10° WORKSHOP NAZIONALE CISAI

MILANO

PREVENZIONE E GESTIONE DELLE CO-MORBIDITÀ ASSOCIATE ALL'INFEZIONE DA HIV

PRESIDENTI
PAOLO BONFANTI
ANTONIO DI BIAGIO

30 SETTEMBRE
1 OTTOBRE
2021

CISAI

FONDAZIONE ASIA

Ottimizzazione della terapia antiretrovirale negli anziani

Andrea Calcagno
Università di Torino

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Potenziale conflitto d'interessi da dichiarare

Tipo di affiliazione o supporto finanziario	Sponsor
Supporto alla Ricerca	Gilead, ViiV
Onorario come Relatore e Consulenze occasionali	Gilead, Janssen-Cilag, Insmed, MSD, ViiV

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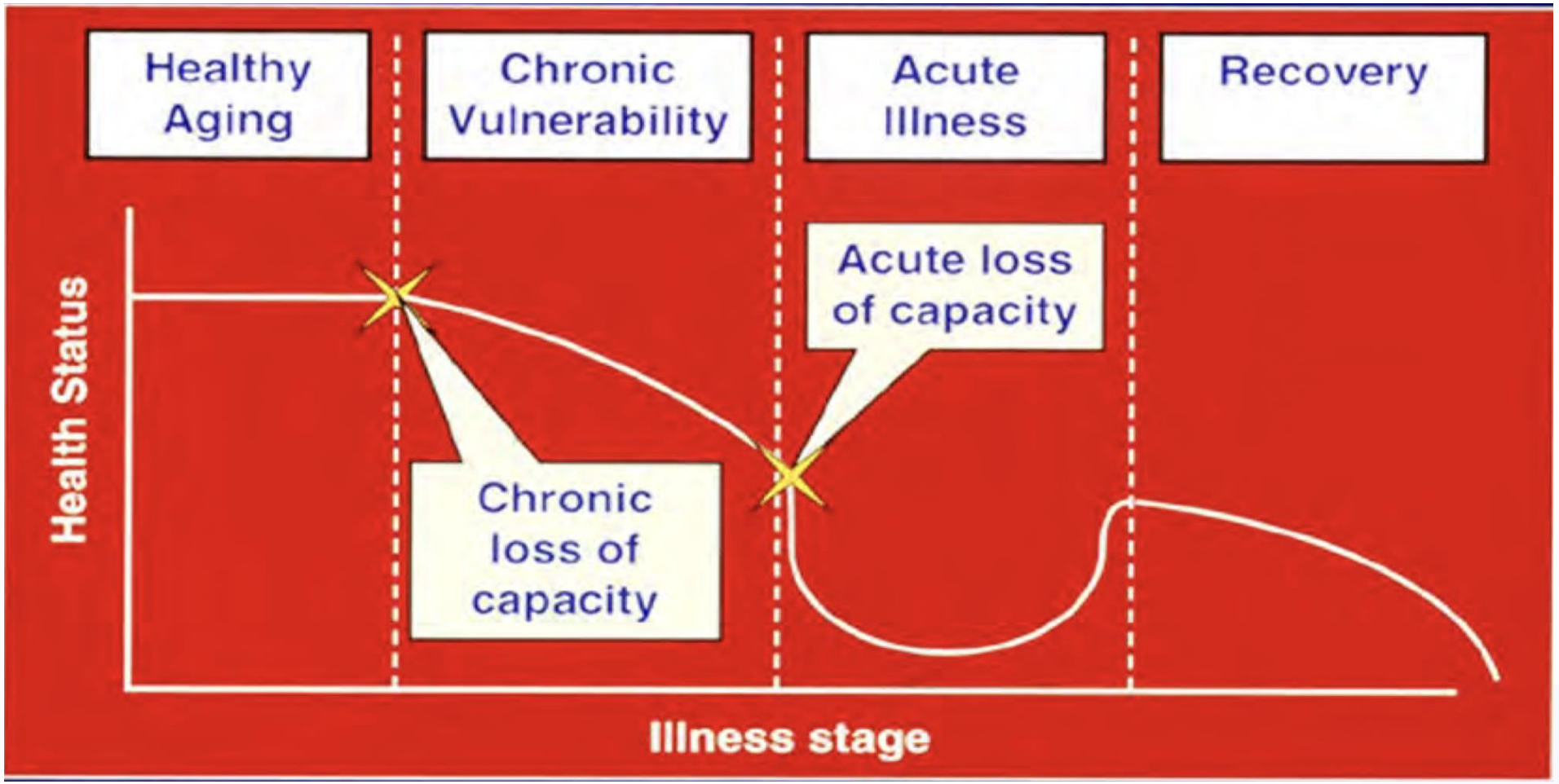

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HIV Outcomes Beyond Viral Suppression 2

Patient-reported outcomes to enhance person-centred HIV care

Meaghan Kall, Fabienne Marcellin, Richard Harding, Jeffrey V Lazarus, Patrizia Carrieri

Quality of life has been proposed as the fourth 90 to complement the UNAIDS 90-90-90 targets to monitor the global HIV response, highlighting a need to address the holistic needs of people living with HIV beyond viral suppression. This proposal has instigated a wider discussion about the use of patient-reported outcomes (PROs) to improve the treatment and care of an ageing HIV population with increasing comorbidities and a disproportionate burden of social problems. PROs can provide a first-hand assessment of the impact of HIV treatment and care on patients' quality of life, including symptoms. The field of PRO measures is rapidly expanding but still no gold standard exists, raising concerns about tool selection. Challenges also remain in the collection, interpretation, and use of PRO data to improve the performance of the health system. An emerging concern is how to adapt PROs to different sociocultural and geographical settings.

Lancet HIV 2020; 7: e59–68

Published Online
November 24, 2019
https://doi.org/10.1016/S2352-3018(19)30345-5

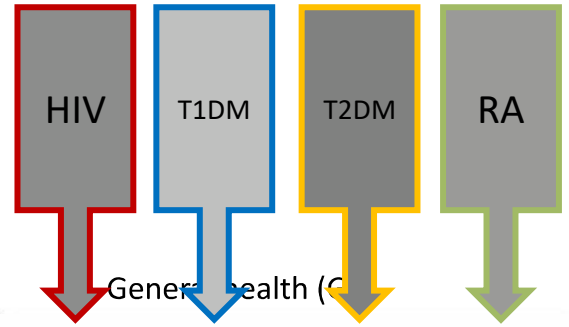
This is the second in a Series of three papers on HIV outcomes beyond viral suppression

HIV/STI Department, National Infection Service, Public Health

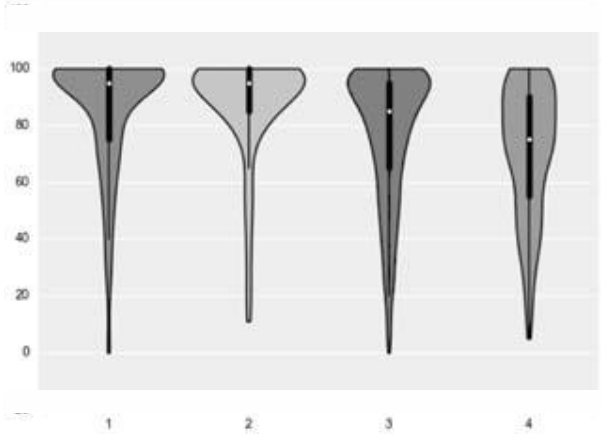
Key messages

- Patient-reported outcomes (PROs) provide vital information about a patient's first-hand account of their experiences that cannot be directly measured and provides a more holistic view of their health and wellbeing
- PROs can be used to instigate and support interventions at all levels (ie, clinical, institutional, and population) to ensure optimal HIV care and prevent ill health
- Recent technological advances have made PROs more accessible to patients and investigators, streamlining data collection and analysis (ie, with electronic PROs and linkage to medical records)
- Further research is needed to show the utility of PROs in the field of HIV, making a clear link between improvements in PROs to improvements in health and clinical care
- New PROs need to be developed and existing PROs cross-culturally adapted to populations with special attention to children and adolescents, the elderly, and settings in which key populations are highly stigmatised or criminalised
- Patient involvement in the development of PROs is vital to ensure their usability and acceptability in the population of interest

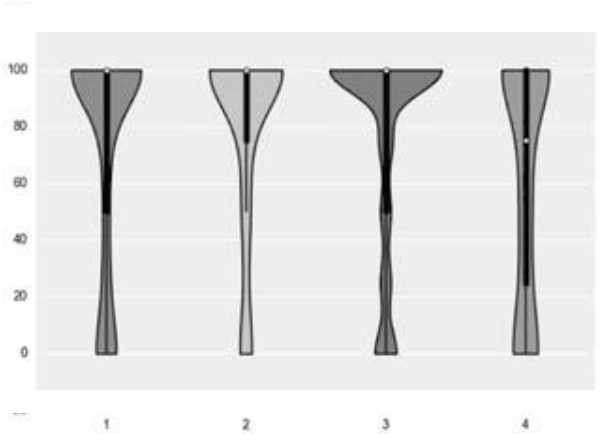
Global Health in PLWH



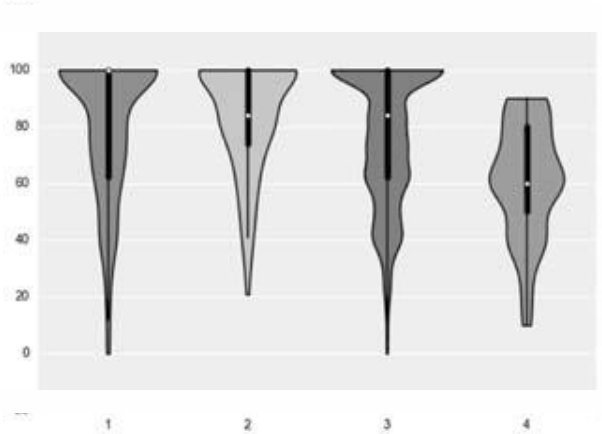
Physical functioning (PF)



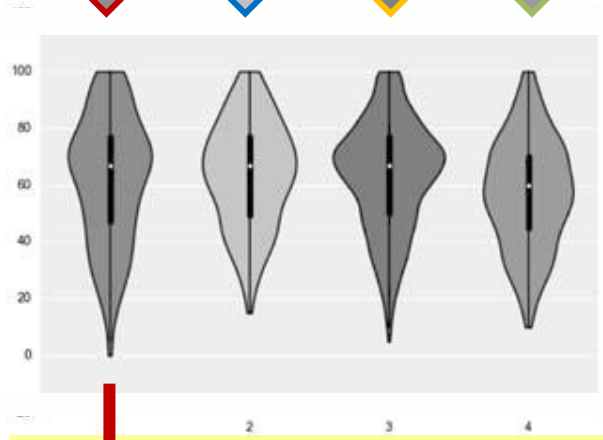
Role - physical (RP)



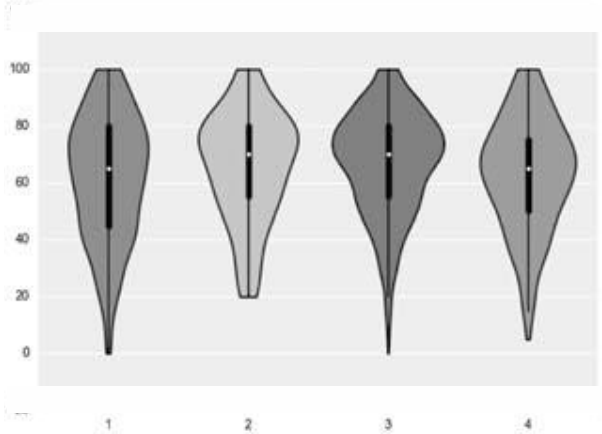
Bodily pain (BP)



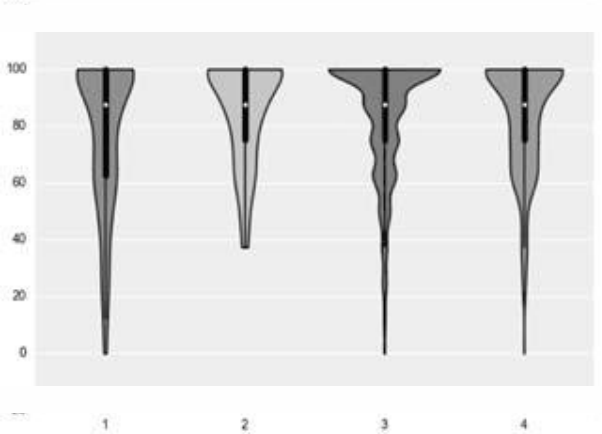
General health (G



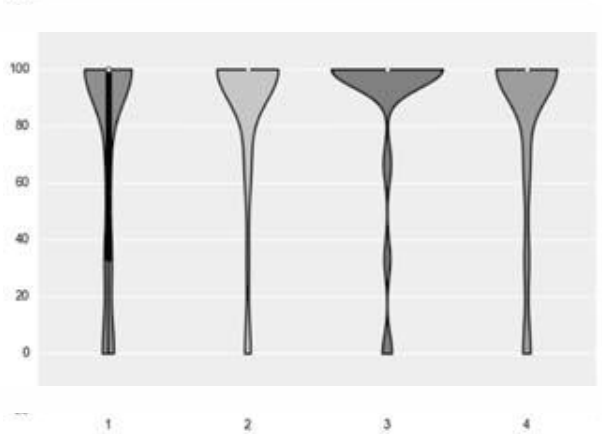
Vitality (VT)



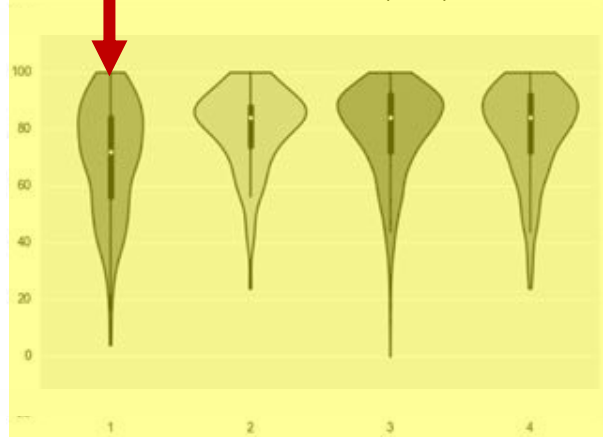
Social functioning (SF)



Role - emotional (RE)



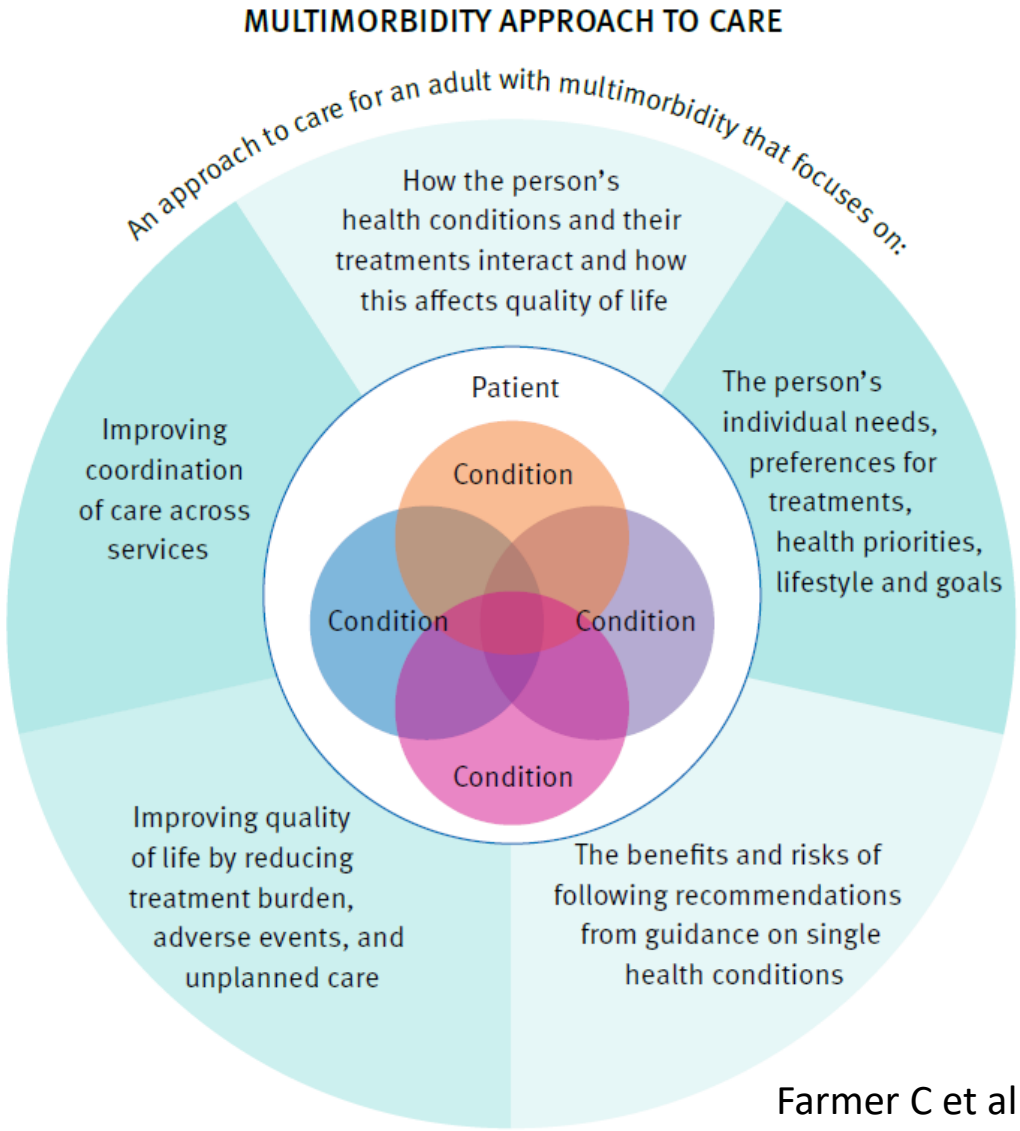
Mental health (MH)



Engelhard EAN, et al. AIDS 2018

MM

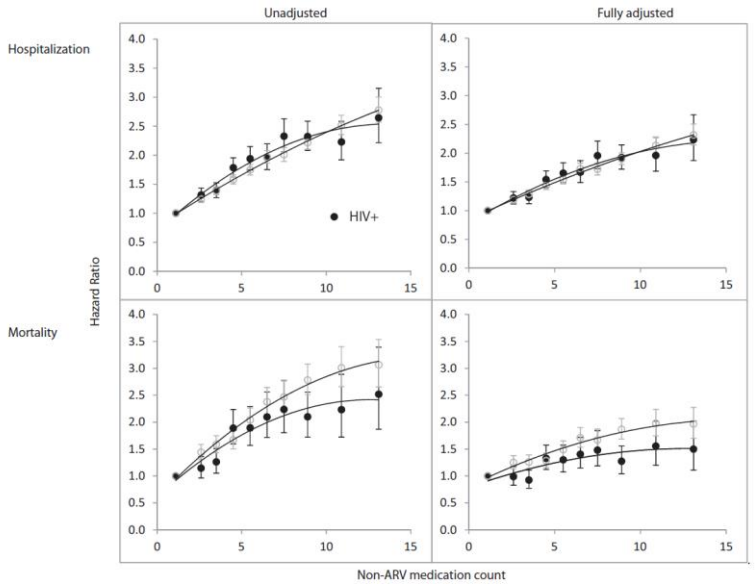
Clinical assessment and management of multimorbidity: summary of NICE guidance



Farmer C et al BMJ 2016

PP

Non-HIV polypharmacy and adverse health outcomes



- HIV infected
- HIV uninfected

Association between increased number non-HIV medications and increased risk for **hospitalization** or **mortality** for both PLWH and uninfected individuals.

