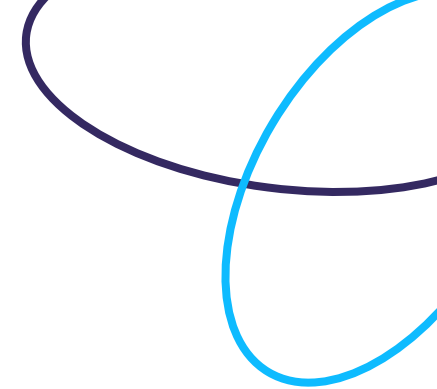


LMAP
2023

LIVERPOOL MASTERCLASS IN
ANTIVIRAL PHARMACOLOGY



Managing complex multimorbidity: From expectation to clinical practice

Dr Lauren Walker

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Marjorie



- Hypertension
- Atrial fibrillation
- Mitral valve replacement
- Dyslipidemia
- Depression
- Osteoporosis
- Type 2 diabetes mellitus
- COPD, 80 pack year passive smoking history, open wood fire
- 2 moderate COPD exacerbations in the past 12 months

Weight: 52 kg

Height: 149cm (BMI 23.4 kg/m²)

BP: 138/94 mmHg

Na: 129

Creatinine: 120 umol/L

eGFR: 50 ml/min

Creatinine clearance: 82 ml/min

Potassium: 5 mmol/L

HbA_{1c}: 58 mmol/mol

Total cholesterol: 6.2 mmol/L

(HDL 1.2 mmol/L, triglycerides 3.1 mmol/L,
LDL 5.0 mmol/L)

Medication:

1. Perindopril 5mg
2. Amlodipine 5mg
3. Atorvastatin 10 mg OD
4. Warfarin
5. Escitalopram 10 mg OD
6. Digoxin 125 micrograms OD
7. Alendronic acid 70 mg weekly
8. cholecalciferol 5600 UI/weekly
9. Metformin 1000 mg twice daily
10. Fluticasone propionate + salmeterol twice daily (Diskus inhaler)
11. Salbutamol (as needed)
12. Movicol oral powder TDS
13. Aspirin 75 mg OD
14. Temazepam 10mg nocte
15. Ferrous sulfate 200 mg tablets TDS
16. Lansoprazole 30 mg OD
17. Longtec 5mg MR BD
18. Carbocisteine 375 mg BD

BD, twice a day; BP, blood pressure; eGFR, estimated glomerular filtration rate; HbA_{1c}, haemoglobin A_{1c}; IV, intravenous; MR, modified release; OD, once daily; PO, oral administration; QDS, four times a day; TDS, three times a day

Patient journey

Age 50

Age 70

1993

1997

2003

2007

2011

2012

2013

Hypertension

COPD
Depression

Back pain
Type II diabetes
Osteoporosis
Vitamin D
deficiency

Polyarthrititis
Back pain
COPD exac

Atrial
fibrillation
Metallic MV
replacement
Cataract
removal

CKD
stage III
COPD exac

Depressive
episodes x3
COPD exac x2
AKI stage 1
Cellulitis
epistaxis

Multi-risk scoring tools - Marjorie

A multi-risk scoring tool is available from:

www.liverpool-multimorbidity.org*

Calculators included:

- Framingham 10-year CVD Risk Score
- HAS-BLED
- CHA₂DS₂-VASc
- MDRD GFR Equation
- Child-Turcotte-Pugh (CTP)
- FRAX

Liverpool Combined Comorbidities Calculator

Select Calculators	Complete Form
<input checked="" type="checkbox"/> Framingham 10-year CVD Risk Score	Age: <input type="text" value="70"/>
<input checked="" type="checkbox"/> HAS-BLED	Sex: <input checked="" type="radio"/> FEMALE <input type="radio"/> MALE
<input checked="" type="checkbox"/> CHA ₂ DS ₂ -VASc	Diabetes history: <input type="radio"/> NO <input checked="" type="radio"/> YES
<input type="checkbox"/> MDRD GFR Equation	Smoker: <input type="radio"/> NO <input checked="" type="radio"/> YES
<input checked="" type="checkbox"/> FRAX	Stroke/TIA/thromboembolism history: <input checked="" type="radio"/> NO <input type="radio"/> YES
<input type="checkbox"/> Child-Turcotte-Pugh (CTP)	Alcohol use (Units/week): <input checked="" type="radio"/> 0-2 units <input type="radio"/> 3-7 units <input type="radio"/> ≥8 units
<input type="button" value="Clear All"/>	Total cholesterol (Set Units: <input type="checkbox"/> mg/dL <input checked="" type="checkbox"/> mmol/L): <input type="text" value="6.200"/>
	HDL cholesterol (Set Units: <input type="checkbox"/> mg/dL <input checked="" type="checkbox"/> mmol/L): <input type="text" value="1.200"/>
	Systolic BP (mmHg): <input type="text" value="138"/>
	Blood pressure being treated with medicines: <input type="radio"/> NO <input checked="" type="radio"/> YES

