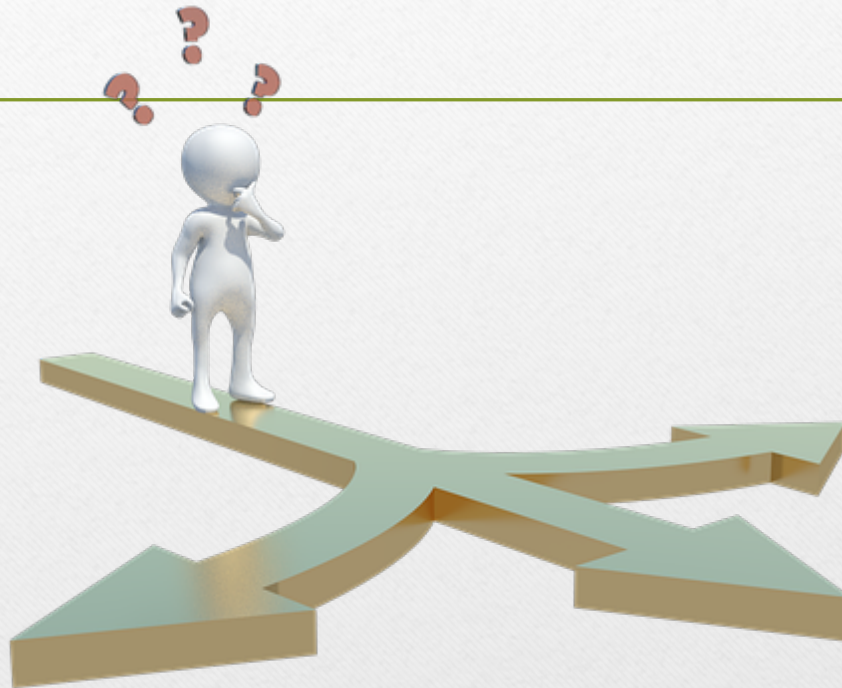*Canadian Institute of Health Information. Adverse drug reaction-related hospitalizations among seniors, 2006-2011. March 2013*

Utilisé avec permission C.Tannenbaum

Lab Tests

- Serum Creatinine = 130 umol/l (stable)

- Weight : 70 kg (Lost 2,5 kg in past 2 months)   Height : 1,70 m

- Na 135 mmol/L; K 4,2 mmol/L; TSH 10 m/UI

- ClCr = 40 ml/min

- HbA1$_c$ 7,1 %

- Blood glucose at home: This week between 4 et 7 mmol/l (according to his daughter)

- Blood pressure : 116/73 mm Hg; 113/84 mm Hg, 120/60 mm Hg

« How do we start »?

Match medical problems and medications

Medical problems	Medications
Falls **Orthostatic hypotension** **(Geriatric syndrome)**	Citalopram 20 mg 1x/d Sitagliptin/Metformin (50 mg/1000 mg) 1 CO BID Glyburide 5 mg 1x/d prn Telmisartan 80 mg + HCTZ 12,5 mg 1x/d Pantoprazole 40 mg 1x/d Atorvastatin 40 mg 1x/d
	Lorazepam 1 mg qhs regular Acétaminophen/Méthocarbamol (500 mg/400 mg) 1 CO q4-6H PRN (took 4 x/d x 4 days regular
Confusion **(Geriatric syndrome)**	Citalopram 20 mg 1x/j Glyburide 5 mg 1x/j prn Lorazepam / mg 1 CO at bedtime Acetaminophen/Methocarbamol (500 mg/400 mg) 1 CO q4-6H PRN Sitagliptin/Metformin (50 mg/1000 mg) 1 CO BID Glyburide 5 mg 1x/j prn
Diabetes	Sitagliptin/Metformin (50 mg/1000 mg) 1 CO BID Glyburide 5 mg 1x/d prn
Hypertension	Telmisartan 80 mg + HCTZ 12,5 mg 1x/d
Cholesterol	Atorvastatine 40 mg 1x/d
Hypothyroidism	Levothyroxine 0,075 mg 1x/j
Depression	Citalopram 20 mg 1x/j
Leg pain	Atorvastatine 40 mg 1x/j
Insomnia	Lorazepam 1 mg 1 x/at bedtime
Constipation	Colace 100 mg 1cap 2 x/j Lax-a-day 17 g po daily
Other problems	? ASA, ? Pantoprazole

Clinical Frailty Scale

1. Very fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2. Well – People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.