Justice AC. AIDS 2018

Variable	Falls (+) N=643	No Falls (-) N=1565	Unadjusted p-value	p-value	Adjusted OR (95% CI)
Age (mean ±SD)	59.0 (58.5–59.5)	57.5 (57.2–57.8)	<0.0001	**0.0008**	1.03 (1.01–1.04)
Female Gender (%)	110 (17.1)	161 (10.3)	<0.0001	**0.0016**	1.56 (1.18–2.05)
Total Meds* (mean ±SD)	11.2 (10.6–11.7)	7.5 (7.2–7.7)	<0.0001	**<0.0001**	1.09 (1.07–1.11)

Each additional medication taken increased the odds of a fall by nearly 10%

Older age, female gender, total number of non-HIV medications associated with increased risk of having a fall.

➔ both studies conclude that future research is needed to determine the impact of polypharmacy reduction for the prevention of harmful outcomes

Thai L et al. 9th International Workshop on HIV and Aging 2018

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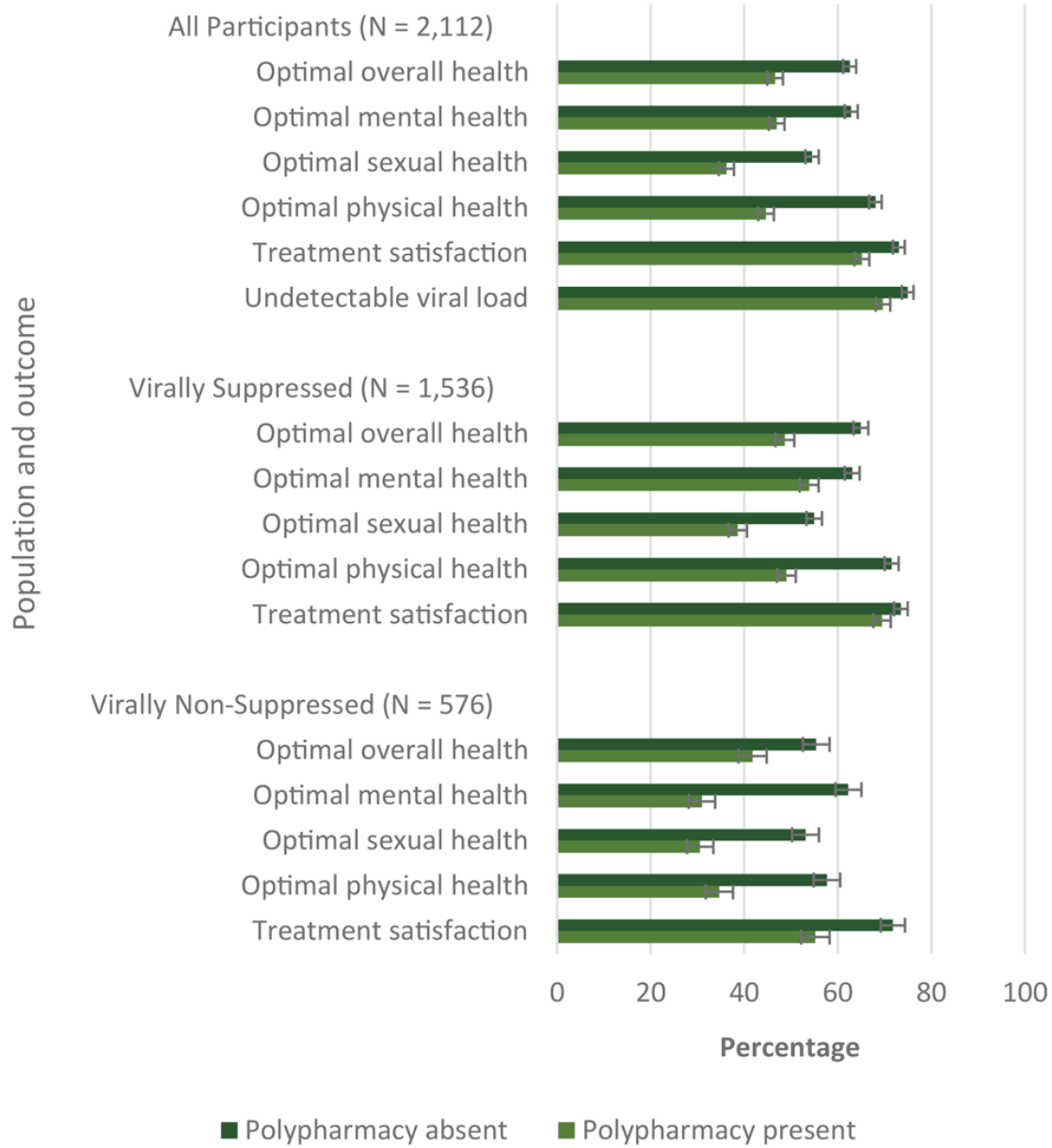
PP and Quality of Life n=2112

Variable	No.	Subjective Measures of Quality of Life, %				
		Optimal Overall Health[b]	Optimal Mental Health[b]	Optimal Sexual Health[b]	Optimal Physical Health[b]	Treatment Satisfaction
Total	2,112	55.8	56.1	46.8	58.1	69.6
Gender						
Male	1,486	58.1	56.1	46.6	60.1	72.5
Female	571	50.1	54.6	46.4	51.1	62.9
Other	55	54.5	70.9	58.2	78.2	60.0
Sexual orientation						
Heterosexual	804	48.5	47.1	43.2	48.4	59.0
Homosexual	1,023	61.8	61.4	48.1	65.3	77.8
Other	285	55.1	62.5	52.6	60.0	70.2
Gender/sexual orientation						
Men who have sex with men	953	62.4	61.7	48.2	66.3	78.4
Men who have sex with women	420	50.7	43.8	44.8	48.8	60.0
Women who have sex with women	58	45.8	50.1	41.5	47.2	57.7
Women who have sex with men	369	51.7	56.9	43.1	48.3	69.0
Other/indeterminate	312	55.1	62.5	52.6	60.6	69.9
Age, y						
<50	1,464	57.2	54.1	50.6	59.7	67.6
≥50	648	52.8	60.6	38.3	54.6	74.1
Year of HIV diagnosis						
2017–2019	488	51.8	53.1	46.9	56.4	64.1
2010–2016	805	58.4	55.7	51.6	58.6	70.3
Before 2010	819	55.7	58.4	42.1	58.7	72.2
Geographic region						
European Union	964	57.5	60.3	51.2	62.8	72.1
North America	583	55.6	50.1	39.5	52.5	71.2
Other	565	53.3	55.2	46.9	56.1	63.7
Home ownership						
Own	653	55.7	56.7	44.7	55.4	72.0
Rent	825	57.8	57.3	47.9	61.3	70.9
Other	634	53.3	53.9	47.6	56.8	65.5



Okoli C, et al. Preventing Chronic Dis 2020

Quali caratteristiche legate alle terapie in ELWH?

PLOS ONE

RESEARCH ARTICLE

Assessing the health status and mortality of older people over 65 with HIV

Gina Turrini[1]*, Stephanie S. Chan[1], Pamela W. Klein[2], Stacy M. Cohen[2], Antigone Dempsey[2], Heather Hauck[2], Laura W. Cheever[2], Andre R. Chappel[1]

1 U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation, Office of Health Policy, Washington, DC, United States of America, **2** Division of Policy and Development, U.S. Department of Health and Human Services, Health Resources and Services Administration, HIV/AIDS Bureau, Rockville, Maryland, United States of America

* gina.turrini@hhs.gov

- Medicare 2011-2016
- 43708 ELWH vs. 1029518 controls

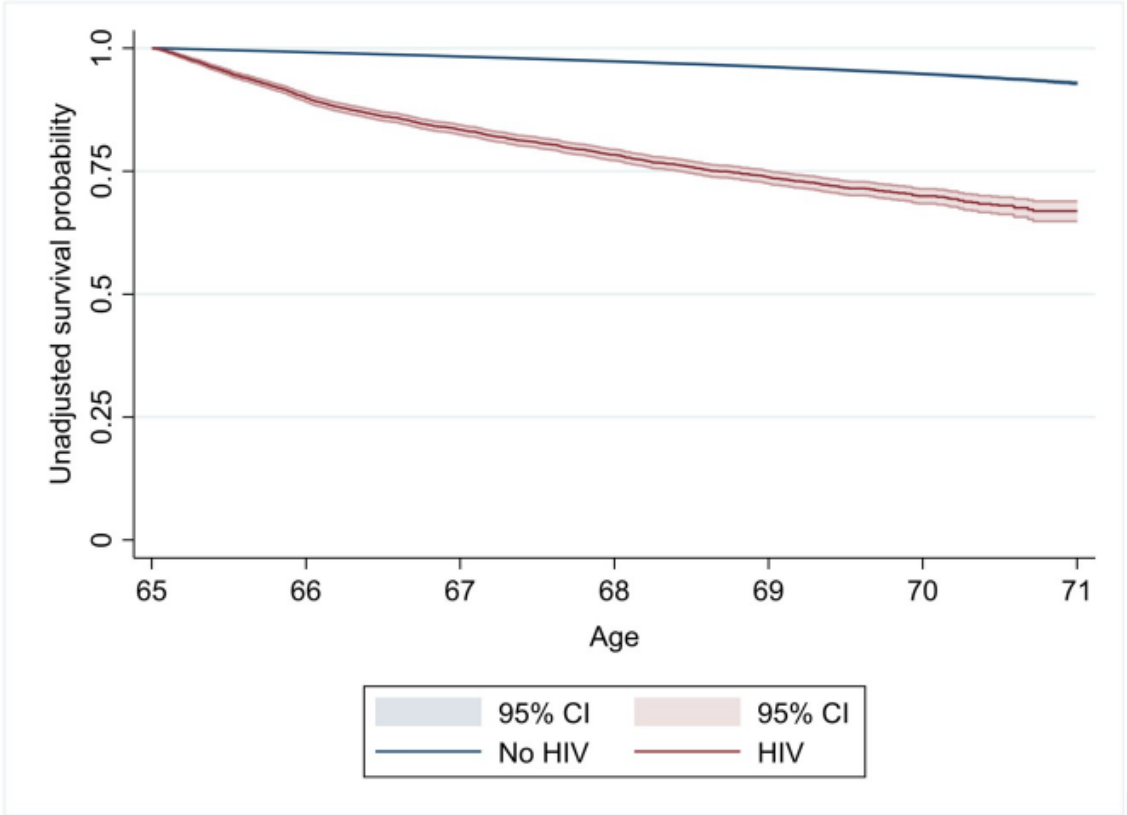


Fig 1. Kaplan-Meier plot of unadjusted survival by HIV status. Years since age 65.

CISAI FONDAZIONE ASIA

PLOS ONE

RESEARCH ARTICLE

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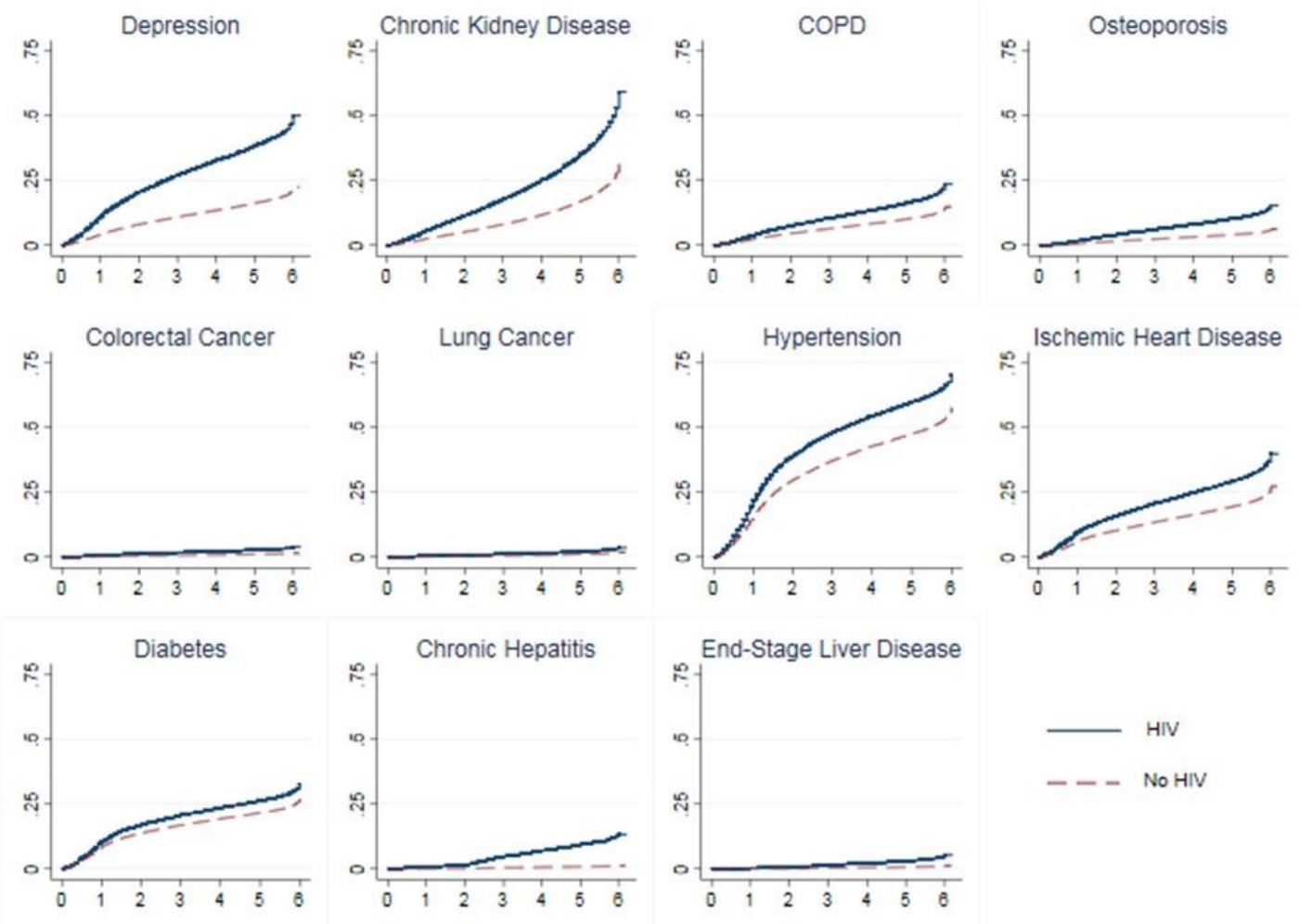
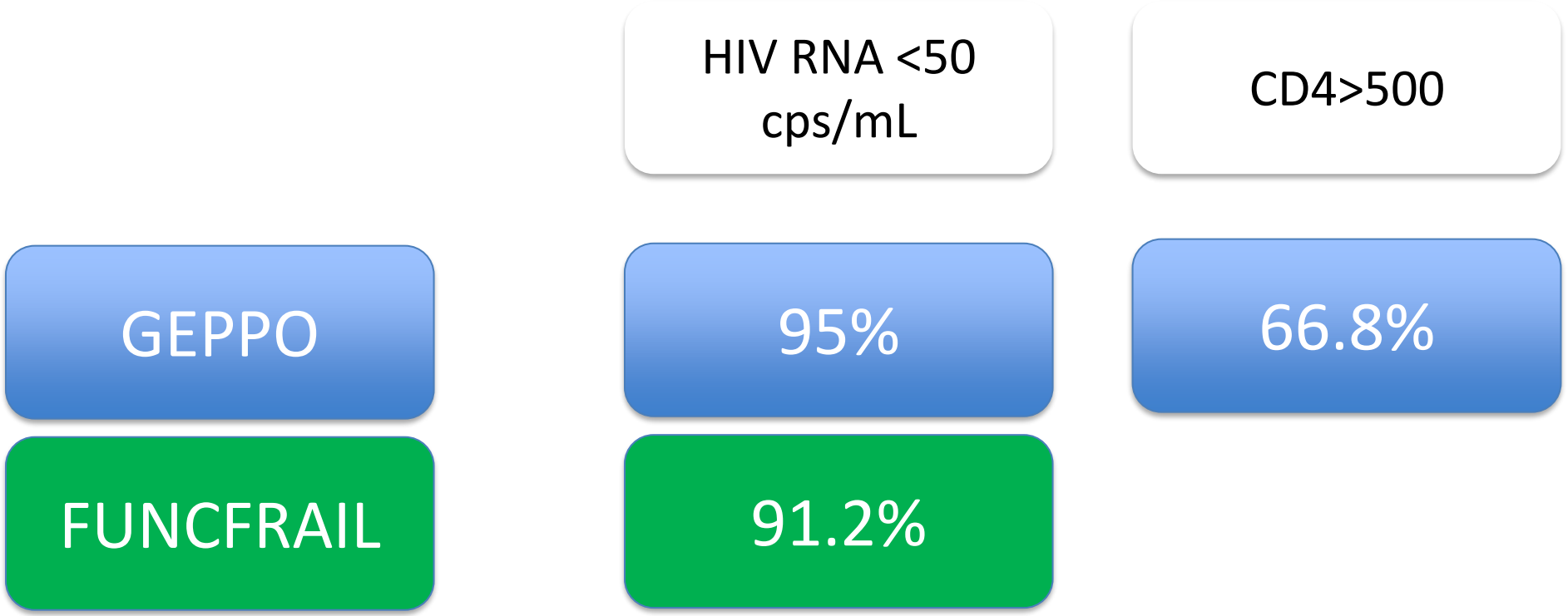
1 U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation, Office of Health Policy, Washington, DC, United States of America, **2** Division of Policy and Development, U.S. Department of Health and Human Services, Health Resources and Services Administration, HIV/AIDS Bureau, Rockville, Maryland, United States of America