FRAX® Fracture Risk Assessment Tool

BMI: 23.4

The ten year probability of fracture (%) without BMD:

Major osteoporotic: 12%

Hip Fracture: 4.0%

www.liverpool-multimorbidity.org/

Comorbidity Results Report

Date Produced: 15 August 2023

Tools Selected

- Framingham
- HAS-BLED
- CHA₂DS₂-VASc Score for Atrial Fibrillation Stroke Risk
- FRAX® Fracture Risk Assessment Tool

Report Detail

Framingham Risk Score for Cardiovascular Disease

21 Points

10-year risk of developing cardiovascular disease: **30%**

HAS-BLED Score for Major Bleeding Risk

2 Points

Risk was 4.1% in one validation study (Lip 2011) and 1.88 bleeds per 100 patient-years in another validation study (Pisters 2010).

Anticoagulation can be considered, however patient does have moderate risk for major bleeding (~2/100 patient-years).

CHA₂DS₂-VASc Score for Atrial Fibrillation Stroke Risk

4 Points

Stroke risk was 4.8% per year in >90,000 patients (the Swedish Atrial Fibrillation Cohort Study) and 6.7% risk of stroke/TIA/systemic embolism.

One recommendation suggests a 0 score for men or 1 score for women (no clinical risk factors) is "low" risk and may not require anticoagulation; a 1 score for men or 2 score for women is "low-moderate" risk and should consider antiplatelet or anticoagulation; and a score ≥2 for men or ≥3 for women is "moderate-high" risk and should otherwise

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ALT, alanine aminotransferase; **AP**, alkaline phosphatase; **AST**, aspartate transaminase; **CHA₂DS₂-VASc**, congestive heart failure, hypertension, age ≥75 (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), vascular disease, age 65 to 74, female; **Cr**, creatinine; **CVD**, cardiovascular disease; **HAS-BLED**, Hypertension, Abnormal liver/renal function, Stroke history, Bleeding history or predisposition, Labile INR, Elderly, Drug/alcohol usage; **INR**, international normalised ratio; **MDRD GFR**, Modification of Diet in Renal Disease study equation for estimating Glomerular Filtration Rate; **TIA**, transient ischemic attack

Prescribing by indication – age 70

R2 Overprescribing review: "...clinical indications must be routinely recorded at the point of prescribing"

Indication	Prescription	Problems/Solutions
CVD		
1.Hypertension 138/94	Perindopril 5mg Amlodipine 5mg	↑ ↑
2.Metallic mitral valve	Warfarin*	
3.Atrial Fibrillation	Digoxin 125 microg* Aspirin 75mg	Fatigue, BB Primary prevention
4. Dyslipidaemia	Atorvastatin 10mg	↑
CNS:		
Depression	Escitalopram 10mg OD* Temazepam 10mg nocte*	SSRI ↑bleeding, Na ACB* = 6
Respiratory:		
COPD	Fluticasone propionate + salmeterol twice daily (Diskus inh) Salbutamol (as needed) Carbocisteine 375 mg BD	LAMA+LABA X ICS? Or Trimbow? X Wrong dose, no cough
MSK:		
1. Osteoporosis	Alendronic acid	
2. Back pain	Longtec 5mg BD*	Drug holiday
Anaemia?	Ferrous sulfate 200mg TDS	Check ferritin
Constipation	Movicol	osmotic needs stimulant
Type 2 DM HbA_{1c} 58	Metformin 1g BD*	Add DPP4 (linagliptin liver exc)
CKD III – eGFR 50 ml/min		



10 years later....