3. Managing well – People whose medical problems are well controlled, but are not regularly active beyond routine walking.

4. Vulnerable – While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up", and/or being tired during the day.

5. Mildly frail – These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6. Moderately frail – People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.

7. Severely frail – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8. Very severely frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. Terminally Ill – Approaching the end of life. This category applies to people with a life expectancy <6 months, who are not otherwise evidently frail.

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia,** recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia,** they cannot do personal care without help.

Figure 1. Clinical frailty scale. Adapted with permission from Moorhouse P, Rockwood K. Frailty and its quantitative evaluation (49).

https://www.dal.ca/site/gmr/our-tools/clinical-frailty-scale.html

Is Mr. Giroux

1. Fit
2. Vulnerable
3. Frail

Upper, middle, and lower quartiles for life expectancies for women (A) and men (B) on the basis of the US life tables
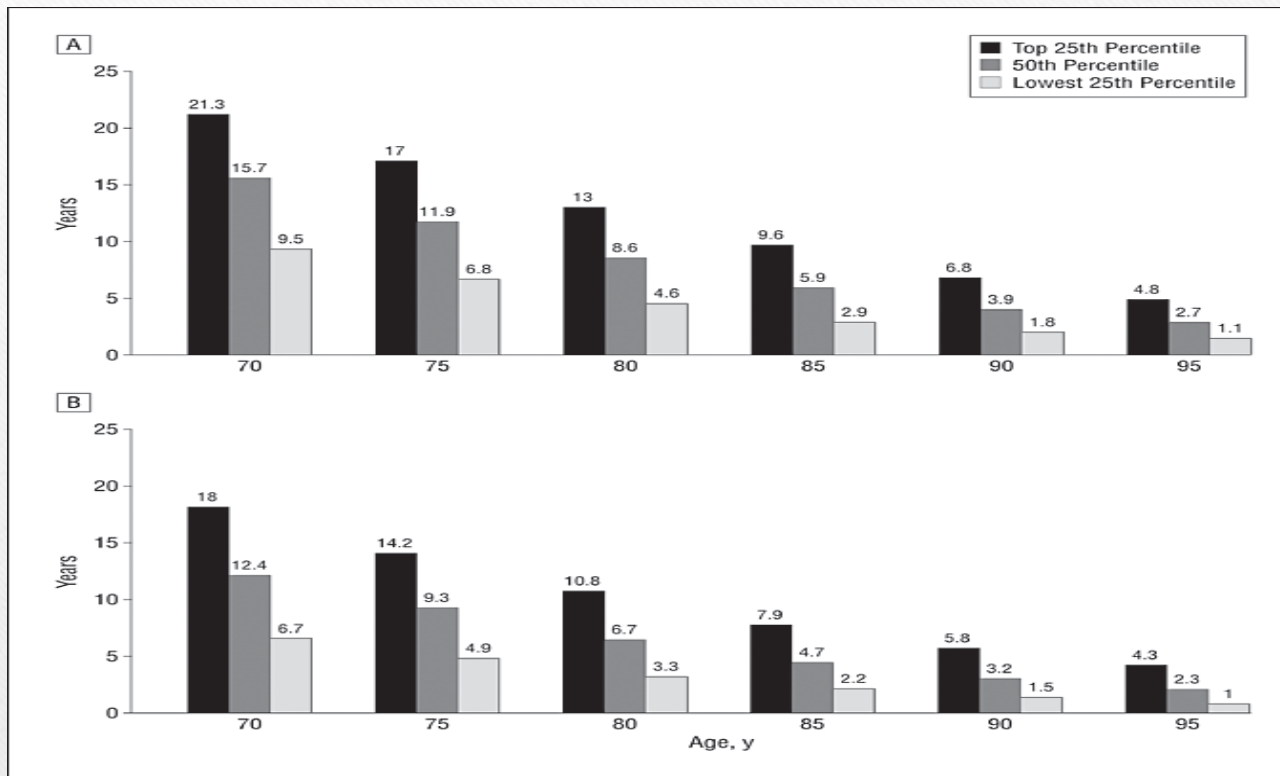
Holmes, H. M. et al. Arch Intern Med 2006;166:605-609.

