

Future challenges for clinical care of an ageing population infected with HIV: a “geriatric -HIV” modelling study

Guaraldi G¹, De Francesco D², Malagoli A¹,
Theou O³, Zona S¹, Carli F¹, Dolci G¹, Mussini C¹,
Kirkland S⁴, Mussi C⁵, Cesari M⁶, Rockwood K⁷

1 Department of Medical and Surgical Sciences for Adults and Children, Clinic of Infectious Diseases, University of Modena and Reggio Emilia;
2 HIV Epidemiology and Biostatistics Group (HEBG) at UCL – London;
3 Geriatric Medicine Research, Dalhousie University;
4 Department of Community Health & Epidemiology, Dalhousie University;
5 Geriatrics Division, University of Modena and Reggio Emilia, Modena, Italy;
6 Gérontopôle, Centre Hospitalier Universitaire de Toulouse, Toulouse, France;
7 (1) Geriatric Medicine Research, Dalhousie University; (2) Geriatric Medicine, Institute of Brain & Behavioural Sciences, University of Manchester



Background

- The average age HIV-positive patients' is constantly increasing;
 - HIV-specialist physician' average age is constantly increasing;
- ... this is a matter of fact



5 years
1st day of school



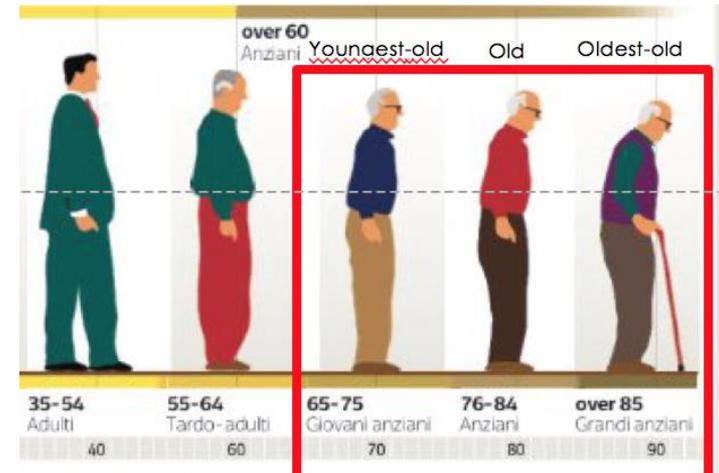
25 years
MD degree



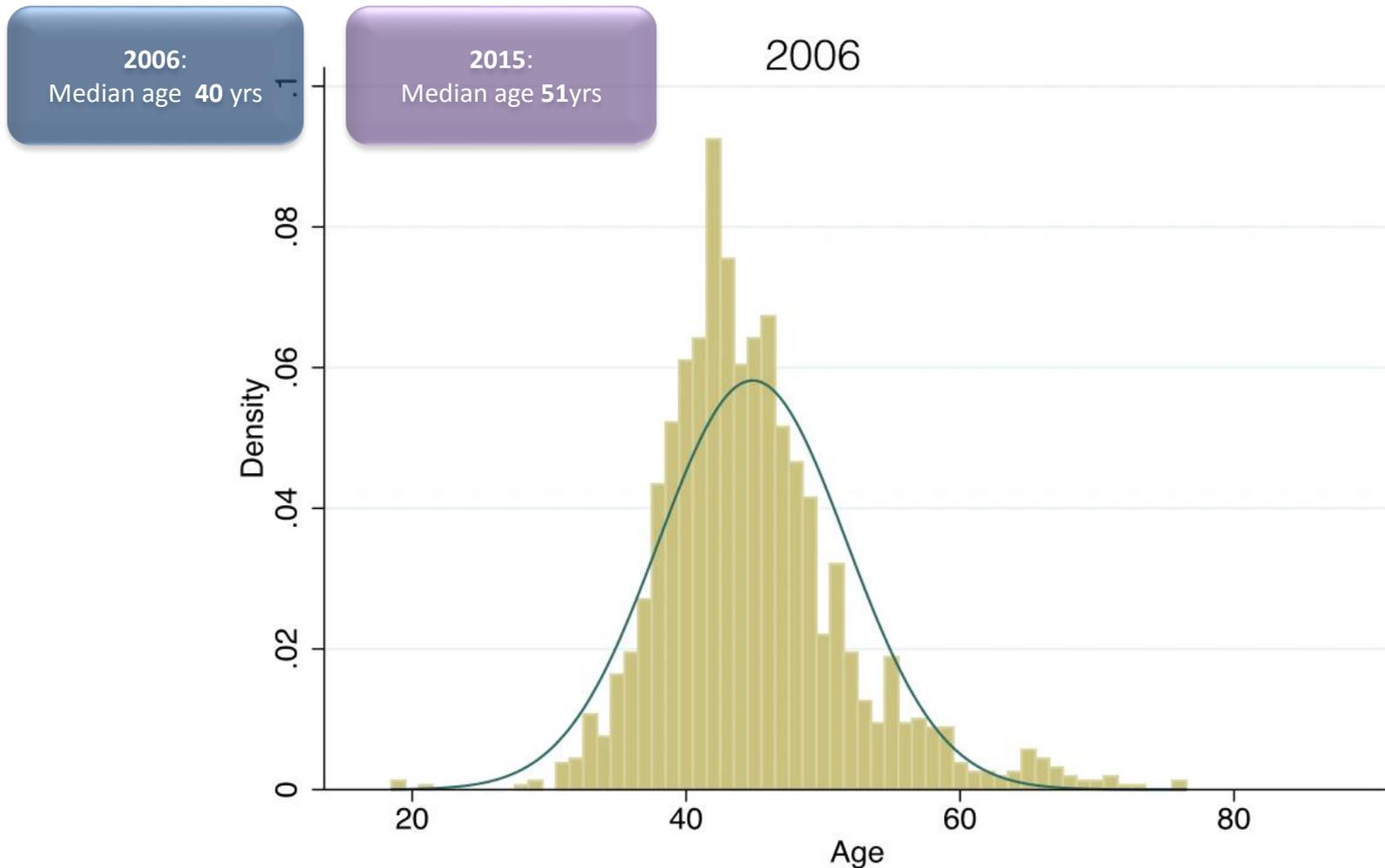
50 years,
NOT YET OLD!

A geriatric definition of old-Age:

65-75 YRS: Youngest old, 76-84 YRS: Old; >85: Oldest-old



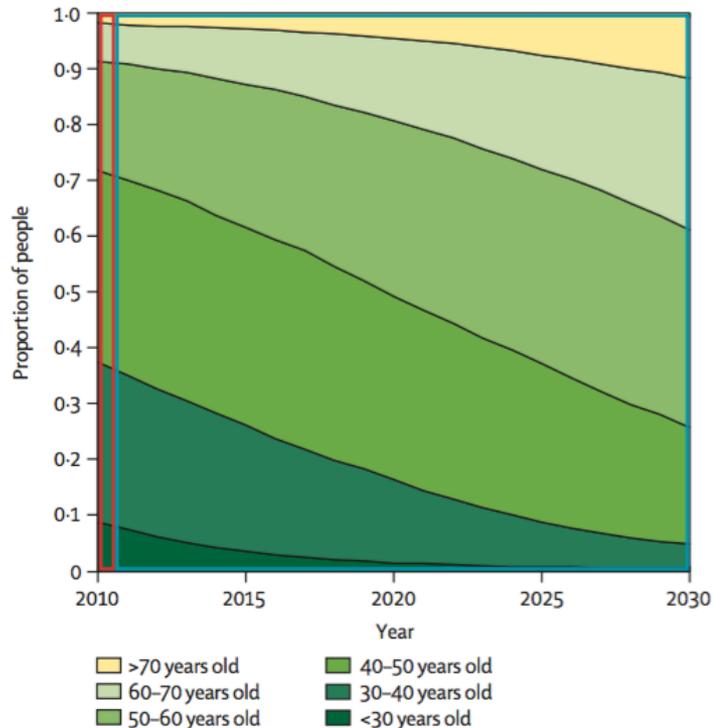
Age distribution of HIV+ patients attending MHMC