* gina.turrini@hhs.gov



Immunovirological outcomes in ELWH cohorts



Nozza S, et al. JAC 2017; Calcagno A, et al. JAIDS 2017

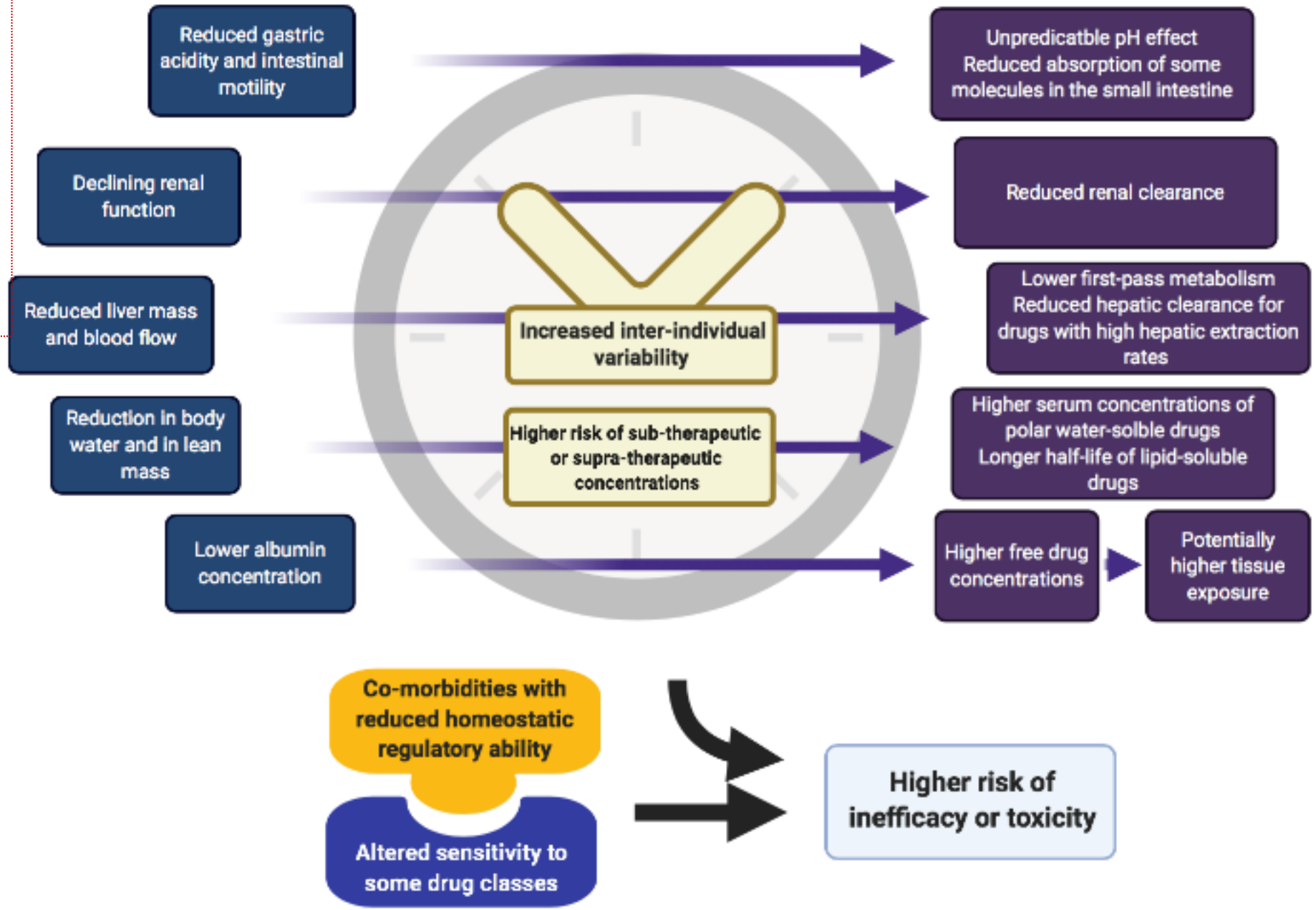
Età e tossicità

Table 5 Estimates of relationship between increased age (per 5 years older) and the development of a laboratory abnormality from unadjusted and adjusted analyses of the risk of an abnormal laboratory measurement

	All patients			Patients receiving drugs known to be related to specific toxicities[†]		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Abnormal triglycerides						
Unadjusted	1.11	1.06, 1.15	0.0001	1.11	1.06, 1.16	0.0001
Adjusted for baseline characteristics*	1.07	1.02, 1.12	0.004	1.07	1.02, 1.12	0.005
Also adjusted for pre-HAART triglycerides	0.98	0.92, 1.05	0.53	0.98	0.91, 1.05	0.56
Abnormal cholesterol						
Unadjusted	1.21	1.16, 1.26	0.0001	1.21	1.16, 1.27	0.0001
Adjusted for baseline characteristics	1.23	1.17, 1.28	0.0001	1.23	1.17, 1.29	0.0001
Also adjusted for pre-HAART cholesterol	1.12	1.05, 1.20	0.0009	1.14	1.06, 1.22	0.0004
Abnormal bilirubin						
Unadjusted	1.03	0.99, 1.08	0.19	1.10	0.89, 1.35	0.38
Adjusted for baseline characteristics	1.02	0.97, 1.77	0.51	1.06	0.85, 1.32	0.61
Also adjusted for pre-HAART bilirubin	1.01	0.95, 1.06	0.82	1.01	0.77, 1.31	0.97
Abnormal haemoglobin						
Unadjusted	1.10	1.05, 1.16	0.0002	1.09	1.02, 1.16	0.02
Adjusted for baseline characteristics	1.11	1.06, 1.17	0.0001	1.11	1.03, 1.19	0.005
Also adjusted for pre-HAART haemoglobin	1.07	1.01, 1.14	0.03	1.06	0.98, 1.16	0.15
Abnormal ALT						
Unadjusted	1.05	1.00, 1.09	0.04	1.09	0.98, 1.20	0.11
Adjusted for baseline characteristics	1.02	0.98, 1.07	0.38	1.03	0.92, 1.15	0.58
Also adjusted for pre-HAART ALT	1.00	0.95, 1.06	0.97	1.01	0.89, 1.15	0.85

Sabin CA, et al. HIV Medicine 2008

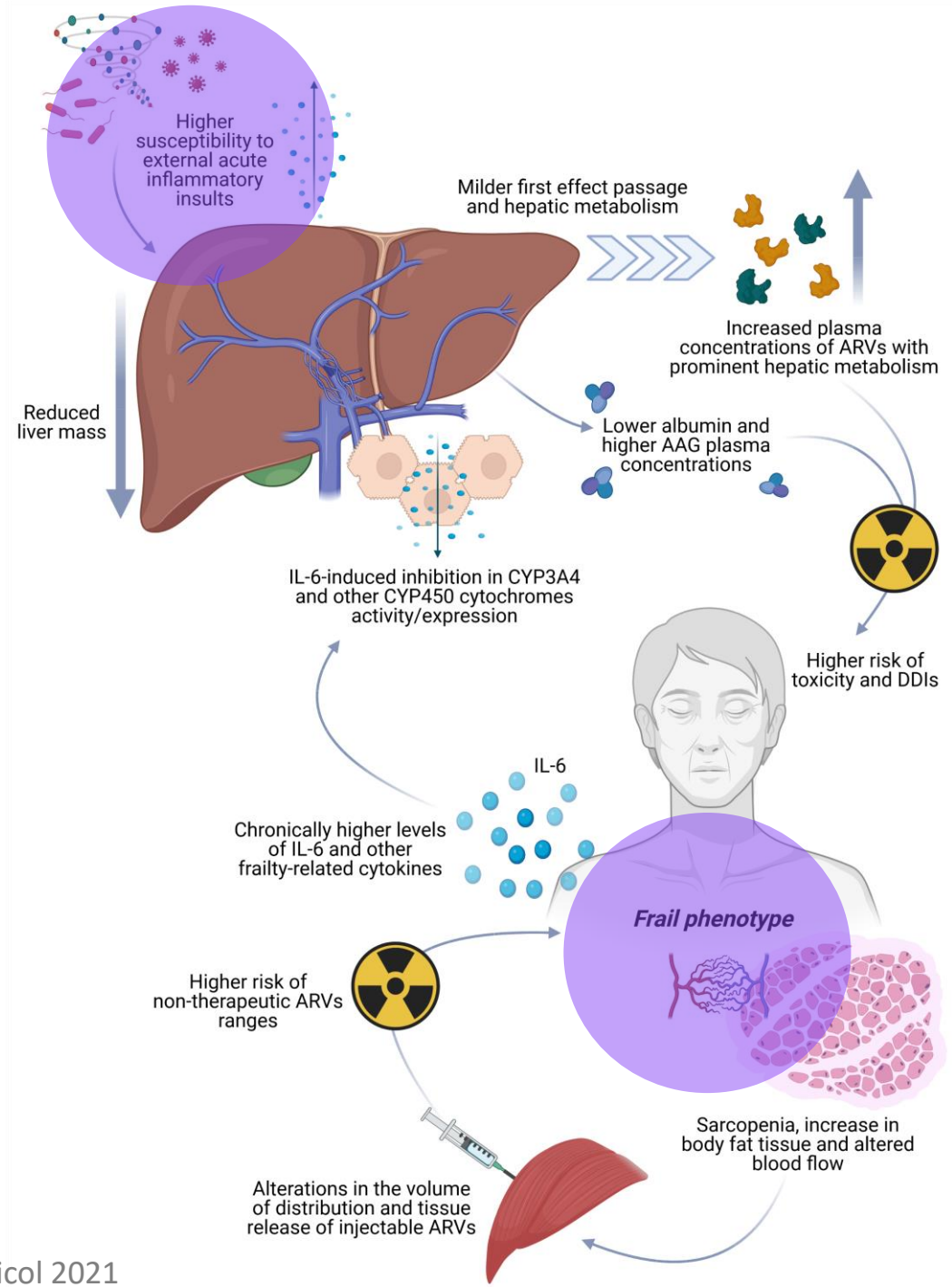
PK/PD changes in ELWH



Calcagno A, et al. Expert Opin Drug Met and Toxicol 2021

Drug	Drug class	Toxicity/tolerability associated with PK	Effect of Age on PK	Potential for toxicity in elderly patients
Zidovudine	N(t)RTIs	No	Small effect on clearance	High
Lamivudine		No	No effect	Low
Abacavir		No	No effect	Intermediate
Emtricitabine		No	No effect	Low
Tenofovir disoproxil fumarate		Yes	Yes	High
Tenofovir alafenamide		No	Unknown	Low
Efavirenz	NNRTIs	Yes	No effect	High
Nevirapine		No	No effect	Intermediate
Etravirine		No	No effect	Low
Rilpivirine		No	No effect	Low
Long acting Rilpivirine		No	Unknown	Low
Doravirine		No	Minimal effect	Low
Lopinavir/r	PIs	Yes	Marginal effect on hepatic and renal clearance	Intermediate
Atazanavir/r or /c		Yes	Marginal effect on hepatic and renal clearance	Intermediate
Darunavir/r or /c		No	Marginal effect on hepatic and renal clearance	Intermediate
Older Protease Inhibitors*/r		Yes	Marginal effect on hepatic and renal clearance	Intermediate
Raltegravir	INSTIs	No	No effect	Low
Elvitegravir/c		No	No effect	Intermediate
Dolutegravir		Weak	Modest effect on clearance	Low°
Bictegravir		No	Marginal effect on clearance	Low°
Long acting cabotegravir		No	Unknown	Low
Maraviroc	EI, AI; R5I	No	Marginal effect on hepatic and renal clearance	Low
Fostemsavir		No	Unknown	Low
Enfuvirtide		No	No	Low
Ibalizumab		No	Unknown	Low

Calcagno A, et al. Expert Opin Drug Met and Toxicol 2021

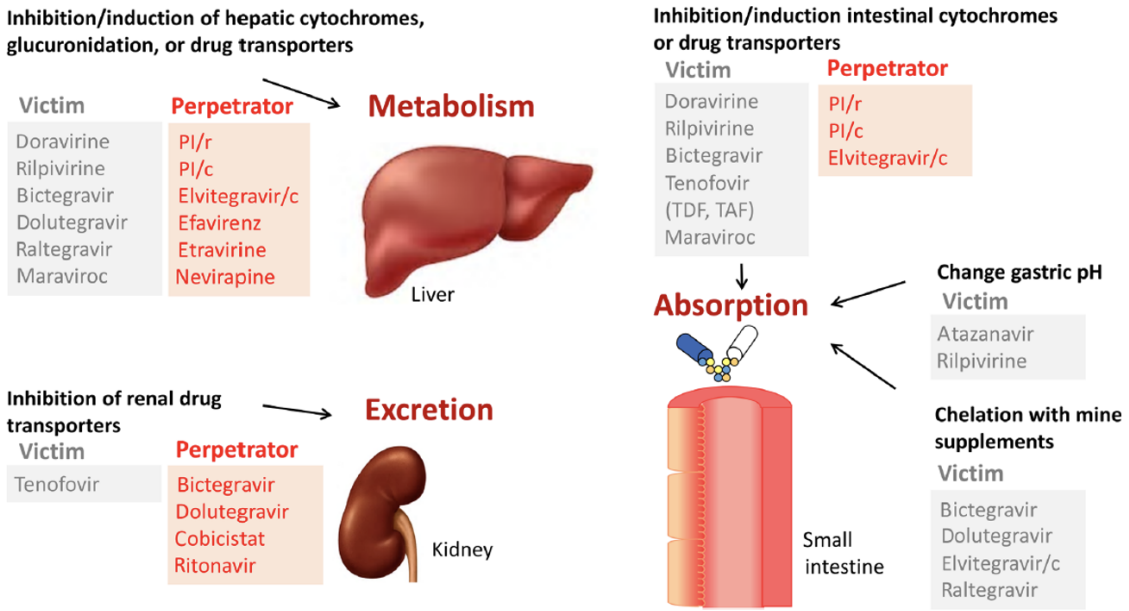


Calcagno A, et al. Expert Opin Drug Met and Toxicol 2021

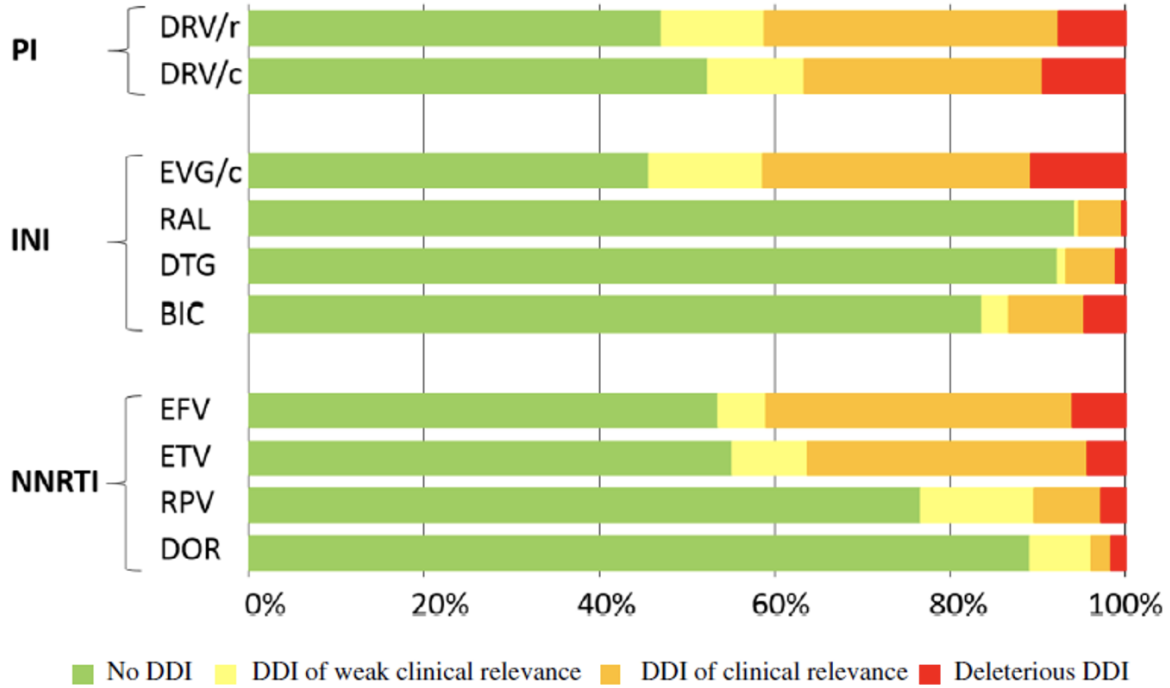
CISAI FONDAZIONE ASIA

Drug-drug interactions with antiretroviral drugs

Mechanisms of drug-drug interactions with antiretrovirals



Drug-drug interactions profiles of various antiretrovirals considering >750 medications



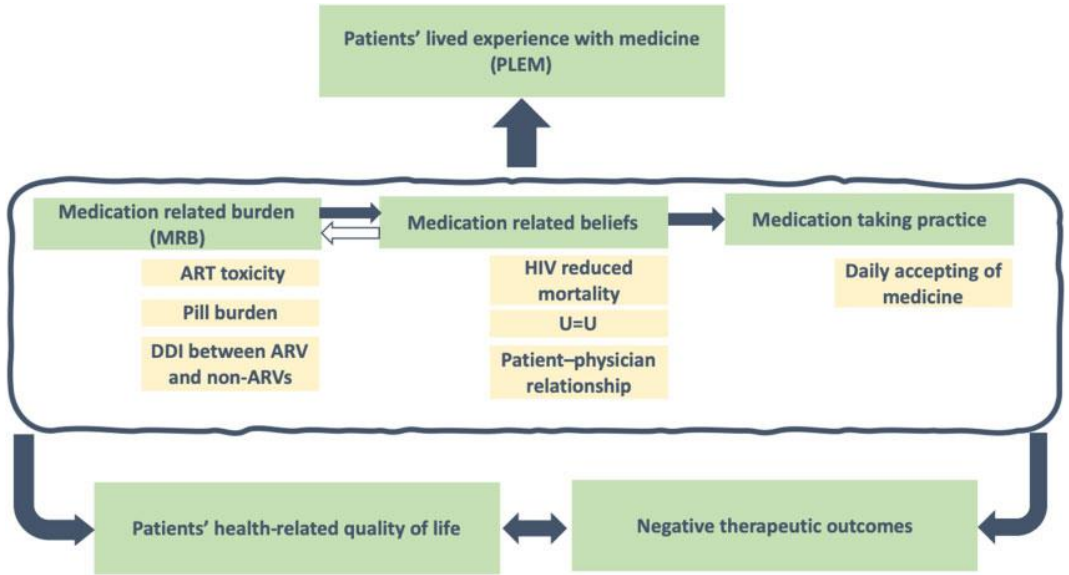
Back D & Marzolini C. J Int AIDS Soc 2020