ARCHIVES OF
INTERNAL MEDICINE

Remaining number of years of life according to age and functional status
Men

Green: Fit   **Red: Vulnerable**   **Orange: Frail**

Age	Fit (Green)	Vulnerable (Red)	Frail (Orange)
70 ans	18	12,4	6,7
75 ans	14,2	9,3	4,9
80 ans	10,8	6,7	3,3
85 ans	7,9	4,7	2,2
90 ans	5,8	3,2	1,5
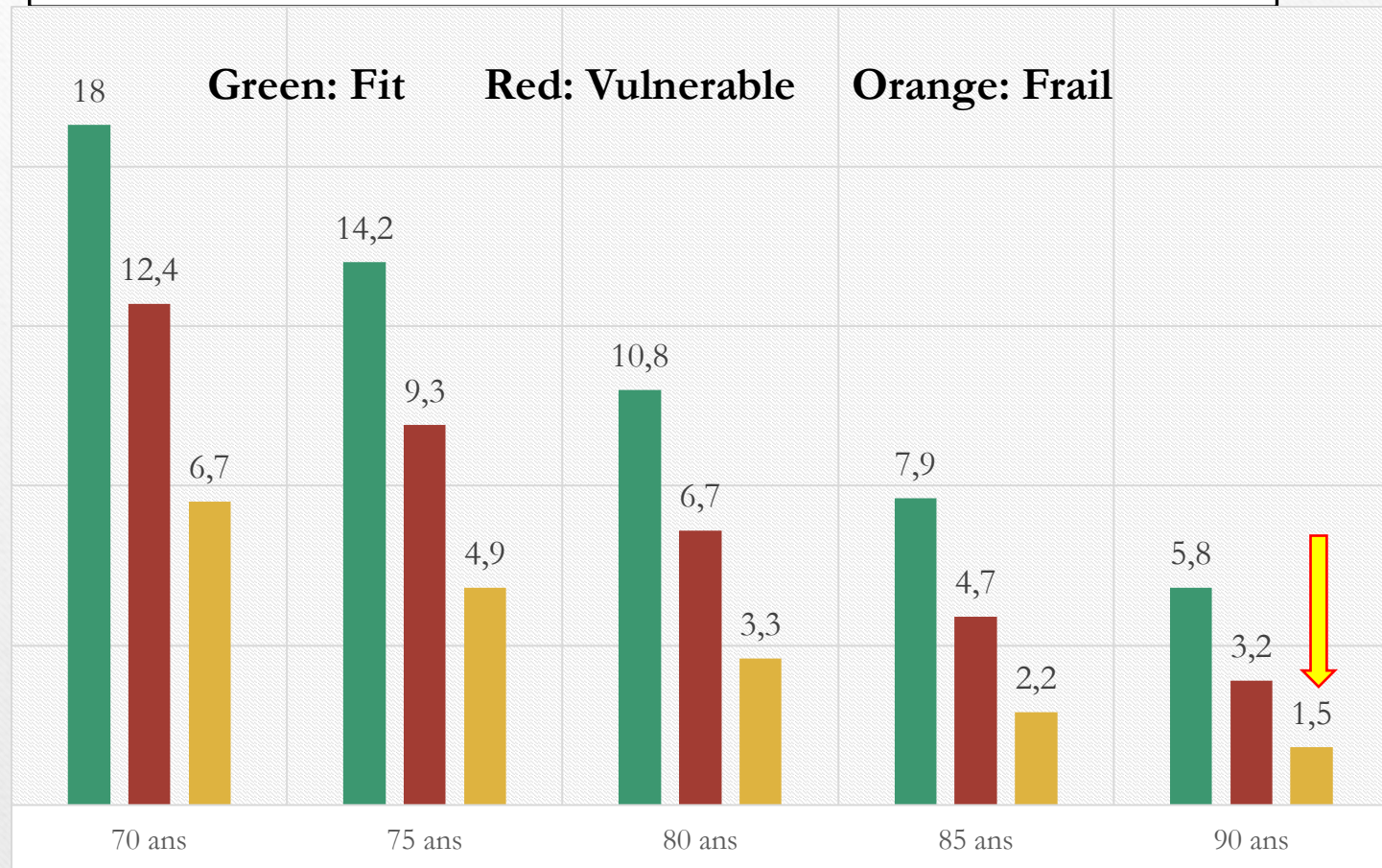
Walter & Covinsky 2001