Patient journey

2013
Age 70

2017

2018

2019

2020

2021

2022

2023
Age 80

Fall
NOF

Polyarthritis
Back pain
COPD exac x3
Bladder
instability

HFrEF

Constipation
Falls
Postural
hypotension
Moderate frailty

Pneumonia
Dizziness "off
legs"
TIA
fluid overload

Ischaemic
foot,
foot ulcer
Depressive
episodes x3
Arm
haematoma
Faecal impaction
Immobile,
housebound - care
home
Severe frailty

? End of life

Multi-risk scoring

www.liverpool-multimorbidity.org*

Risk scores are largely unchanged a decade later but the *patient* is radically changed

Major increased risk is for osteoporotic fracture


FRAX® Fracture Risk Assessment Tool

BMI: 21.9

The ten year probability of fracture (%) without BMD:

Major osteoporotic: 31%

Hip Fracture: 18%

www.liverpool-multimorbidity.org/ **Comorbidity Results Report** 

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CHA₂DS₂-VASc Score for Atrial Fibrillation Stroke Risk

6 Points

Stroke risk was 9.7% per year in >90,000 patients (the Swedish Atrial Fibrillation Cohort Study) and 13.6% risk of stroke/TIA/systemic embolism.

One recommendation suggests a 0 score for men or 1 score for women (no clinical risk factors) is "low" risk and may not require anticoagulation; a 1 score for men or 2 score for women is "low-moderate" risk and should consider antiplatelet or anticoagulation; and a score ≥ 2 for men or ≥ 3 for women is "moderate-high" risk and should otherwise

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Multi-risk Scoring Tool. Available at: <http://www.liverpool-multimorbidity.org/>. [accessed August 2023].



Prescribing by indication – age 80

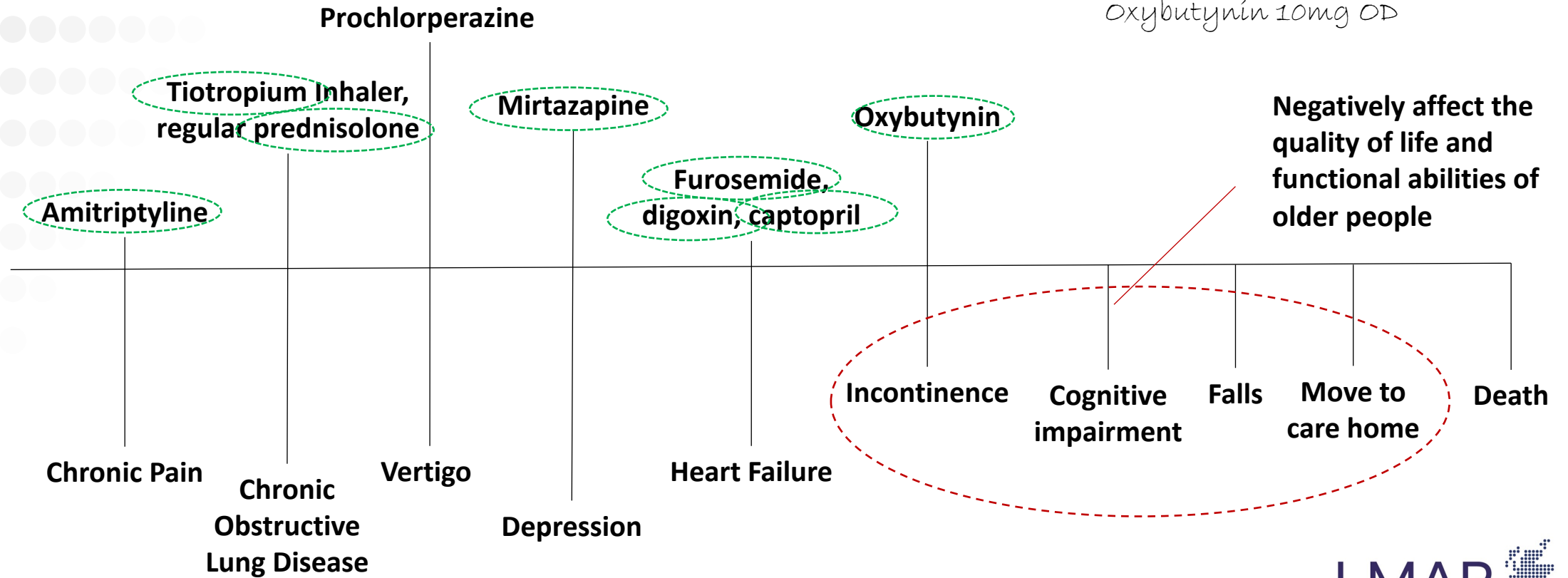
R2 Overprescribing review: "...clinical indications must be routinely recorded at the point of prescribing"