Future challenges for clinical care of an ageing population infected with HIV: a modelling study



Mikaela Smit, Kees Brinkman, Suzanne Geerlings, Colette Smit, Kalyani Thyagarajan, Ard van Sighem, Frank de Wolf, Timothy B Hallett, on behalf of the ATHENA observational cohort

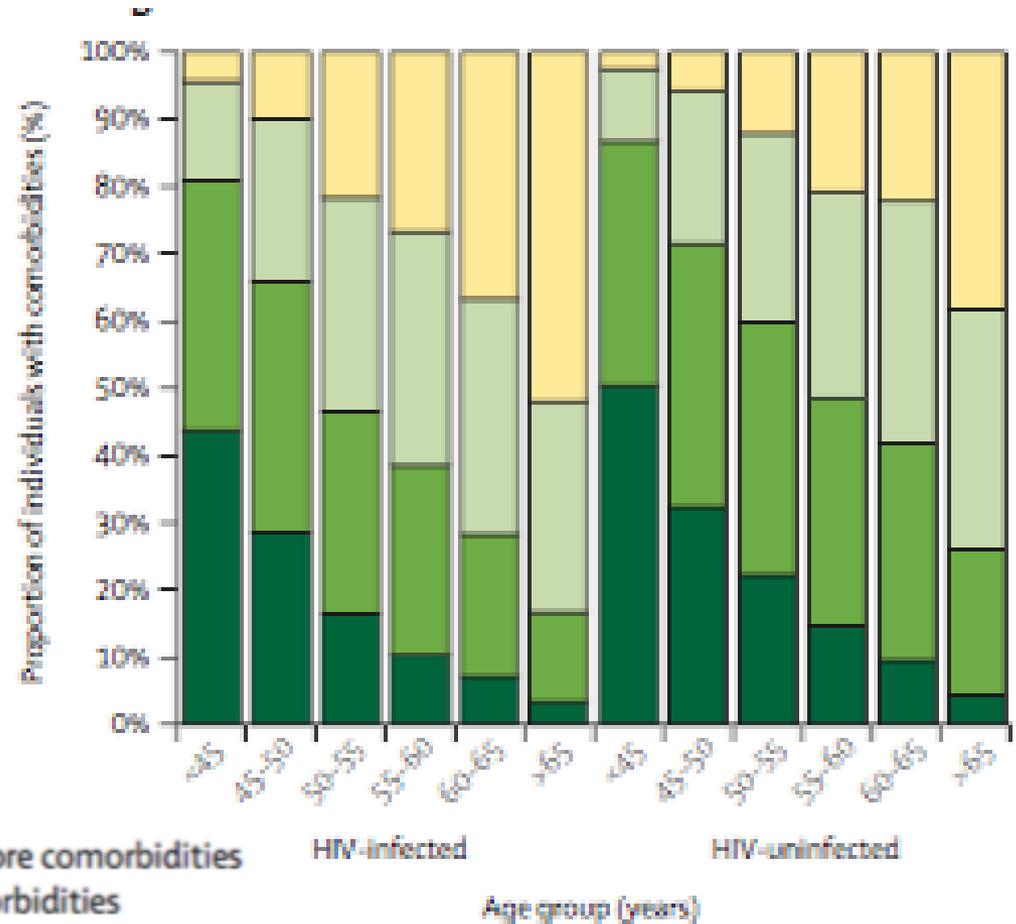
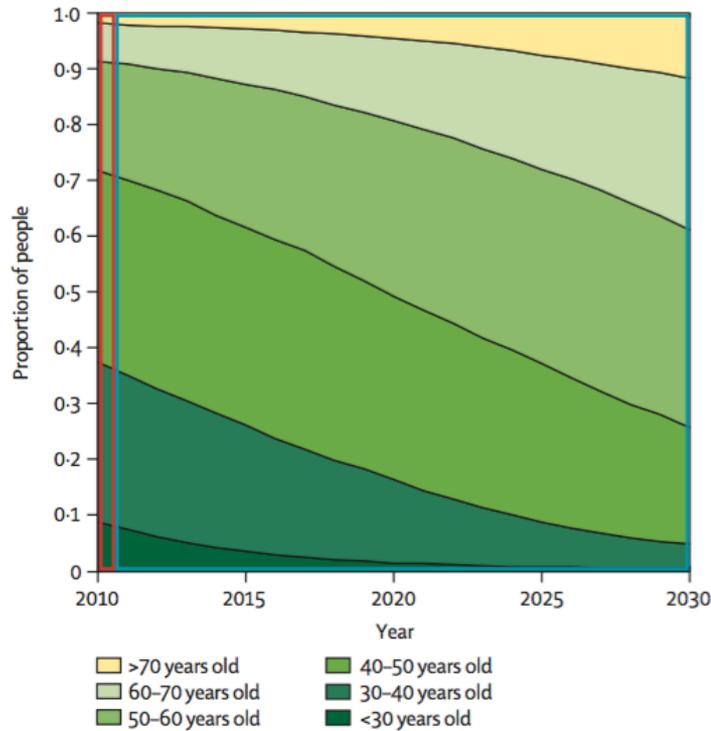