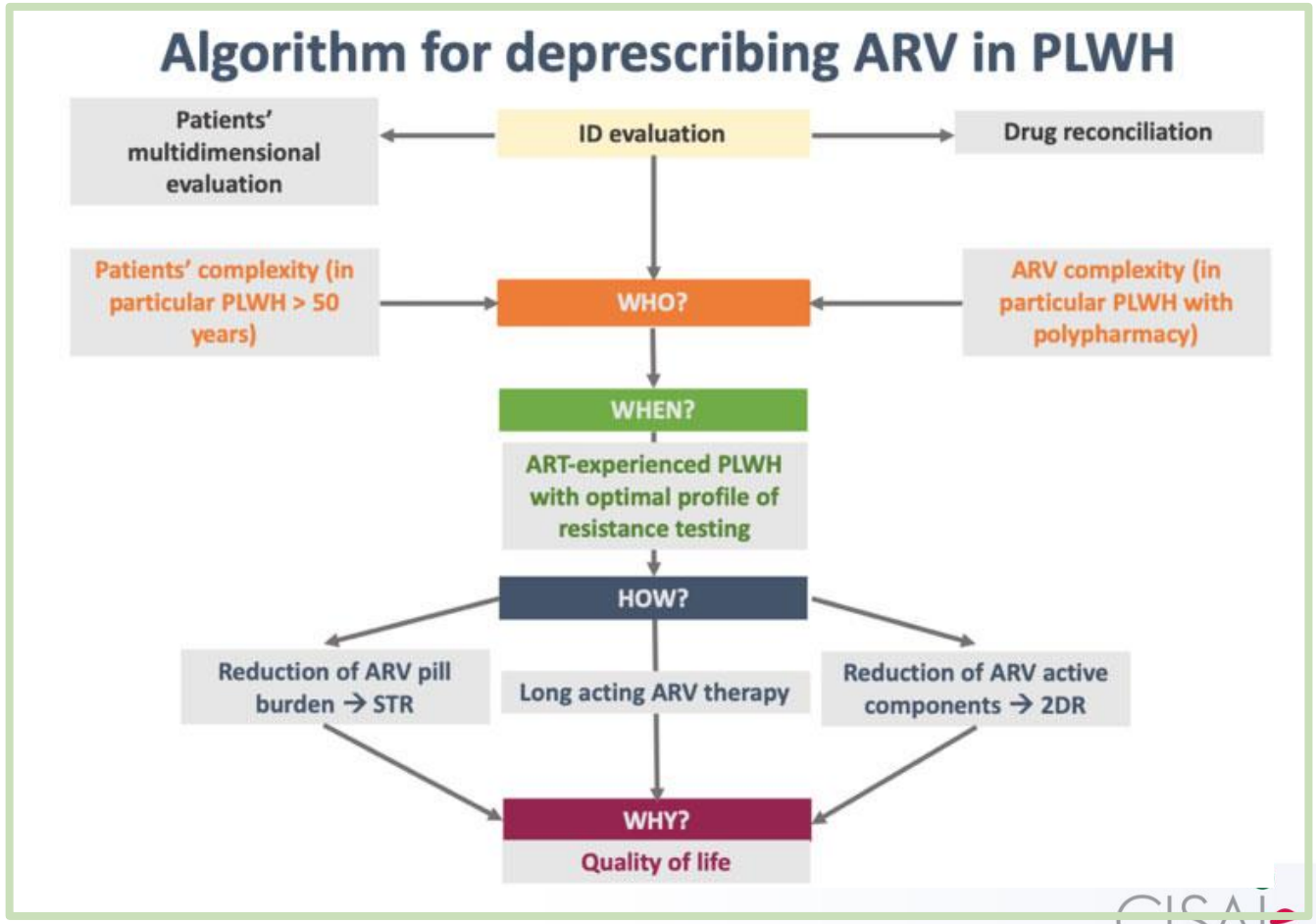
J Antimicrob Chemother
doi:10.1093/jac/dkaa329

Journal of Antimicrobial Chemotherapy

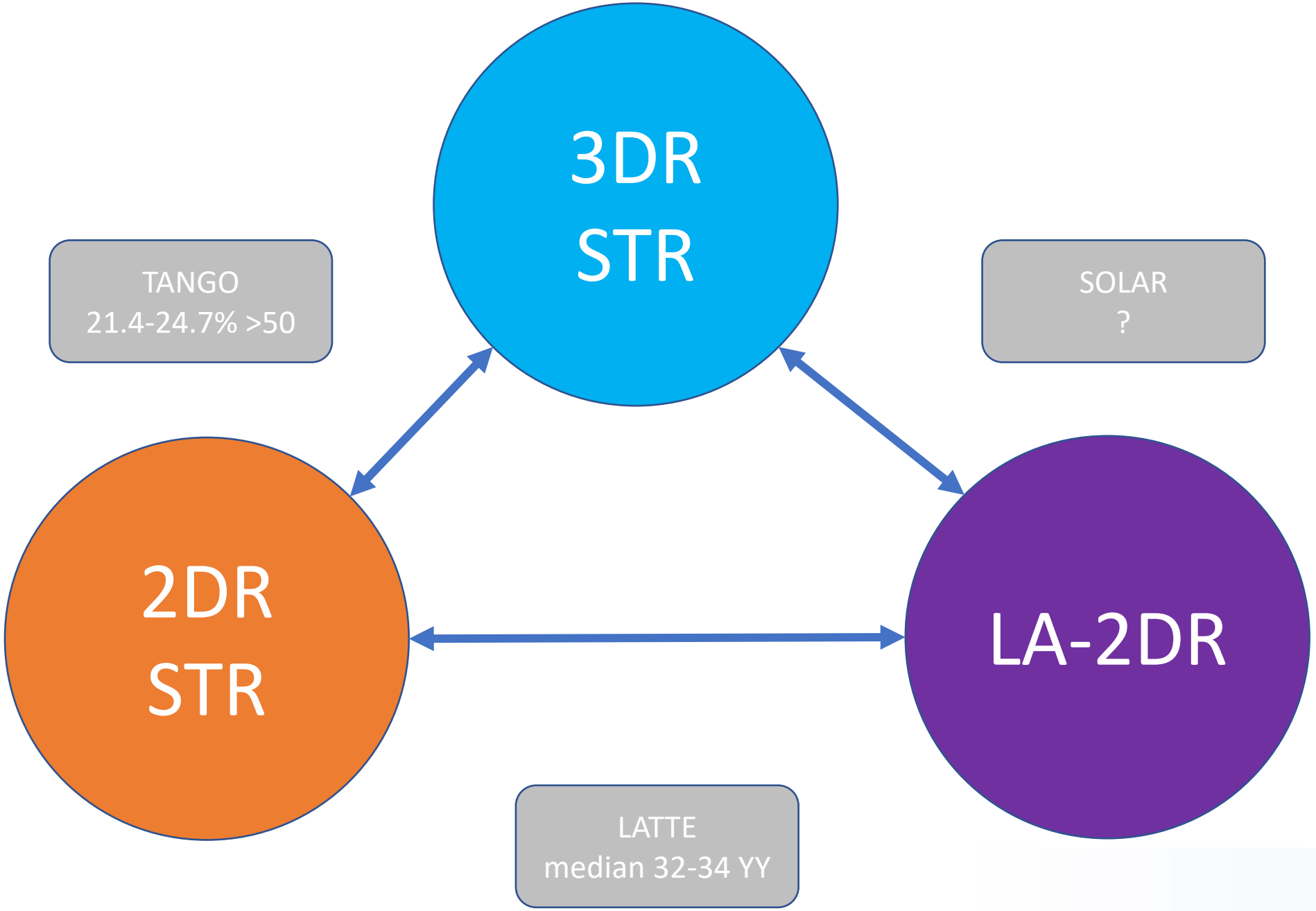
A patient-centred approach to deprescribing antiretroviral therapy in people living with HIV

Giovanni Guaraldi [1,2]*, Jovana Milic[1–3], Simone Marcotullio[4] and Cristina Mussini[1,2]



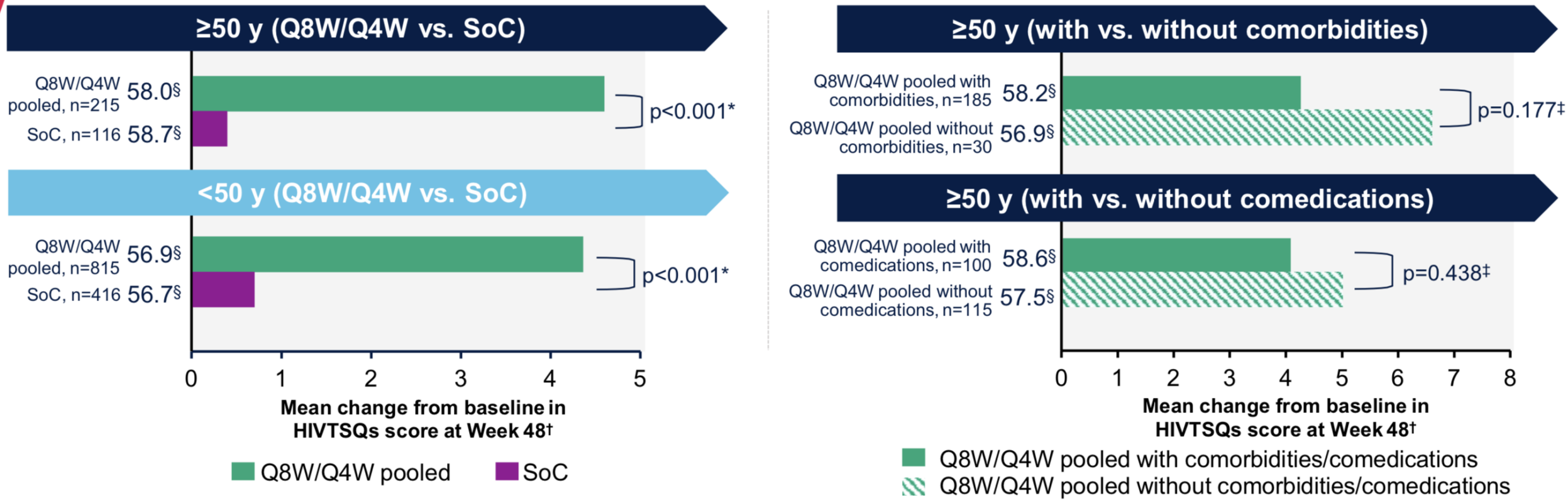


Guaraldi G, et al. JAC 2020


3DR
STR
TANGO
21.4-24.7% >50
SOLAR
?
2DR
STR
LA-2DR
LATTE
median 32-34 YY

CAB + RPV LA in Adults ≥50 Years of Age:

High Treatment Satisfaction Irrespective of Age Group or Comorbidities/Comedication

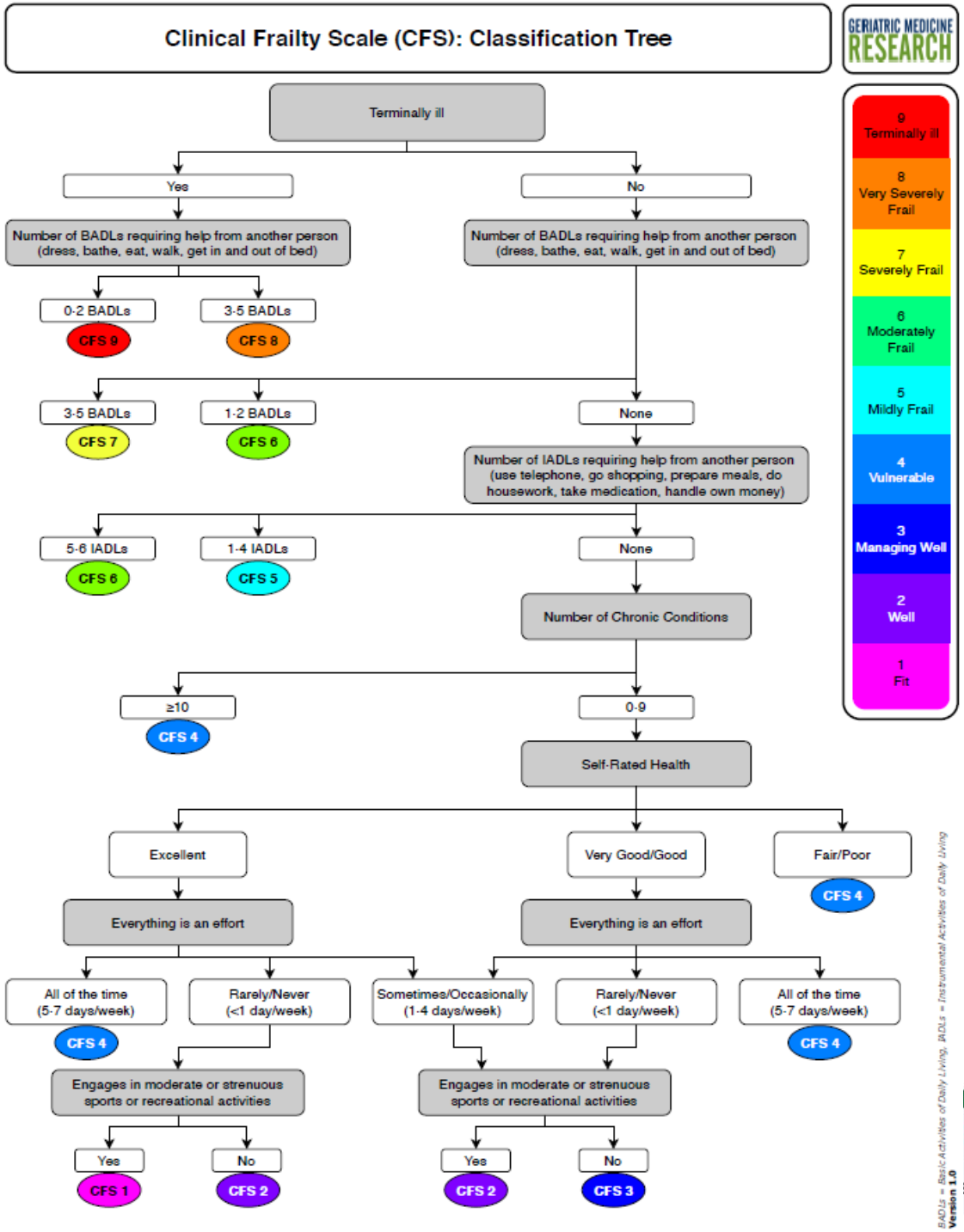


- Irrespective of age group, mean change from baseline in HIVTSQs score was significantly greater in participants receiving LA therapy in comparison to participants receiving SoC
- When stratified for the presence of comorbidities and comedications, no significant differences were observed in mean change from baseline in HIVTSQs score for participants aged ≥50 y receiving LA therapy

*P-value for difference of means ([Q4W+Q8W]–CAR). †As HIVTSQs score was not collected at Week 48 in the ATLAS and FLAIR study, Week 44 values from ATLAS and FLAIR were pooled with Week 48 scores from ATLAS-2M.
‡P-value for difference of means (individuals with comorbidities/comedications vs. individuals without). §Mean baseline HIVTSQs score.
CAB, cabotegravir; CAR, current antiretroviral regimen; HIVTSQs, HIV Treatment Satisfaction Questionnaire (status version); LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; SoC, standard of care; RPV, rilpivirine; y, years.

Perchè non iniziare in certi pazienti?