Adapted from : https://slideplayer.fr/slide/12363028/Lang

Table 1

Glycemic targets in older people with diabetes

Status	Functionally independent	Functionally dependent	Frail and/or with dementia	End of life
Clinical Frailty Index[*]	1–3	4–5	6–8	9
A1C target *Low-risk hypoglycemia* (i.e. therapy does **not** include insulin or SU)	≤7.0%	<8.0%	<8.5%	A1C measurement not recommended. Avoid symptomatic hyperglycemia or any hypoglycemia.
A1C target *Higher-risk hypoglycemia* (i.e. therapy includes insulin or SU)		7.1–8.0%	7.1–8.5%	
CBGM				
Preprandial	4–7 mmol/L	5–8 mmol/L	6–9 mmol/L	Individualized
Postprandial	5–10 mmol/L	<12 mmol/L	<14 mmol/L	

A1C, glycated hemoglobin; *CBGM*, capillary blood glucose monitoring; *SU*, sulfonylurea.

[*] Clinical Frailty Score (1 - very fit to 9 - terminally ill). Please see Figure 1.

Meneilly G, et coll Can J Diabetes 2018;42:S283-95

Table 2

Guideline recommendations for key clinical outcomes for older people with diabetes from Diabetes Canada (DC), American Diabetes Association (ADA) and International Diabetes Federation (IDF)

Measure	ADA	DC	IDF
A1C	Healthy: <7.5% Complex/Intermediate: <8.0% Very Complex/Poor Health: <8.5%	Functionally independent: ≤ 7.0% Functionally dependent: 7.1–8.0% Frail and/or dementia: 7.1–8.5% End of life: A1C measurement not recommended. Avoid symptomatic hyperglycemia and any hypoglycemia.	Functionally independent: 7.0%–7.5% Functionally dependent: 7.0%–8.0% Sub-level frail: <8.5% Sub-level dementia: <8.5% End of life: avoid symptomatic hyperglycemia
Blood Pressure	Healthy: <140/80 mmHg Complex/Intermediate: <140/80 mmHg Very Complex/Poor Health: <150/90 mmHg	Functionally independent with life expectancy >10 years: <130/80 mmHg Functionally dependent, orthostasis or limited life expectancy: individualize BP targets	Functionally independent: <140/90 mmHg Functionally dependent: <140/90 mmHg Sub-level frail: <150/90 mmHg Sub-level dementia: <140/90 mmHg End of life: strict BP control may not be necessary
LDL-C	<1.8 mmol/L	<2.0 mmol/L or >50% reduction from baseline	<2.0 mmol/L and adjusted based on CV risk

Adapted from ADA (42) and IDF (40).