In the ATHENA cohort, proportion of patients on ART aged ≥ 50 years old will increase from 28% to 73% between 2010 and 2030

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The burden of NCDs mostly driven by larger increases in cardiovascular disease

While people generally accumulate more health problems with age, not everyone of the same age experiences the same health status or risk for adverse outcomes



83 years old;
HTN, Hyperlipidemia, prior MI



83 years old;
HTN, Hyperlipidemia, prior MI

Frailty has been proposed as a measure of biological (opposed to chronological) aging and a measure of overall health status

Objective

We aimed to estimate levels of Frailty and its implications for HIV care in Italy up to 2030.

Falls and Instrumental Activities of Daily Living (IADL) were used as proxy of geriatric syndromes and disability in the geriatric population

Methods

- ✓ Geriatric age categories were chosen: <35, 35-49, 50-64, 65-75, >75
- ✓ An individual-based model of the ageing population of the Modena HIV Metabolic Clinic cohort (MHMC) was constructed using data collected between 2009 and 2015 from 2982 patients.
- ✓ The model follows patients enrolled to the clinic up to 2015 and generates new entries on a yearly basis up to 2030. Number, age and gender of new entries were modelled using trends observed in the period 2009-2015.
- ✓ The relationship between age and gender, falls and disability, observed in 2014-2015 at MHMC was postulated to constant over time.

Methods

- **Frailty Index (FI)**, quantified as the proportion of deficits present out of a total of 37. FI at enrolment was generated from a Gamma distribution with age- and gender-specific parameters estimated using the MHMC 2009-2015 data.
- We defined Frail a patient with FI between 0.3 and 0.4 and Most-frail a patient with $FI > 0.4$.
- Changes in the FI over a one-year period and death rates were modelled following a validated mathematical model developed in a large Canadian ageing population with parameters adjusted to best represent the changes observed in the MHMC 2009-2015 population.

Geriatric syndromes were evaluated by means of a self-reported fall frequency in the past 12 months and defined as one or more **falls** (i.e. unexpectedly dropping to the floor or ground from a standing, walking, or bending position).