ARV deprescribing – Patients' complexity



Co-morbidities clusters

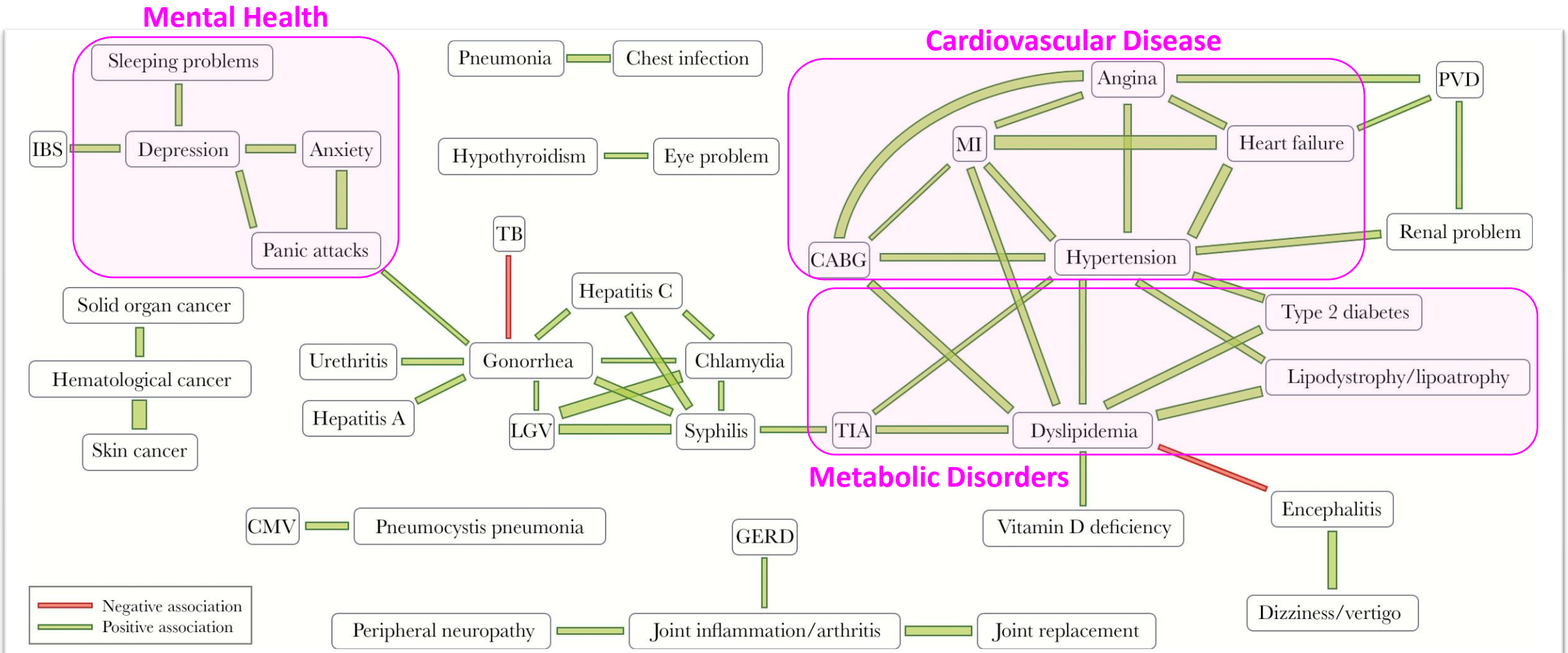


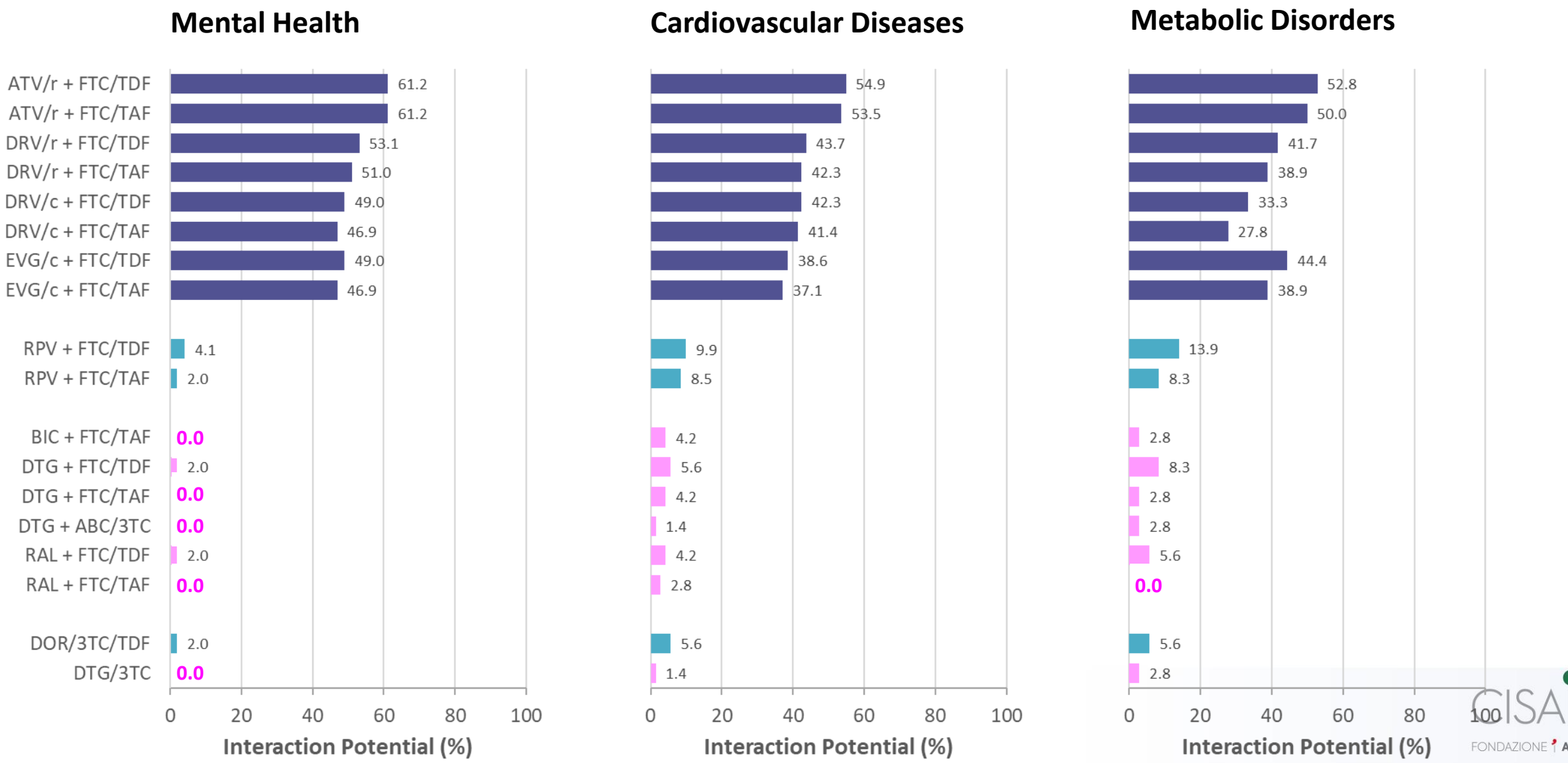
Figure 1. Significant non-random associations between comorbidities (as indicated by a significant Somers' D at the 0.1% significance level) in all POPPY PLWH (n = 1073). The thickness of the line is directly proportional to the absolute value of the Somers' D. Abbreviations: CABG, coronary artery bypass graft; CMV, cytomegalovirus; GERD, gastro-esophageal reflux disease; IBS, irritable bowel syndrome; LGV, lymphogranuloma venereum; MI, myocardial infarction; PLWH, people living with HIV; PVD, peripheral vascular disease; TB, tuberculosis; TIA, transient ischemic attack.

De Francesco D, et al. Open Forum Infect Dis. 2018 Oct 24;5(11):ofy272.

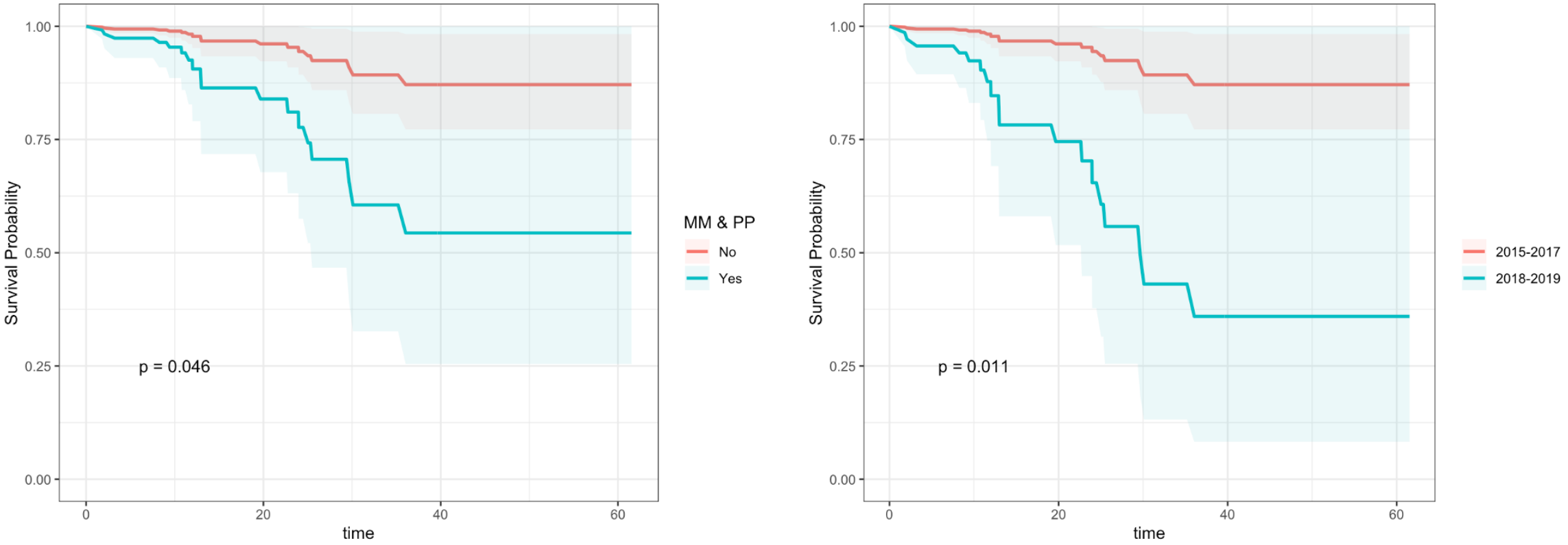
Comorbidity Clusters - Comedications

	Mental Health	Cardiovascular Diseases	Metabolic Disorders
Drug Classes	Anxiolytics Hypnotics Sedatives Antidepressants	Beta blockers Calcium channel blockers Hypertensives Heart failure agents	Antidiabetic drugs Lipid lowering agents
Comedications	49	71	36

Comorbidity Clusters – Interaction Potential



Use of two drugs regimens in a cohort of geriatric people with HIV (GEPPO cohort): is time for deprescribing?



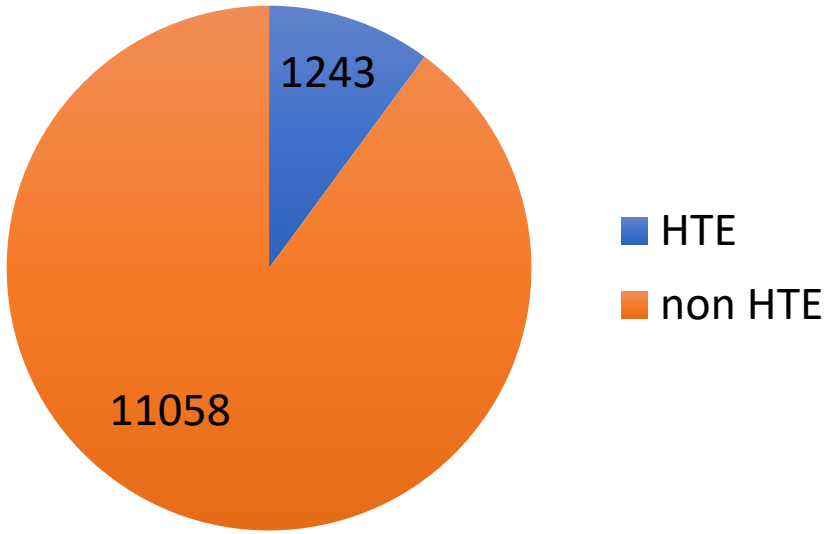
Nozza S, et al. ICAR 2020

CISAI
FONDAZIONE ASIA

Why not starting with certain index drugs?

ART complexity

Heavily treatment experienced
ICONA, 2008-2018 (10,1%)



Endpoints	n.events 3-year	3-year probability (95%CI)	n. events 5-year	5-year probability (95%CI)	n. events 8-year	8-year probability (95%CI)
VF>200	13	2.3 (1.1, 3.6)	16	3.3 (1.6, 5.0)	19	5.0 (2.5, 7.4)
AIDS	9	1.5 (0.5, 2.4)	21	3.8 (2.2, 5.4)	24	4.7 (2.8, 6.6)
NADC	17	2.8 (1.5, 4.1)	38	6.8 (4.7, 8.9)	47	9.0 (6.5, 11.5)
Death	1	0.2 (0.0, 0.5)	2	0.4 (0.0, 1.0)	4	0.9 (0.0, 1.8)
Composite (AIDS, NADC or Death)	24	3.9 (2.4, 5.5)	58	10.4 (7.9, 13.0)	68	12.8 (10.0, 15.7)

Lo Caputo S, et al. ICAR 2019

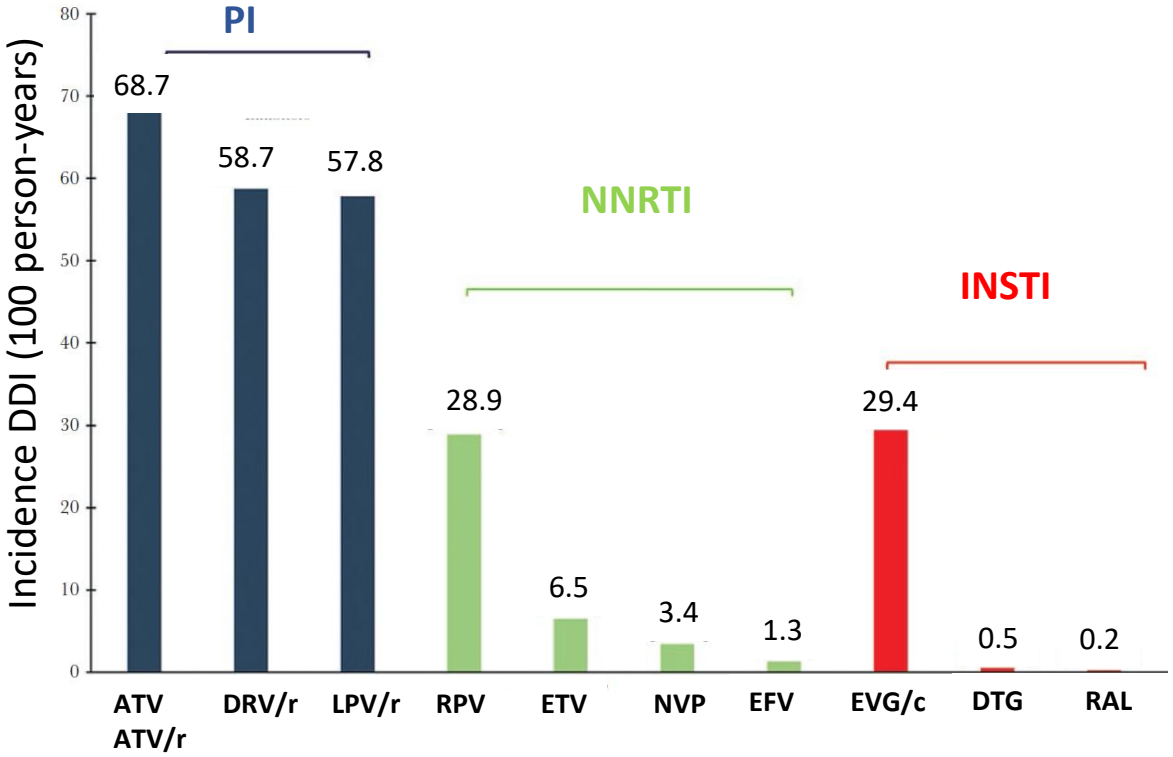
CISAI
FONDAZIONE ASIA

Risk and cost associated with DDIs in elderly PLWH

Frequency, risks and costs attributable to «red flag DDIs» (Liverpool database) using French nationwide health e-records for 2016:

- 9076 PLWH, mean age: 71 ± 5 years, median non-HIV comeds (IQR): 14 (9-21)
- **16.8%** ≥ 1 DDI, unboosted INI associated with lower risk for DDI (OR: 0.02), boosted PIs increased risk for DDI (OR: 4.12)
- **Presence of DDIs associated with additional 2693 USD/year**

Incidence of DDI per 100 person-years



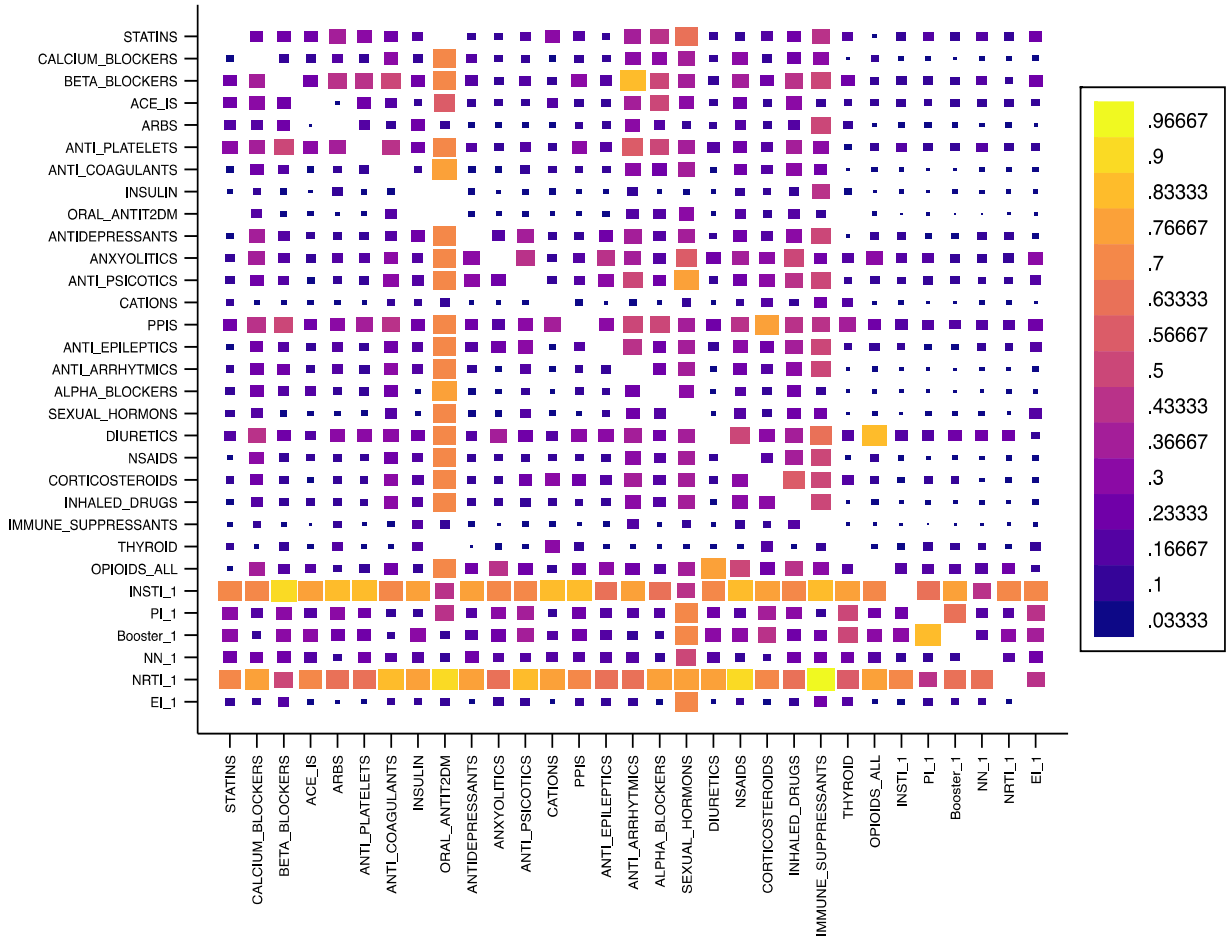
10 most frequent encountered DDIs

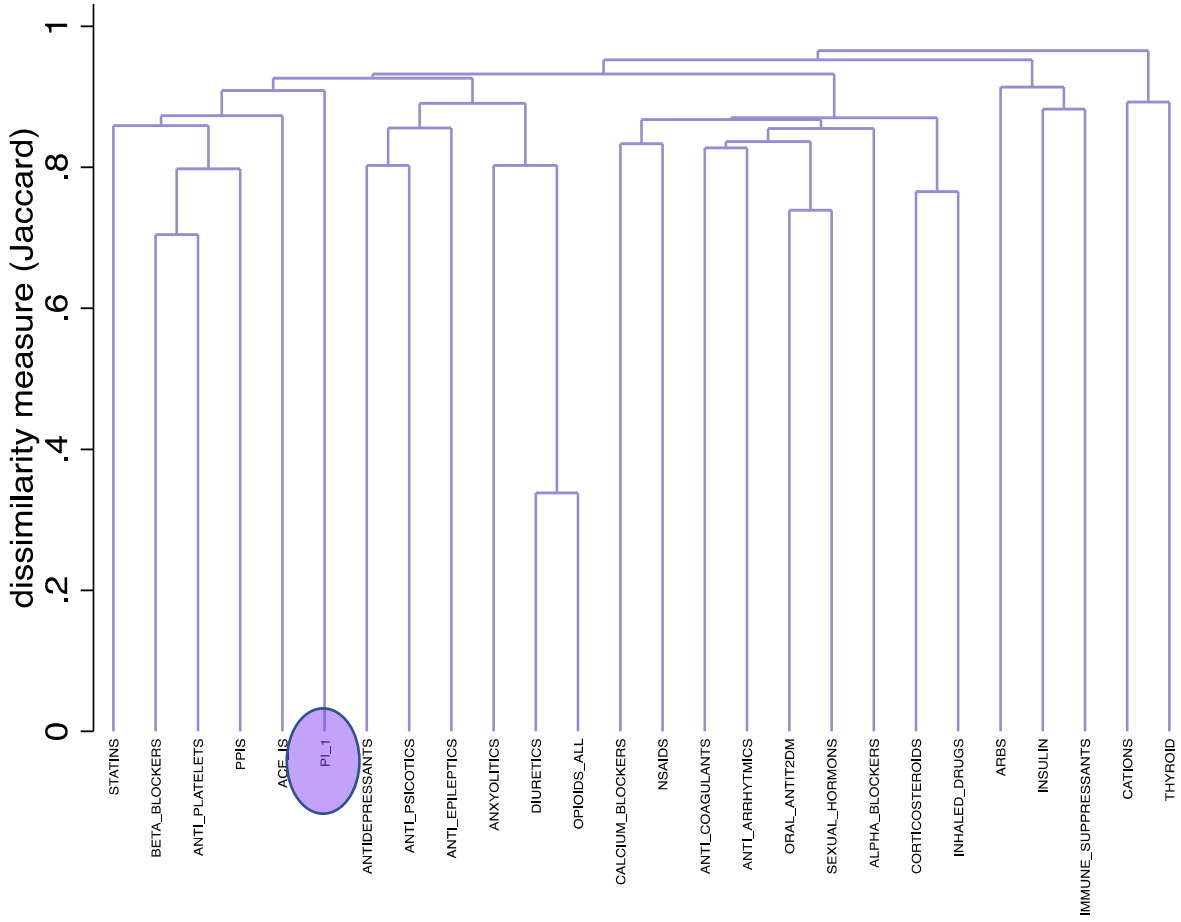
	DNCIs, No. (%)	Risk
PI or boost/inhaled glucocorticoids[b]	739 (29)	Cushing syndrome
Atazanavir or rilpivirine/proton pump inhibitors[c]	676 (27)	↓ ARV efficacy
PI or boost/lercanidipine	285 (11)	hypotension & cardiac disorders
PI or boost/alfuzosin	233 (9)	severe hypotension
PI or boost/domperidone	136 (5)	QT prolongation
PI or boost/amiodarone	82 (3)	QT prolongation
PI or boost/simvastatin	79 (3)	rhabdomyolysis
PI or boost/apixaban or rivaroxaban	67 (3)	bleeding
PI or boost/piroxicam	51 (2)	respiratory depression & hematologic abnorm.
Darunavir/injectable lidocaine	38 (2)	QT prolongation