A1C, glycated hemoglobin; *BP*, blood pressure; *CV*, cardiovascular; *LDL-C*, low density lipoprotein cholesterol.

What would be the therapeutic objectives for M. Giroux Diabetes and Hypertension

- Frail elderly

- HbA1$_c$ = 7,1 %;

- Preprandial glucose: between 4 and 10 mmol/L

- Blood pressure: 116/93 mm Hg; 123/84 mm Hg, 120/60 mm Hg (? 0rthostatic hypotension)

- Patient is confused, had 2 falls

Therapeutic objectives
For M. Giroux

- HbA1$_c$ <8,5%;

- Preprandial glucose: 6-9 mmol/L

- Postprandial glucose: <14 mmol/L

- Blood pressure: <150/90 without orthostatic hypotension

Medication cascade

Drug 1 → Side effect → Drug 2 → Side effect

Medication cascade

Canagliflozin
- Day 0

Urinary inf/incontinence
- Day 60
- Day 75

Clavulin, tamsulosin
- Day 60
- Day 75

Falls, orthostatic hypotension
- Day 80
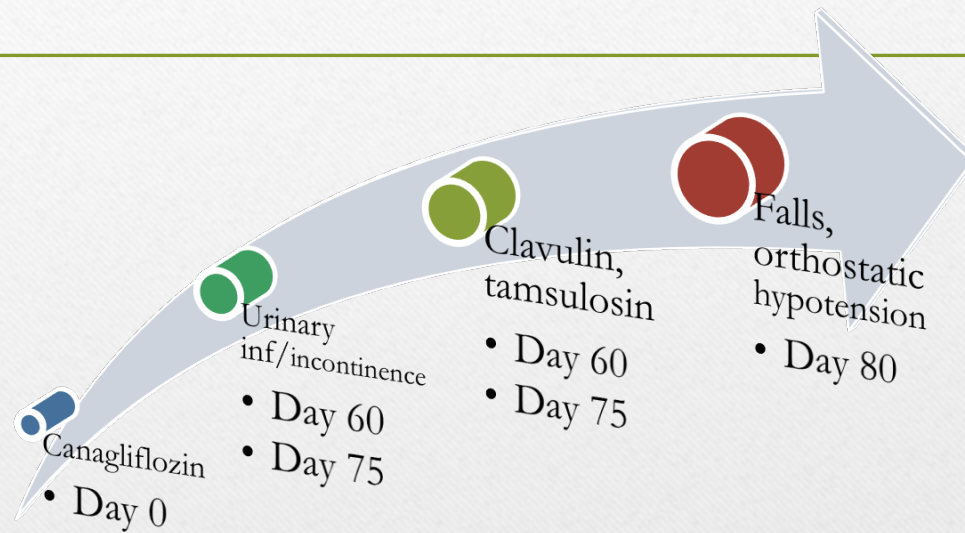
Potential medication cascade for M. Giroux

Atorvastatin → **Leg pain** → **Methocarbamol** → **Anticholinergic-confusion**

| Skeletal muscle relaxants	Most muscle relaxants poorly tolerated by older adults	Avoid	Moderate	Strong
Carisoprodol	because some have anticholinergic adverse effects,			
Chlorzoxazone	sedation, increased risk of fractures; effectiveness at			
Cyclobenzaprine	dosages tolerated by older adults questionable			
Metaxalone				
Methocarbamol				
Orphenadrine				

Genitourinary

Attention: Cyclobenzaprine (Flexeril)

Beers Criteria 2019. J Am Ger Society 2019;67:674–694.