Disability was assessed with **IADL**: 8 categories of activities of daily function (housekeeping, money management, cooking, transportation, telephone use, shopping, laundry, medication management) and defined as impairment in ≥ 1 categories.

Results

Socio-demographic, anthropometric and lifestyle characteristics

	HIV-positive (N=2982)
Gender, n (%)	
Female	951 (31.9%)
Age in years, median (IQR)	49 (45, 54)
BMI (kg/m ²), median (Q1, Q3)	23.5 (21.4, 26.0)
Waist (cm), median (Q1, Q3)	87 (81, 94)
Smoking, n (%)	
No smoking	1756 (58.9%)
1-10 cigarettes per day	516 (17.3%)
>10 cigarettes per day	672 (22.5%)

HIV-specific characteristics

	HIV-positive (N=2982)
Likely route of transmission, n (%)	
Homosexual sex	881 (29.5%)
CDC classification "C", n (%)	699 (23.4%)
Years since HIV diagnosis, median (Q1, Q3)	19.7 (12.8, 24.4)
Currently on cART, n (%)	2810 (92.5%)
Duration of cART (years), median (Q1, Q3)	5.2 (2.6, 7.8)
Currently on NRTIs, n (%)	2319 (82.5%)
Currently on PIs, n (%)	1550 (55.2%)
Currently on NNRTIs, n (%)	1103 (39.3%)
Currently on other drugs, n (%)	569 (20.6%)
CD4 count (cells/ μ L), median (Q1, Q3)	648 (474, 841)
Nadir CD4 count (cells/ μ L), median (Q1, Q3)	200 (86, 300)