Desmessine L et al. Open Forum Infect Dis 2019

CISAI FONDAZIONE ASIA

Co-medication clustering





Calcagno A, et al. BJCP 2021

CISAI
FONDAZIONE ASIA

Fattori di rischio per sintomi NPS in corso di DTG

sesso F, età avanzata, uso di abacavir, PK?

- Più elevate C_{trough} di DTG in pazienti giapponesi sintomatici e in pazienti francesi che avevano interrotto il farmaco
- Scomparsa dei sintomi con dosaggio ridotto (a giorni alterni in una paziente di basso BMI)
- Maggiore prevalenza di depression in pazienti con DTG C_{trough} nel quartile più elevato
- Età avanzata associate a esposizione maggiore di DTG

- Non segnalata maggiore incidenza di sintomi NPS con DTG 50 mg bid o con DTG + atazanavir (associate a PK più elevata)
- Predisposizione genetica? (polimorfismi in *UGT1A1* e/o *SLC22A2*)

Yagura H, et al. BMC Inf Dis 2017; Menard A, et al. AIDS 2017; Parant F, et al. Current Drug Safety 2018; Borghetti A, et al. JAC 2018; Elliot E, et al. CID 2018; Calcagno A, et al. Cin Pharm 2020

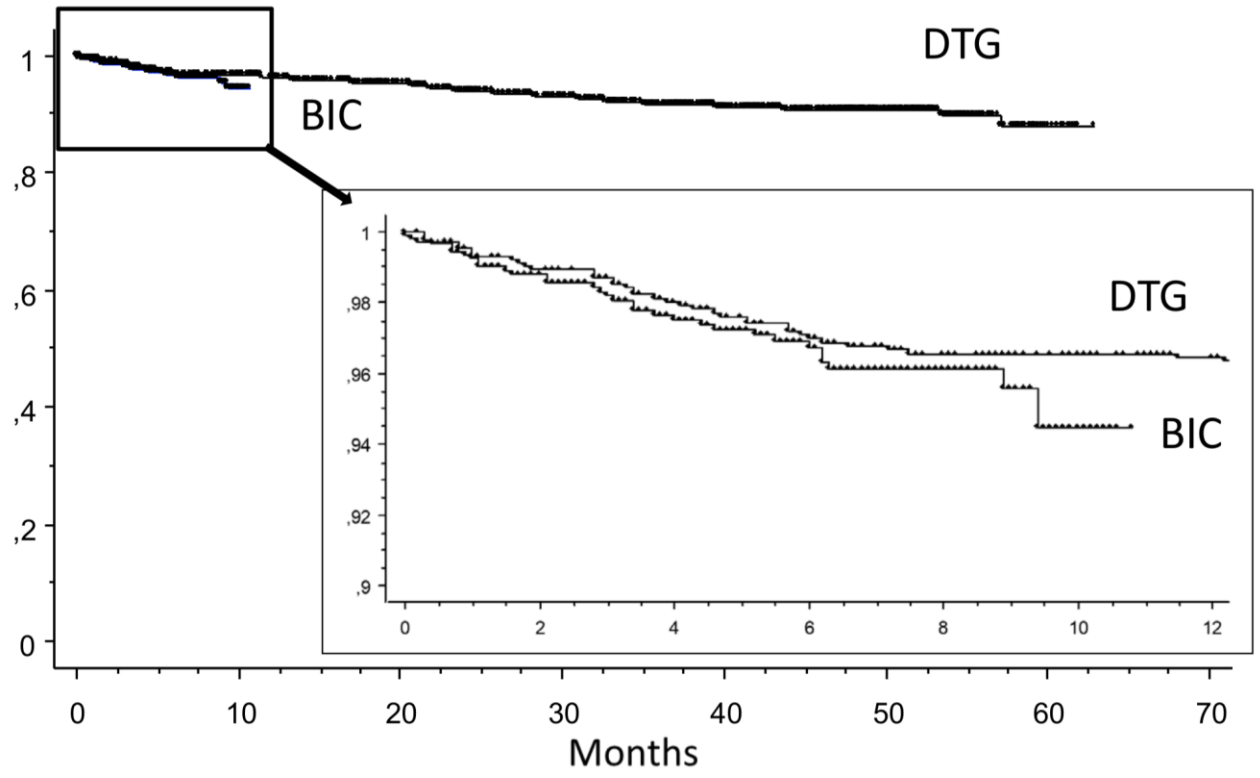
Dati preliminari su NPS con Bictegravir

943 pazienti → 5.3% tasso di discontinuazione (3.3% per NPS)

All'analisi multivariata associazione con:

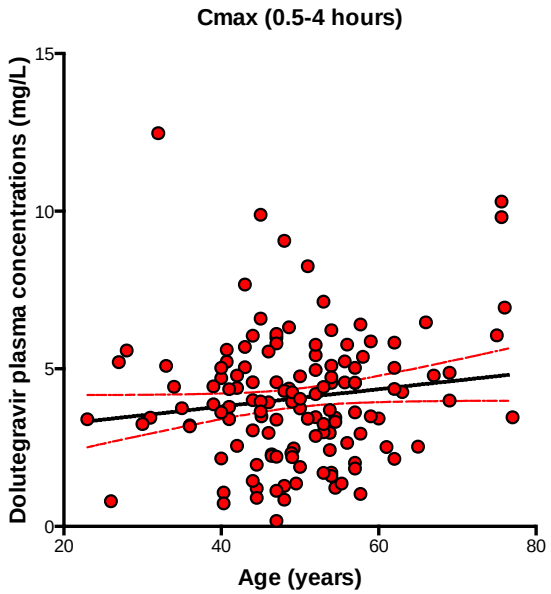
- depressione
- centro di cura

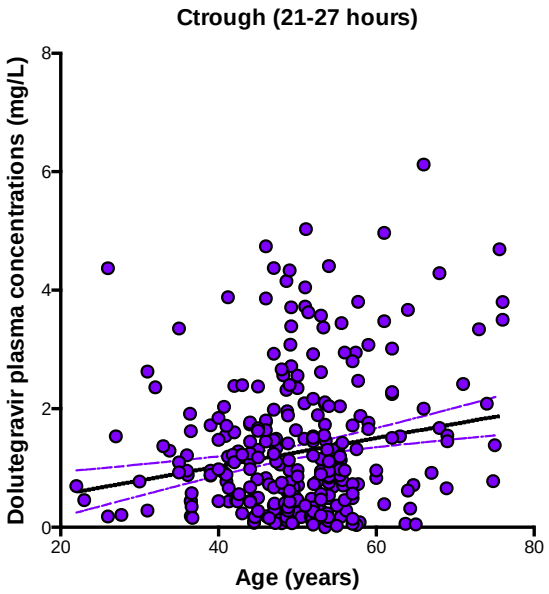
Non osservato un effetto di età, genere, etnia o eventi avversi precedenti con DTG

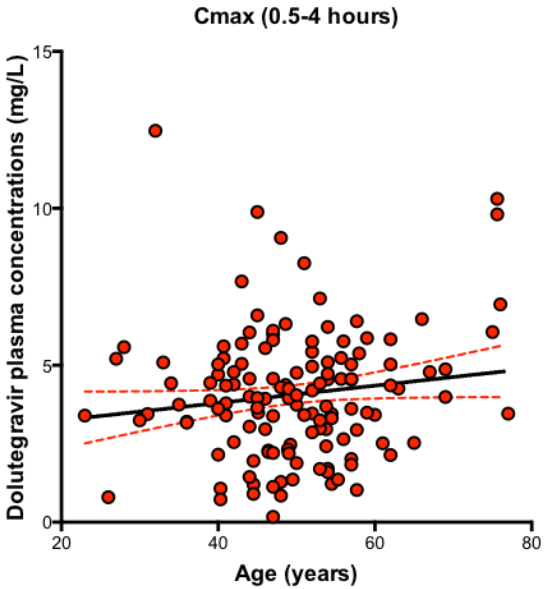


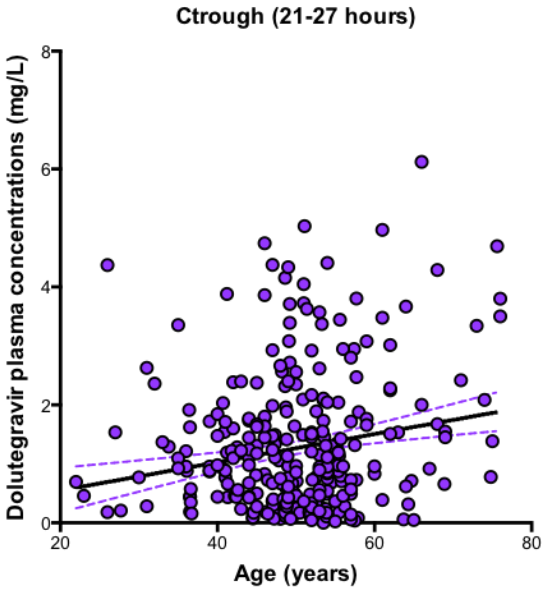
Hoffmann C, et al. Antiviral Therapy 2020

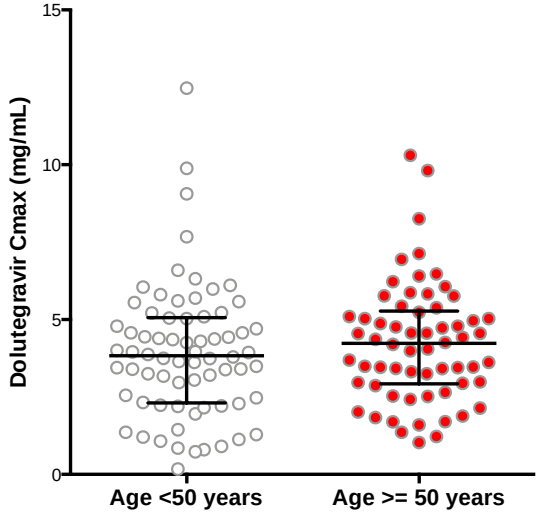
DTG PK in plasma and CSF

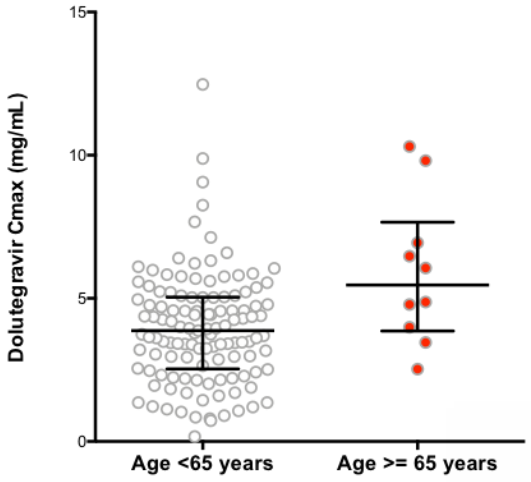


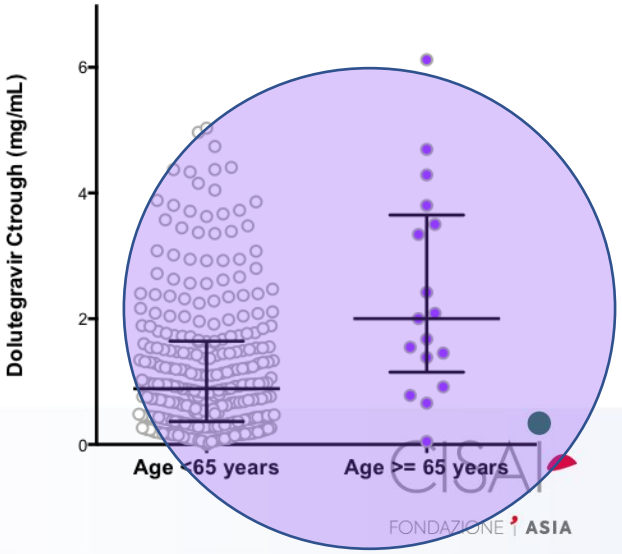






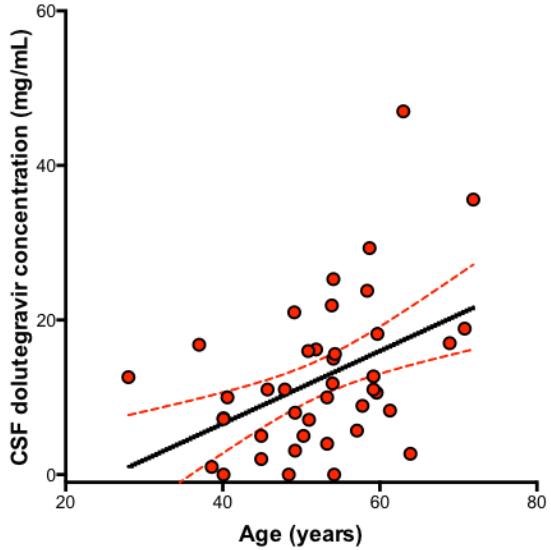


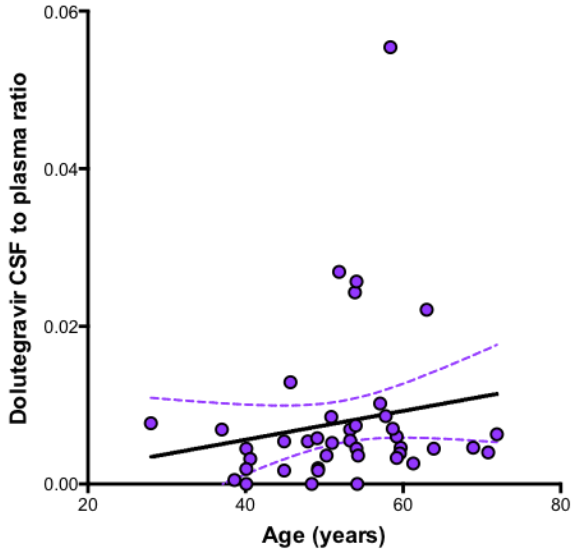


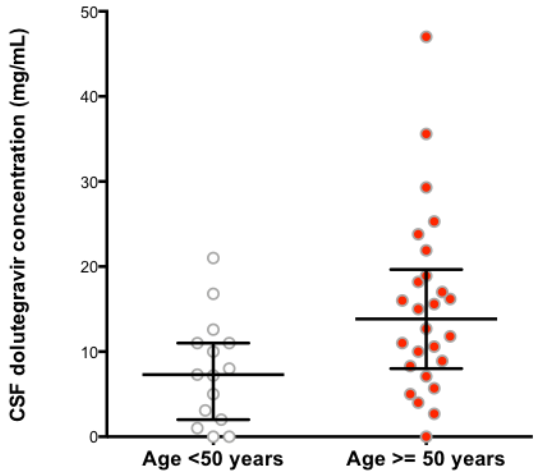


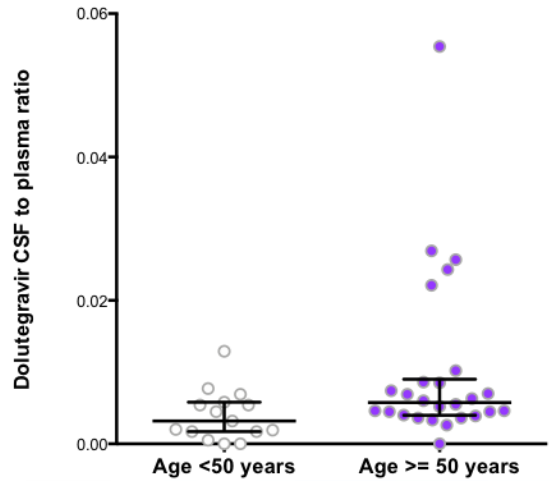
Calcagno A, et al. Clinical Pharmacokinetics 2020

CSF DTG PK









Calcagno A, et al. Clinical Pharmacokinetics 2020

Economic and clinical burdens and associated health disparities in HIV/AIDS management using big data: potentially inappropriate use and deprescribing of benzodiazepines

Medicare claims in 2017

Potentially inappropriate use of benzodiazepines was defined as having any benzodiazepine claims in individuals 65+ years or having benzodiazepine claims for more than four weeks in individuals 18–64 yy

235/1211

19.4%

Less IU of BDZ in PLWH >65, Blacks and Hispanics

More Inpatient, Outpatient and ER Visits!
Higher Costs

Li, et al. AIDS Care 2020

CISAI FONDAZIONE ASIA

Recommendations for deprescribing benzodiazepines in HIV-infected patients (adapted from ref. 94)

ANALYZE THE USE OF THESE DRUGS IN THE CONTEXT OF MANAGING ASSOCIATED COMORBID CONDITIONS

- Other sleep disorders (eg, restless leg syndrome)
- Uncontrolled anxiety, depression, mental or physical status that may cause or aggravate insomnia.
- Effective benzodiazepine, especially for anxiety.
- Cessation of alcohol consumption.