Cyclobenzaprine (Flexeril)

Cyclobenzaprine

Amitriptyline

Chemical structure related to Amitriptyline

http://www.anticholinergicscales.es/
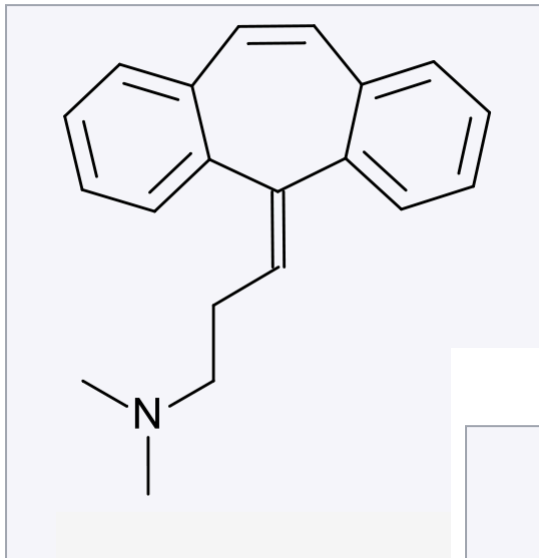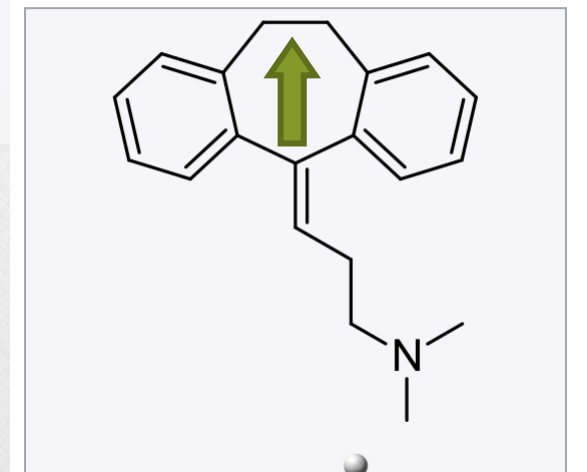
DBI Results (Note: This scale, unlike the above, considers drug dose prescribed in the calculation)

Medication		DBI
CITALOPRAM (20 mg)		0.67
LORAZEPAM (1 mg)		0.50
METHOCARBAMOL (2000 mg)		0.80
Results	HIGH RISK	1.97

Drug Burden Index

Automatic renewal

Discuss the following with the patient/guardian

An evidence-based consensus exists for using the drug for the indication given in its current dosing rate in this patient's age group and disability level, and the benefit outweighs all possible known adverse effects — Yes

No/Not sure

Indication seems valid and relevant in this patient's age group and disability level — No → STOP DRUG

Yes

Do the known possible adverse reactions of the drug outweigh possible benefit in old, disabled patients? — Yes → STOP DRUG

No

Any adverse symptoms or signs that may be related to the drug? — Yes → SHIFT TO ANOTHER DRUG

No

Is there another drug that may be superior to the one in question? — Yes → SHIFT TO ANOTHER DRUG

No

Can the dosing rate be reduced with no significant risk?

No → Continue with the same dosing rate

Yes → Reduce dose

Medical problems55	Medications	Therapeutic objectives	Solution
Falls	*Citalopram 20 mg 1x/d* *Sitagliptin/Metformin* *(50 mg/1000 mg) 1 CO BID* *Telmisartan 80 mg + HCTZ 12,5 mg 1x/j* *Glyburide 5 mg po 1x/j prn* *Pantoprazole 40 mg 1x/j* *Atorvastatin 40 mg 1x/j* *Lorazepam 1 mg q hs*	*Prevention of falls, fractures*	*See other problems*
Confusion	*Acétaminophen/Methocarbamol* *(500 mg/400 mg) 1 CO q4-6H PRN* *Glyburide 5 mg po 1x/d prn* *Citalopram 20 mg 1x/d* *Lorazepam 1 mg q hs*	*Prevent delirium*	*CAM* *Glucose level*
Diabetes	*Sitagliptin/Metformin(50 mg/1000 mg) 1 CO BID* *Glyburide 5 mg po 1x/j prn*	*Glycémie prépandiale 6 et 9 mmol/L* *Postprandiale <14 mmol/L* *HbA1c < 8,5%*	*CrCl = 40 ml/min* *Stop Glyburide* *Decrease dose of Sitagliptin to 50 mg daily* *Metformin 500 mg po bid*