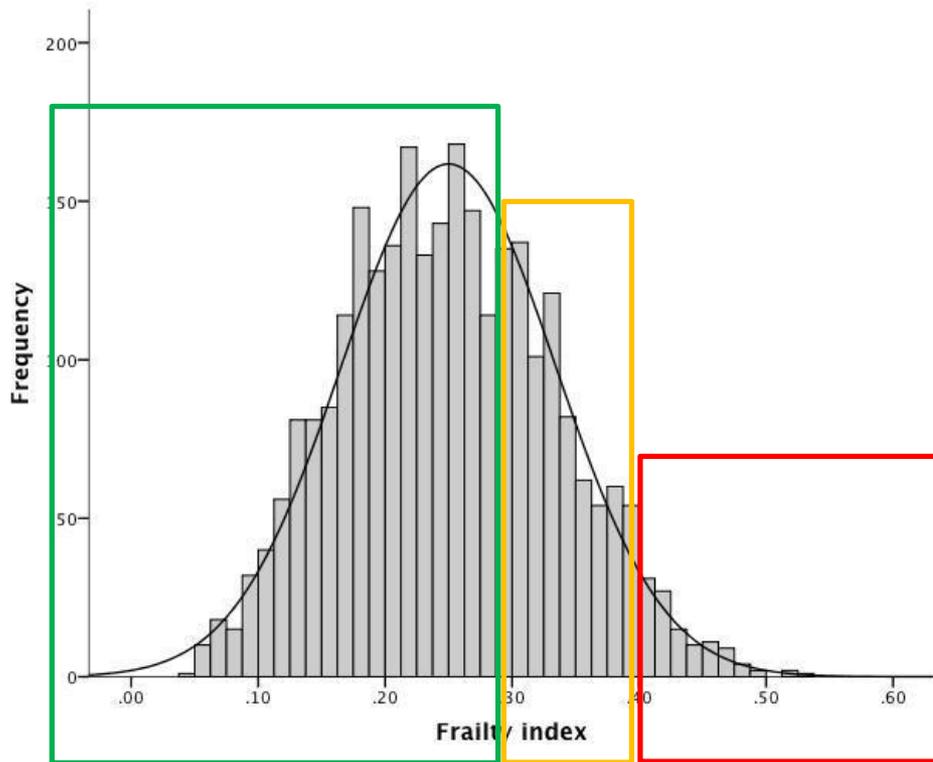
Prevalence of comorbidities

	MHMC (N=2982)
Cardiovascular disease, n (%)	142 (4.8%)
Hypertension, n (%)	1088 (36.5%)
Impaired Fasting Glucose, n (%)	602 (20.2%)
Type 2 Diabetes, n (%)	393 (13.2%)
Lipodystrophy, n (%)	2265 (76.0%)
Dyslipidaemia, n (%)	2449 (82.1%)
NAFLD, n (%)	701 (23.5%)
Renal Insufficiency, n (%)	284 (9.5%)
CKD, n (%)	28 (0.9%)
Liver cirrhosis, n (%)	352 (11.8%)
Vitamin D insufficiency, n (%)	2061 (69.1%)
Osteoporosis, n (%)	269 (9%)
COPD, n (%)	91 (3.1%)
Any AIDS malignancy, n (%)	77 (2.6%)

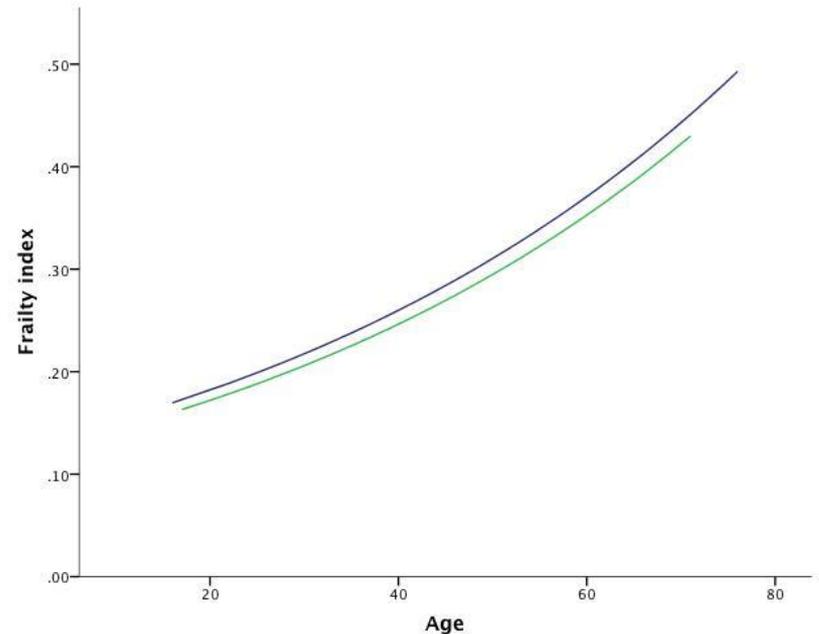
Prevalence of comorbidities

	MHMC (N=2982)	ATHENA (N=10278)
Cardiovascular disease, n (%)	142 (4.8%)	372 (4%)
Hypertension, n (%)	1088 (36.5%)	2379 (23%)
Impaired Fasting Glucose, n (%)	602 (20.2%)	
Type 2 Diabetes, n (%)	393 (13.2%)	578 (6%)
Lipodystrophy, n (%)	2265 (76.0%)	
Dyslipidaemia, n (%)	2449 (82.1%)	
NAFLD, n (%)	701 (23.5%)	
Renal Insufficiency, n (%)	284 (9.5%)	
CKD, n (%)	28 (0.9%)	1399 (14%)
Liver cirrhosis, n (%)	352 (11.8%)	
Vitamin D insufficiency, n (%)	2061 (69.1%)	
Osteoporosis, n (%)	269 (9%)	829 (8%)
COPD, n (%)	91 (3.1%)	
Any AIDS malignancy, n (%)	77 (2.6%)	765 (7%)