INVOLVE THE PATIENT (discuss potential risks, benefits, withdrawal plan, symptoms, and duration)

DEPRESCRIBING RECOMMENDED

- Minimize the use of drugs that aggravate insomnia (eg, caffeine, alcohol)
- Treat underlying conditions.
- Consider consulting a psychologist, psychiatrist, or sleep specialist.

GRADUAL WITHDRAWAL OF DRUGS

(Gradual withdrawal in collaboration with the patient. It is recommended to reduce consumption by 25% every 2 weeks and, if possible, by 12.5% towards the end)

Fortnightly monitoring during withdrawal

Expected benefits:

- Improvement in alertness, cognition, daytime sleepiness, and reduction in falls.
- Withdrawal symptoms:
- Insomnia, anxiety, irritability, sweating, gastrointestinal symptoms (with a mean duration of days to weeks)

- Do not administer drugs to control insomnia.
- Focus on behavior

If symptoms recur:
Consider

- Maintaining the normal dose for the first few weeks, then continue with withdrawal at a slow rate.

Blanco JR, et al. Eur J Clin Pharm 2020

CISAI FONDAZIONE ASIA

Burden anticolinergico

Farmaci anticolinergici bloccano il neurotrasmettitore acetilcolina
→ soprattutto negli anziani (minore densità recettoriale) rischio di deficit cognitivo, demenza, volume cerebrale ridotto, cadute, delirium
→ consigliato utilizzo ridotto nei soggetti >65 anni

Table 5. Modified Anticholinergic Risk Scale

3 Points	2 Points	1 Point
Amitriptyline	Amantadine	Carbidopa-levodopa
Atropine/scopolamine	Baclofen	Entacapone
Benztropine	Cetirizine	Haloperidol
Chlorpromazine	Cimetidine	Methocarbamol
Clomipramine	Clozapine	Metoclopramide
Dicyclomine	Cyclobenzaprine	Mirtazapine
Diphenhydramine	Desipramine	Paroxetine
Doxepin	Loperamide	Pramipexole
Fluphenazine	Loratadine	Quetiapine
Flurazepam	Nortriptyline	Ranitidine
Hydroxyzine	Olanzapine	Risperidone
Hyoscyamine products	Prochlorperazine	Selegiline
Imipramine	Pseudoephedrine	Trazodone
Meperidine	Tiprolidine	Ziprasidone
Nitrazepam	Tolterodine	
Oxybutynin		
Perphenazine		
Solifenacin		
Trimipramine		

Effects of anticholinergic medication use on brain integrity in persons living with HIV and persons without HIV

Sarah A. Cooley[a], Robert H. Paul[b], Jeremy F. Strain[a], Anna Boerwinkle[a], Collin Kilgore[a] and Beau M. Ances[a,c,d]

Objective: This study examined relationships between anticholinergic medication burden and brain integrity in people living with HIV (PLWH) and people without HIV (HIV−).

Methods: Neuropsychological performance *z*-scores (learning, retention, executive function, motor/psychomotor speed, language domains, and global cognition), and neuroimaging measures (brain volumetrics and white matter fractional anisotropy) were analyzed in PLWH ($n = 209$) and HIV− ($n = 95$) grouped according to the Anticholinergic Cognitive Burden (ACB) scale (0 = no burden, 1–3 = low burden, >3 = high burden). Neuropsychological performance and neuroimaging outcomes were compared between HIV− and PLWH with high anticholinergic burden. Within a cohort of PLWH ($n = 90$), longitudinal change in ACB score over ~2 years was correlated to the rate of change per month of study interval in neuropsychological performance and neuroimaging measures.

Results: A higher number of anticholinergic medications and ACB was observed in PLWH compared with HIV− ($P < 0.05$). A higher ACB was associated with worse motor/psychomotor performance, smaller occipital lobe, putamen, subcortical gray matter and total gray matter volumes in HIV−; and poorer executive function, retention and global cognition, smaller brain volumes (frontal, parietal and temporal lobes, hippocampus, amygdala, cortex, subcortical gray matter and total gray matter), and reduced fractional anisotropy (posterior corpus callosum, perforant pathway) in PLWH. PLWH with high anticholinergic burden performed worse on tests of learning and executive function compared with HIV− with high anticholinergic burden. Longitudinally, PLWH who reduced their ACB over time had better neuropsychological performance and neuroimaging measures.

Conclusion: Anticholinergic medications were associated with worse neuropsychological performance and reduced structural brain integrity, and these effects were more widespread in PLWH. Use of anticholinergic medications should be carefully monitored in older adults with deprescription considered whenever possible.

AIDS 2021, **35**:381–391

Keywords: anticholinergics, cognition, HIV, neuroimaging

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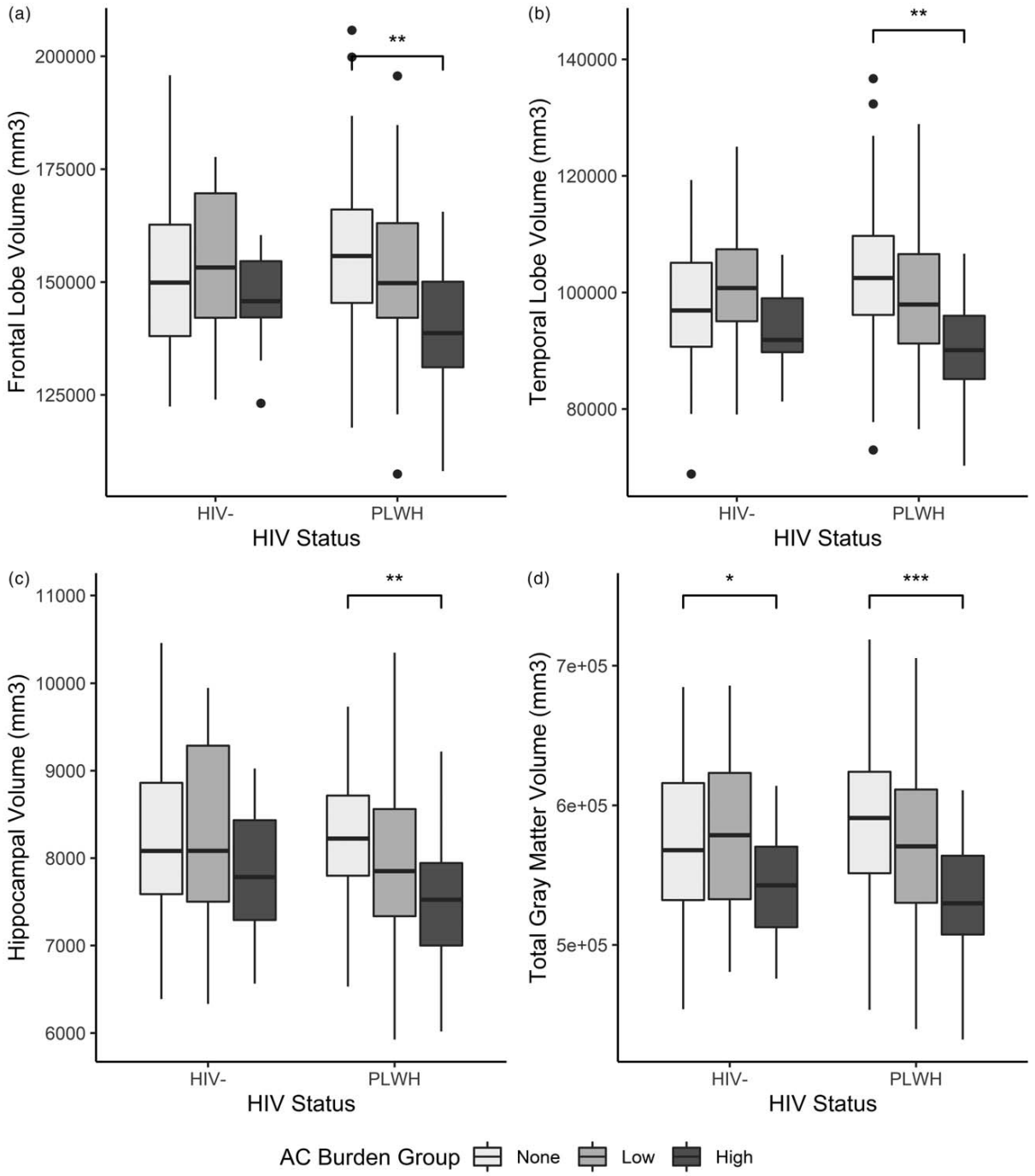

JAMDA 22 (2021) 56–64

JAMDA

journal homepage: www.jamda.com

Review Article

Anticholinergic Burden Measures Predict Older People's Physical Function and Quality of Life: A Systematic Review

Carrie Stewart PhD [a,*], Kaisa Yrjana BSc [a], Mitrysha Kishor BSc [a], Roy L. Soiza MD [b], Martin Taylor-Rowan PhD [c], Terence J. Quinn MD [c], Yoon K. Loke MD [d], Phyo Kyaw Myint MD [a,b]

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Keywords:
Anticholinergics
adverse outcomes
prognostic study
older adults
measurement scales

A B S T R A C T

Objectives: This systematic review (PROSPERO CRD42019115918) compared the evidence behind anticholinergic burden (ACB) measures and their ability to predict changes in older people's physical function and quality of life.
Design: Eligible cohort or case-control studies were identified systematically using comprehensive search terms and a validated search filter for prognostic studies. Medline (OVID), EMBASE (OVID), CINAHL (EMBSCO), and PsycINFO (OVID) databases were searched. Risk of bias, using Quality in Prognosis Studies tool, and quality of evidence, using the Grading of Recommendations, Assessment, Development and Evaluation, were assessed.
Setting and Participants: People aged 65 years and older from any clinical setting.
Measures: Any ACB measures were accepted (including the anticholinergic domain of the Drug Burden Index). Any global/multidimensional measure for physical function and/or quality of life was accepted for outcome.
Results: Thirteen studies reporting associations between ACB and physical function (n = 10) or quality of life (n = 4) were included. Exposure measures included Anticholinergic Cognitive Burden Scale, Anticholinergic Drug Scale, Anticholinergic Risk Scale, Clinician Rated Anticholinergic Score, and the anticholinergic domain of the Drug Burden Index. All studies were rated moderate risk of bias in ≥2 Quality in Prognosis Studies categories with 5 rated high risk in ≥1 categories. Seven of 10 studies (5251 of 7569 participants) reported significant decline in physical function with increased burden. All 4 studies (2635 participants) reporting quality of life demonstrated similar association with increased burden. High risk of biases and inadequate data reporting restricted analysis. There was no evidence to support one measure being superior to another.
Conclusions and Implications: The evidence supports association between increased ACB and future impairments in physical function and quality of life. No conclusion can be made regarding which ACB measure has the best prognostic value. Well-designed longitudinal studies are required to address this. Clinicians should be aware of patient's anticholinergic burden and consider alternative medications where appropriate.

Summary of Results for Studies Exploring Prognostic Relationships Between ACB Scale and Physical Function (n = 10)

Scale/Outcome	Studies	ACB (Baseline)	Physical Function (Baseline)	Statistical Approach	Results (Unadjusted)	Results (Adjusted)
ACBS (Range 0–3) ADL (≥1 ADL)	Brombo et al 2018[24]	ACBS ≤1: 381 (33.9%) ACBS ≥2: 348 (31.0%)	Any ADL: 542 (48.3%)	Multivariable logistic regression OR 95% CI (ACBS ≥1 vs ACBS = 0)	2.38 (1.37,4.13) $P = .002$	2.77 (1.39, 5.54) $P = .004$*
BI (Range 0–100)	Kolanowski et al 2015[29]	ACBS Mild: 81 (81.8%) ACBS Mod/Sev: 25 (25.2%)	NR	Multiple linear regression β (SE)	NR	Mild: −3.41 (2.14) P = NS† Mod/sev: 5.76 (1.99) $P \leq .05$
	Lopez-Matons et al 2018[33]	ACBS ≥1: 26.4%	BI (Mean, SD): 88.9 (18.5)	Difference in the BI scores between exposed and unexposed patients Mean (SD) (95% CI)	−4.3 (3.3) (−10.8, −2.2)	−4.0 (4.5) (−12.9, 4.9)‡
	Pasina et al 2013[34]	ACBS ≥1: 724 (58.8%)	NR	Correlation Pearson coefficient	0.004, $P = .91$	NR
FIM (Range 18–126)	Hershkovitz et al 2018[27]	ACB ≤1: 666 (76.6%) ACB ≥2: 203 (23.4%)	60.5 (17.8) 56.3 (18.7)	Multiple linear regression β (SE)	NR	−0.03 (0.85) $P = .02$§
IADL (Range 0–8)	Koyama et al 2014[31]	ACBS Mean (SD): 1.6 (1.9)	NR	Multiple logistic regression OR (95 % CI)	1.11 (1.04, 1.18) P = NR	1.11 (1.04, 1.19)‖ P = NR

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The authors declare no conflicts of interest.
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E-mail addresses: carrie.stewart@abdn.ac.uk, carrie.stewart1@outlook.com (C. Stewart).

https://doi.org/10.1016/j.jamda.2020.05.065

THE JOURNAL OF CLINICAL PSYCHIATRY

Bipolar Disorder

Reducing Anticholinergic Medication Burden in Patients With Psychotic or Bipolar Disorders

Ana M. Lupu, PharmD; Kimberly Clinebell, MD; Jessica M. Gannon, MD; Justin C. Ellison, PharmD, BCPP; and K. N. Roy Chengappa, MD, FRCPC

ARTICLE ABSTRACT

OBJECTIVE:

Anticholinergic medications are prescribed to treat extrapyramidal side effects (EPS) associated with antipsychotics. Anticholinergic medications cause several side effects and can often be withdrawn during the maintenance phase of antipsychotic treatment without EPS reemergence. The purpose of this quality improvement (QI) project was to reduce anticholinergic medication burden and improve quality of life in patients with severe mental illness.

Come?

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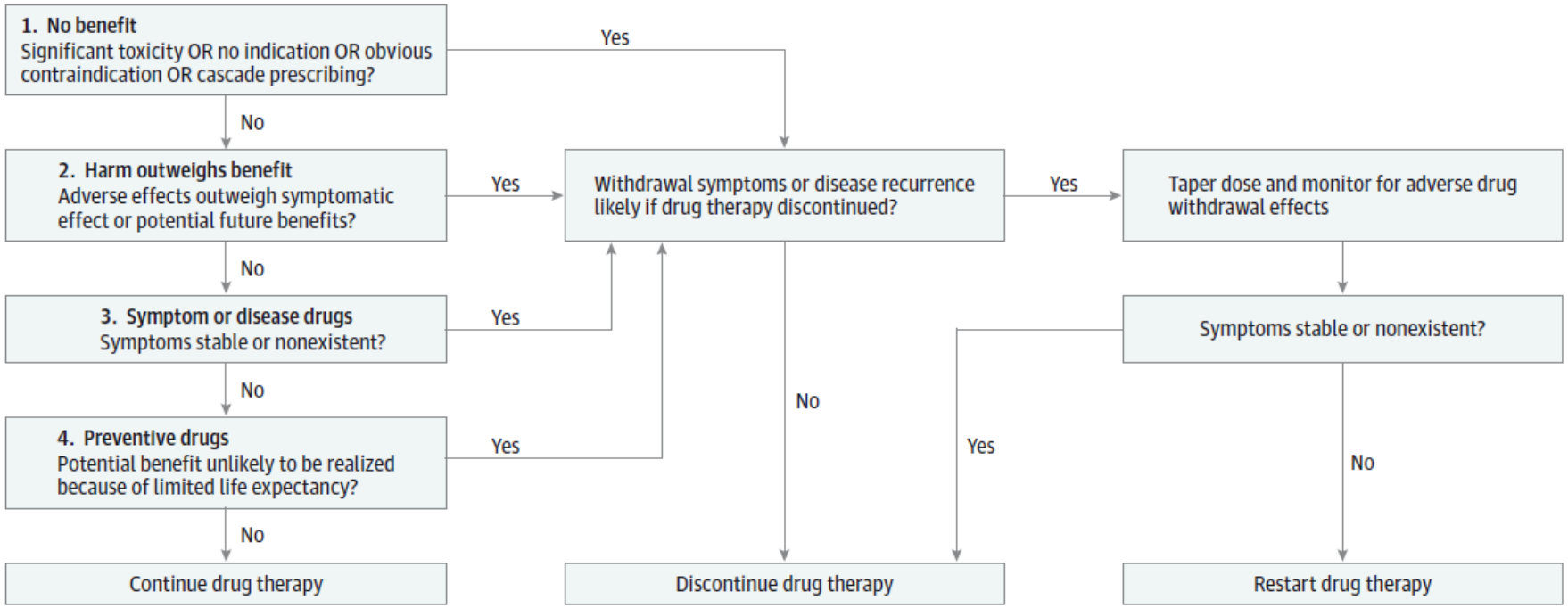
Algorithm for drug discontinuation

Deprescribing = planned and supervised process of dose reduction or stopping of medications that may be causing harm or no longer provide benefit



Website for deprescribing of medications: **MedStopper**: http://medstopper.com

http://deprescribing.org website providing algorithms on deprescribing of PPI, BZD and antidiabetics

Scott IA et al. JAMA Intern Med 2015

CISAI FONDAZIONE ASIA

Technology-based Counselling

AIDS and Behavior (2020) 24:2463–2465
https://doi.org/10.1007/s10461-020-02880-8

NOTES FROM THE FIELD

It is Time to Include Telehealth in Our Measure of Patient Retention in HIV Care

Dima Dandachi[1,2] · Jennifer Freytag[3,4,5] · Thomas P. Giordano[4,5,6] · Bich N. Dang[4,5,6]

Current HIV/AIDS Reports (2019) 16:113–119
https://doi.org/10.1007/s11904-019-00430-z

T ENCE OF PREVENTION (JD STEKLER AND JM BAETEN, SECTION EDITORS)

Check for updates

CrossMark

A Review of Telehealth Innovations for HIV Pre-Exposure Prophylaxis (PrEP)

Rebecca Touger[1] · Brian R. Wood[2]

BMJ Open

Telehealth and texting intervention to improve HIV care engagement, mental health and substance use outcomes in youth living with HIV: a pilot feasibility and acceptability study protocol