Medical problems	Medications	Therapeutic objectives	Solution
HTN	Telmisartan 80 mg + HCTZ 12,5 mg 1x/j	<150/90 without orthostatic hypotension	Discontinue HCTZ BP: Lying and standing Could decrease dose of Telmisatan 40 mg po daily
Cholesterol	Atorvastatin 40 mg po daily (leg pain)	???	Discontinue atorvastastin Discontinue Acetaminophen + Methocarbamol
Diabetes	Sitagliptin/Metformin(50 mg/1000 mg) 1 CO BID Glyburide 5 mg po 1x/j prm	Glycémie prépandiale 6 et 9 mmol/L Postprandiale <14 mmol/L HbA1c < 8,5%	CrCl = 40 ml/min Stop Glyburide Decrease dose of Sitagliptin to 50 mg daily Metformin 500 mg po bid
Hypo thyroidism	Levothyroxine 0,075 mg po daily TSH 10 m/UI	TSH 0,5-5,5 m/UI	Not compliant Keept same dose Repeat in 6 weeks
?	ECASA 80 mg po daily	???	Discontinue
? GI	*Pantoprazole 40 mg po daily*	*???*	*Taper/discontinue*

2019-12-03

Medical problems	Medications	Therapeutic objectives	Solution
Depression	Citalopram 20 mg po q hs	Geriatric Depression Scale	Evaluation GDS Could start tapering
Insomnia	Lorazepam 1 mg po qhs	Prevention of falls, confusion etc	Discuss with patient Start tapering
Compliance			Use of Dispill Need to evaluate

Time	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
8h00	ECASA Sitagliptin Metformin Telmisartan Acetaminophen Levothyroxine	ECASA Sitagliptin Metformin Telmisartan Acetaminophen Levothyroxine	ECASA Sitagliptin Metformin Telmisartan Acetaminophen Levothyroxine	ECASA Sitagliptin Metformin Telmisartan Acetaminophen Levothyroxine	ECASA Sitagliptin Metformin Telmisartan Acetaminophen Levothyroxine	ECASA Sitagliptin Metformin Telmisartan Acetaminophen Levothyroxine	ECASA Sitagliptin Metformin Telmisartan Acetaminophen Levothyroxine
12h00	Acetaminophen	Acetaminophen	Acetaminophen	Acetaminophen	Acetaminophen	Acetaminophen	Acetaminophen
17h00	Metformin Acetaminophen Lax-a-day	Metformin Acetaminophen Lax-a-day	Metformin Acetaminophen Lax-a-day	Metformin Acetaminophen Lax-a-day	Metformin Acetaminophen Lax-a-day	Metformin Acetaminophen Lax-a-day	Metformin Acetaminophen Lax-a-day
22h00	Acetaminophen Citalopram Lorazapem	Acetaminophen Citalopram Lorazapem	Acetaminophen Citalopram Lorazapem	Acetaminophen Citalopram Lorazapem	Acetaminophen Citalopram Lorazapem	Acetaminophen Citalopram Lorazapem	Acetaminophen Citalopram Lorazapem

Total # of medications/day : 9   from 18
Total # of doses/day : 13 from 28

« Time-to-review expiry date »

- « Integrate the culture of deprescribing in the medical culture when a medication is started

- « Medication prescribe for life: should be replaced by « **Time to review- expiry date**

Reeves E et al. Eur J Inter Med 2017

Evaluation of medications

Define priorities with patient

List the medical problems

Evaluate life expectancy

Evaluate if patient is fit, vulnerable or frail

Define the therapeutic objectives for the patient and plan to follow up (efficacy and side eff

Find the best solution for the patient

Plan follow up for effectiveness and safety

Decrease barrier to adherence to treatment

Assure continuity of care: Nurse practitioner, pharmacist

Healthy Aging

Conclusion

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