FI distribution at MHMC

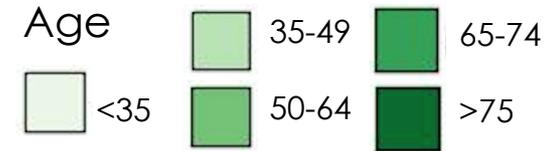
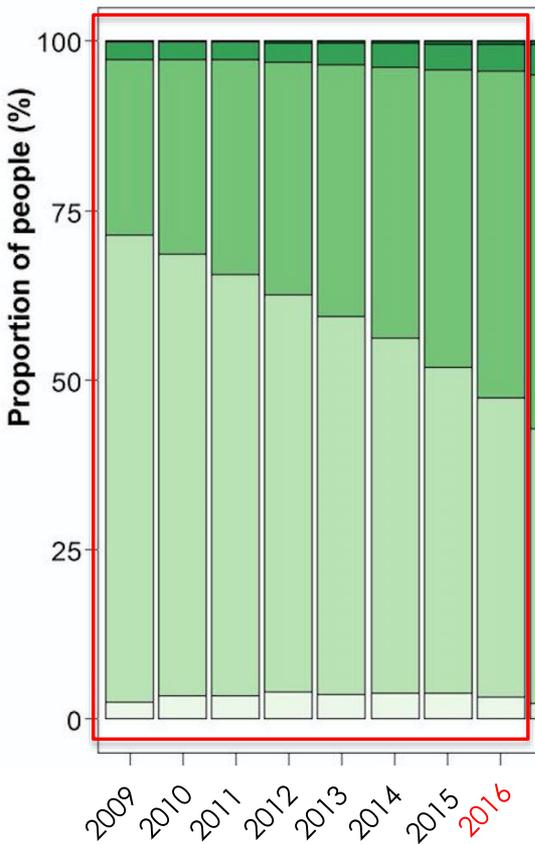


Distribution of frailty index scores at first visit. Bars represent 0.01 frailty index score groupings. Solid line indicates normal distribution.



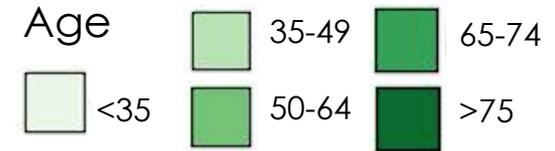
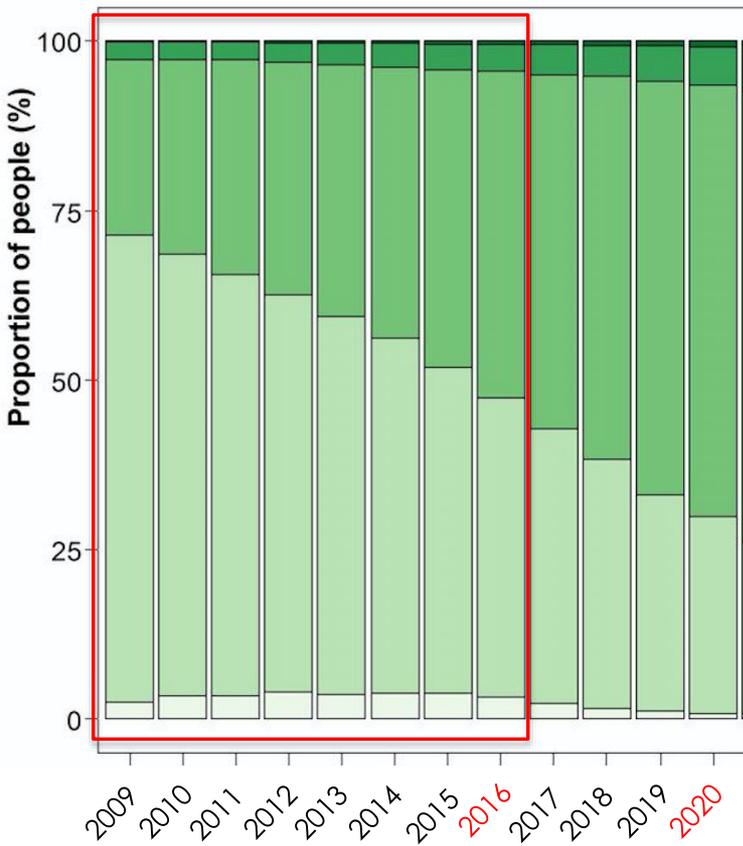
Average frailty index score at each age. Lines represent exponential best fit. Solid line is men, dashed line is women.