Indication	Prescription	Problems/Solutions
CVD 1.Hypertension 110/60	Perindopril 10mg Amlodipine 5mg	X CCB, wean down ACEi
2.Metallic MV 3.Atrial Fibrillation, TIA	Warfarin* Bisoprolol 5mg OD	Wean down
4.HFrEF	Bumetanide 1mg OD, spironolactone 25mg Dapagliflozin 10mg OD Atorvastatin 20mg OD	?stop
5.dyslipidaemia		
CNS: Depression	Escitalopram 10mg OD* Temazepam 10mg*	Support to discontinue if ineffective
Respiratory: COPD	Trimbow Salbutamol (as needed)	
Bladder Instability	Oxybutynin***	X or Switch to mirabegron
MSK: 1. Osteoporosis #NOF 2. Back pain	Longtec 5mg BD* Amitriptyline 50 mg daily*** Gabapentin 300mg TDS	Support to discontinue ACB = 10
Constipation	Movicol	
Type 2 DM HbA_{1c} 46	Metformin* 1g BD, linagliptin	Reduce metformin dose, X linagliptin
CKD III – eGFR 40 ml/min		

Accumulation of medicines risks

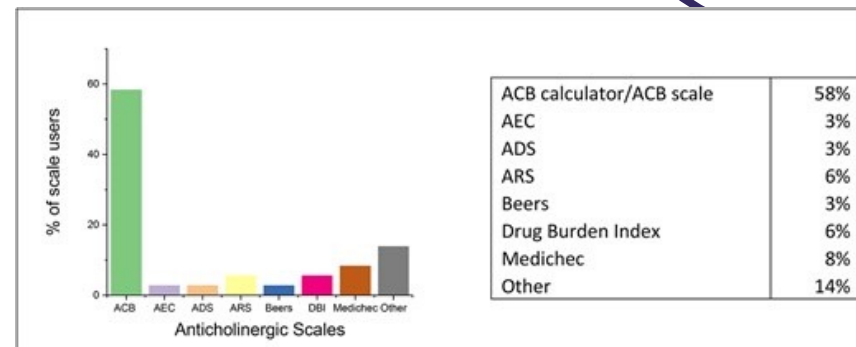
Amitriptyline 50mg nocte
Trimbow inh, tiotropium inh
Prednisolone 30mg 7/7 reducing
Mirtazapine 30mg OD
Furosemide 40mg BD
Digoxin 125 micrograms OD
Captopril 25mg TDS
Oxybutynin 10mg OD

Escalating anticholinergic burden across the life course



age ↑; kidney function ↓; muscle mass ↓; unsteady; frail

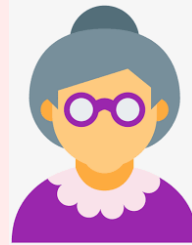
PLWH with high ACB performed worse on tests of learning and executive function compared with HIV- controls with high ACB



- <http://www.acbcalc.com/> (multiple tools, no gold standard)
- score ≥ 3 higher risk of confusion, falls, delirium and death (>65's)
- Every additional ACB point increases risk of death by 26%
- ACB3 **amitriptyline, chlorphenamine, olanzapine, oxybutynin, paroxetine, quetiapine**
- Common – prednisolone, furosemide, anti-histamines, tricyclics
- Stop, dose reduce, exchange: quetiapine (3) -> risperidone (1) in AD, oxybutynin (3) -> mirabegron (0)
- Most computerised prescribing support tools are **not integrated into clinical workflows.**

How might we predict this better and intervene earlier using existing information?

Drugs to treat symptoms



Salbutamol Inh

Asthma

GTN spray

Angina

Cholesterol disorder

High BP

Heart attack

Furosemide

Heart failure

Oxybutynin

Incontinence

Mini stroke

Bumetanide Inh

age ↑; kidney function ↓; muscle mass ↓; unsteady; frail

Many hidden factors influence decision to move from preventative to symptomatic treatment

Simvastatin
Amlodipine

Aspirin,
Bisoprolol,
Ramipril

Dapagliflozin Apixaban

Drugs to prevent disease



Hospitalisation/transition of care

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Thank you!