Angie R Wootton,[1] Dominique A Legnitto,[1] Valerie A Gruber,[2] Carol Dawson-Rose,[3] Torsten B Neilands,[1] Mallory O Johnson,[1] Parya Saberi[1]

Table 1 Study overview

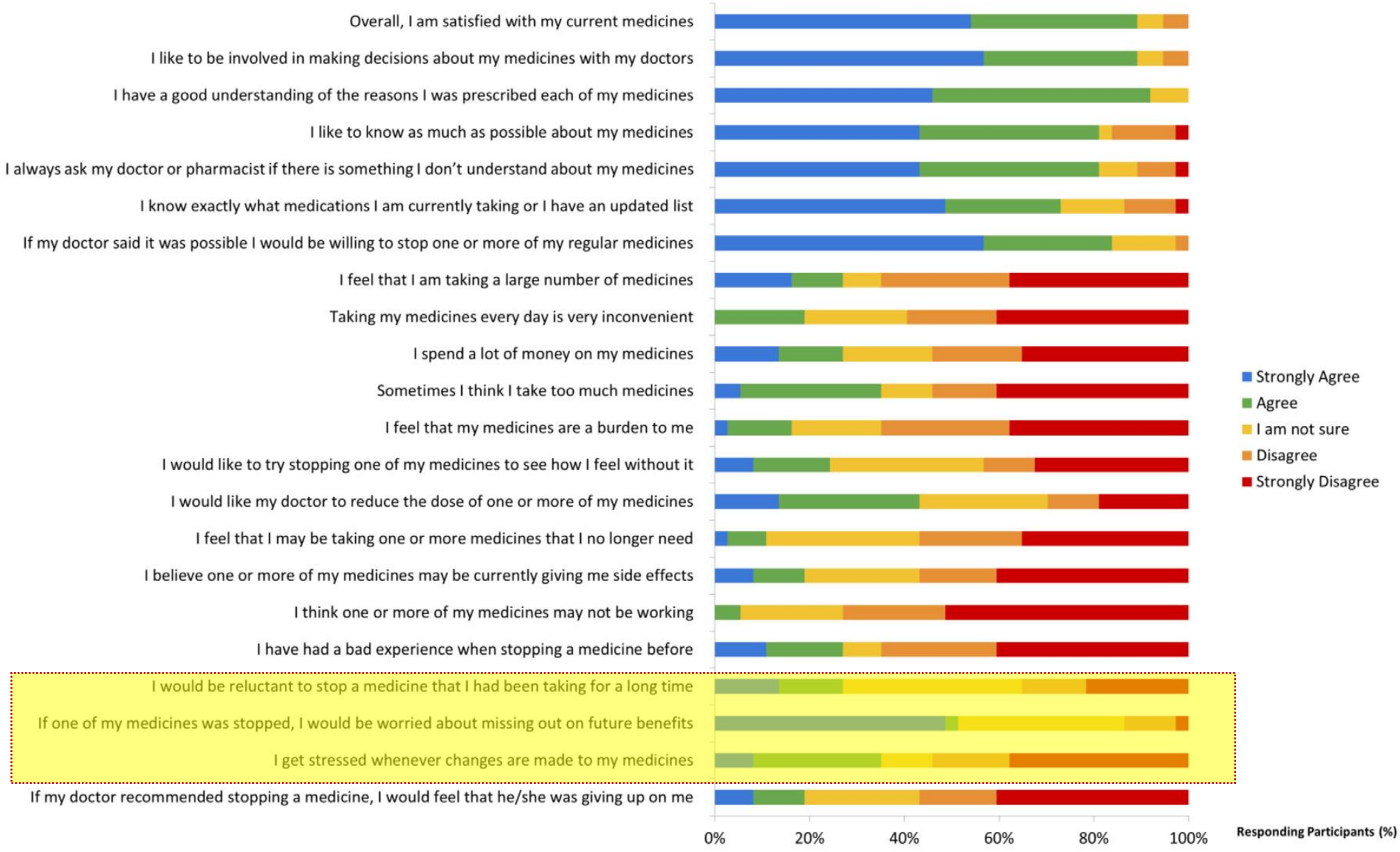
I=intervention arm participants W=waitlist arm participants X=all participants	Months 0	1	2	3	4	5	6	7	8
Screening/enrolment									
Telephone screening	X								
Informed consent		X							
Assessment surveys									
Baseline survey		X							
Follow-up surveys					X				X
Satisfaction and acceptability questionnaire					I				W
Counselling sessions									
Weekly counselling sessions (12)		I	I	I	I	W	W	W	W
Bidirectional text messages									
Monthly check-ins			W	W	W		I	I	I
Session ratings		I	I	I	I	W	W	W	W
Goal reminders		I	I	I	I	W	W	W	W
Session reminders (24 hours and 15 min before telehealth session)		I	I	I	I	W	W	W	W
Community events and resources		X	X	X	X	X	X	X	X
Exit interviews									
Satisfaction survey					I				W
Qualitative exit interviews					I				W

CISAI FONDAZIONE ASIA

Technology-based Counselling – an opportunity?

Elder PLWH opinions

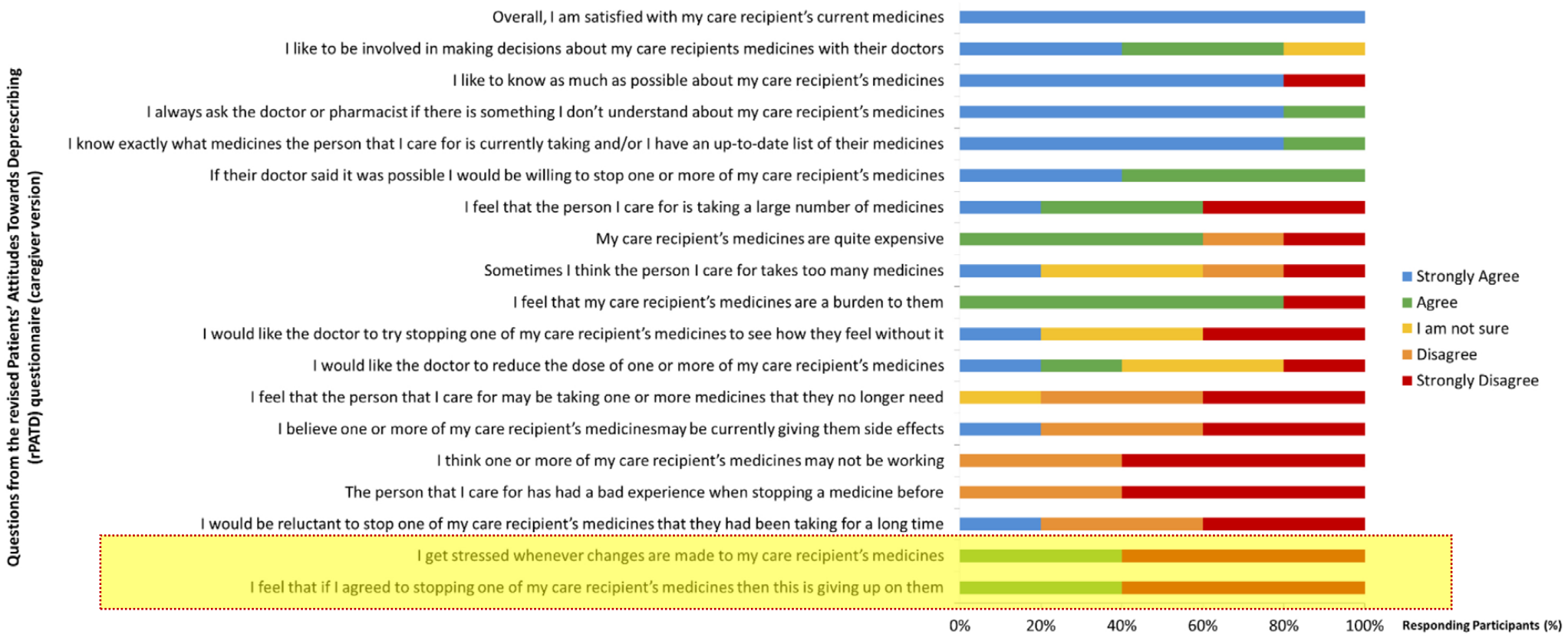
42 Elder PLWH, on cART, 2018



Serrano Gimenez R, et al. Rev Esp Quim 2020

Elder PLWH doctors' opinions

42 Elder PLWH, on cART, 2018



Serrano Gimenez R, et al. Rev Esp Quim 2020

Undertreatment vs. Overtreatment

Two examples of suboptimal care

Editorials

Overtreatment and undertreatment:

time to challenge our thinking

Kearney M, et al. Brit J Gen Practice 017

CISAI FONDAZIONE ASIA

Undertreatment vs. Overtreatment
Two examples of suboptimal care

Implementation of multiple single-condition guidelines

- can lead to pursuit of tight glycaemic or blood pressure control that does not take account of multimorbidity and individual risks and benefits
- **It is easier to prescribe than to have a complex consultation**

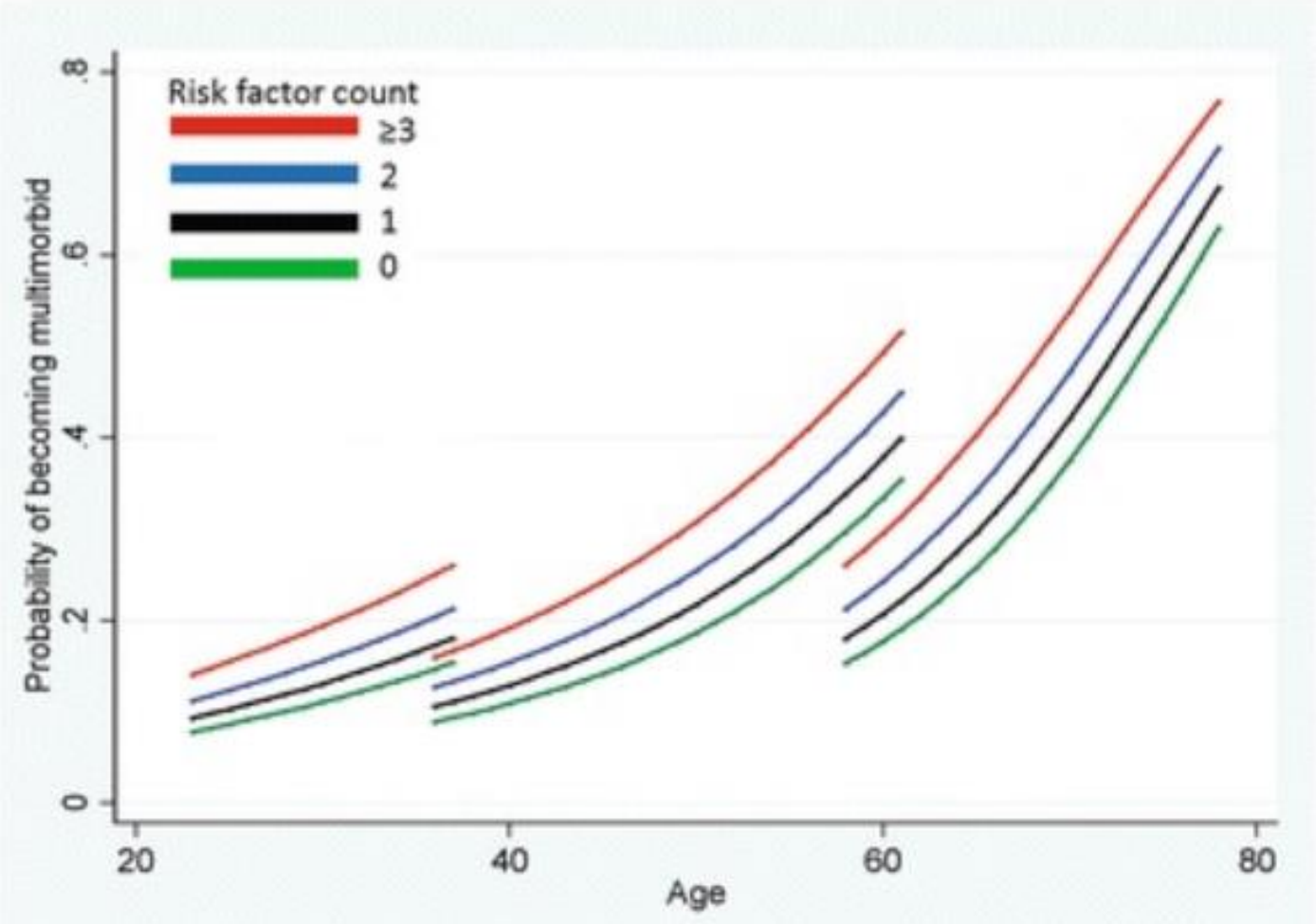
But not taking in care guidelines is highly detrimental

- In people with known atrial fibrillation (AF) who suffer a stroke, 47% have not been anticoagulated before their stroke despite the overwhelming evidence of benefit
- In 17700 patients woth specific preventive treatment clinically indicated before their first stroke, 52% did not receive an anticoagulant, 25% did not receive an antihypertensive, and 49% did not receive a statin

Kearney M, et al. Brit J Gen Practice 017

CISAI FONDAZIONE ASIA

The contribution of risk factors to the predicted probability of developing multimorbidity over 5-year periods across the life course in Twenty-07 cohort



Risk factors

- Smoking
- BMI
- Physical activity
- Fruit & veg consumption
- Alcohol intake

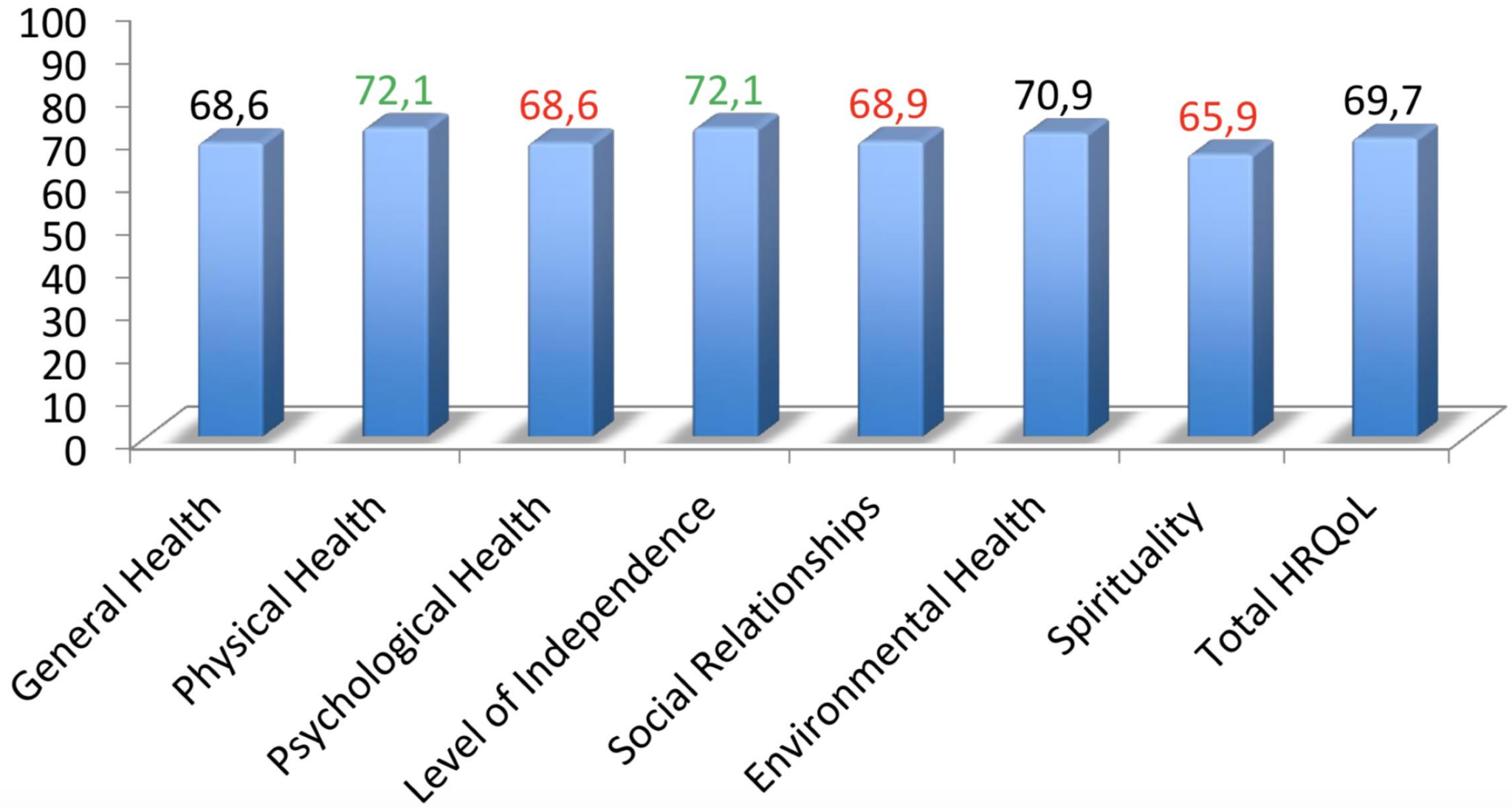
(Adjusted for age, age squared, age cubed, sex, cohort, previous multimorbidity, time between waves, and cohort*sex interaction)

Katikireddi SV et al BMC Med 2017

CISAI FONDAZIONE ASIA

Health-related quality of life of people with hiv living in Spain

1462. Edad media 45 ± 10



Fuster MJ.

seisida
SOCIEDAD ESPAÑOLA INTERDISCIPLINARIA DEL SIDA

Conclusioni

- I pazienti anziani che vivono con HIV hanno un tasso di co-morbidità e co-patologie elevato e, in confronto a controlli HIV-negativi, una qualità della vita peggiore
    - Mortalità significativamente maggiore in US
- Gestione complessiva della salute
- Interventi farmacologici mirati con ottimizzazione della terapia antiretrovirale (pochi dati) e concomitante (pochi dati in ELWH) ma alcuni principi:
    - Evitare interazioni farmacologiche significative
    - Evitare effetto su SNC e pressione
    - De-prescrizione personalizzata

Pintassilgo *et al. BMC Infectious Diseases* (2020) 20:290
https://doi.org/10.1186/s12879-020-05020-8

BMC Infectious Diseases

CORRESPONDENCE

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The Lisbon patient: exceptional longevity with HIV suggests healthy aging as an ultimate goal for HIV care

Ines Pintassilgo[1], Matteo Cesari[2,3], Henrique N. Santos[4], Jovana Milic[5,6,7], Iacopo Franconi[5,6], Cristina Mussini[5,6], Nuno Marques[4] and Giovanni Guaraldi[5,6*]

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Amedeo de Nicolò

geppo cohort

GEriatric Patiens living with HIV/AIDS
a Prospective multidimensional cOhort

Aging is an extraordinary process where you become the person you always should have been.

David Bowie