Observed (red area) and projected age distribution of HIV-infected patients



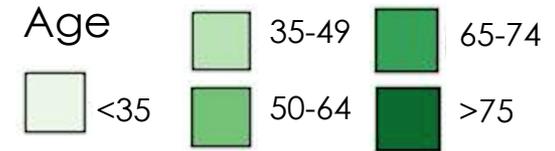
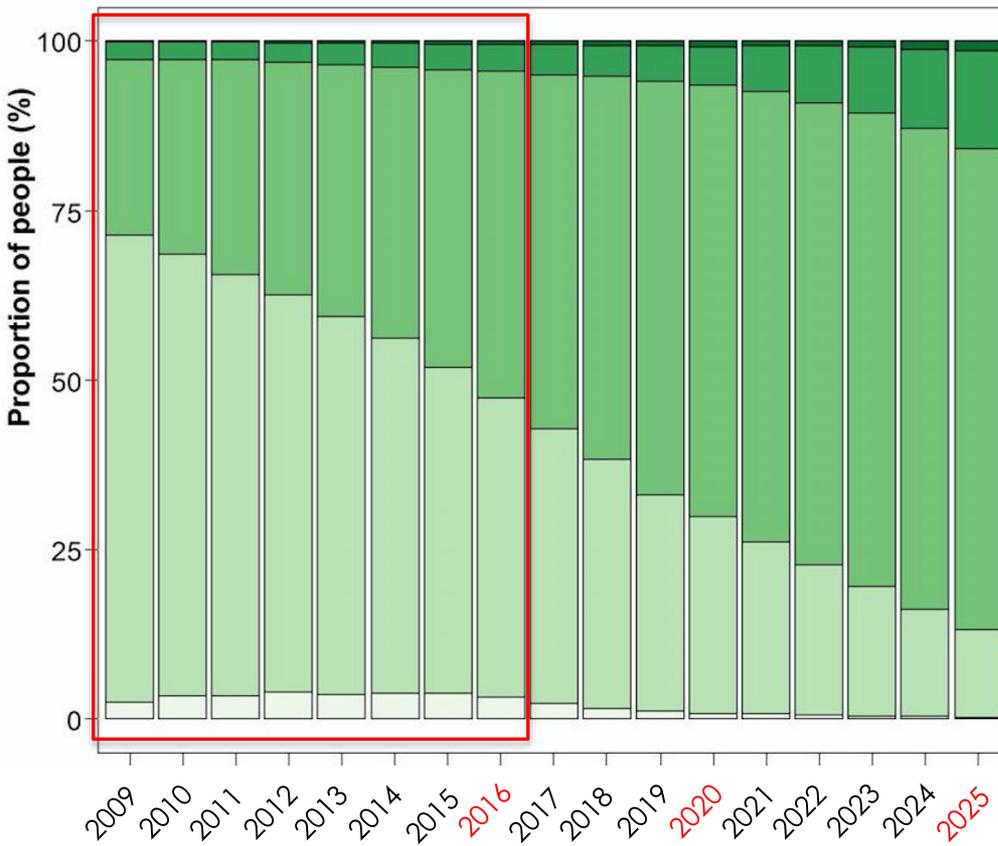
Geriatric Age categories	65-7 yrs	>74 yrs
2016	3.8%	0.5%

Observed (red area) and projected age distribution of HIV-infected patients



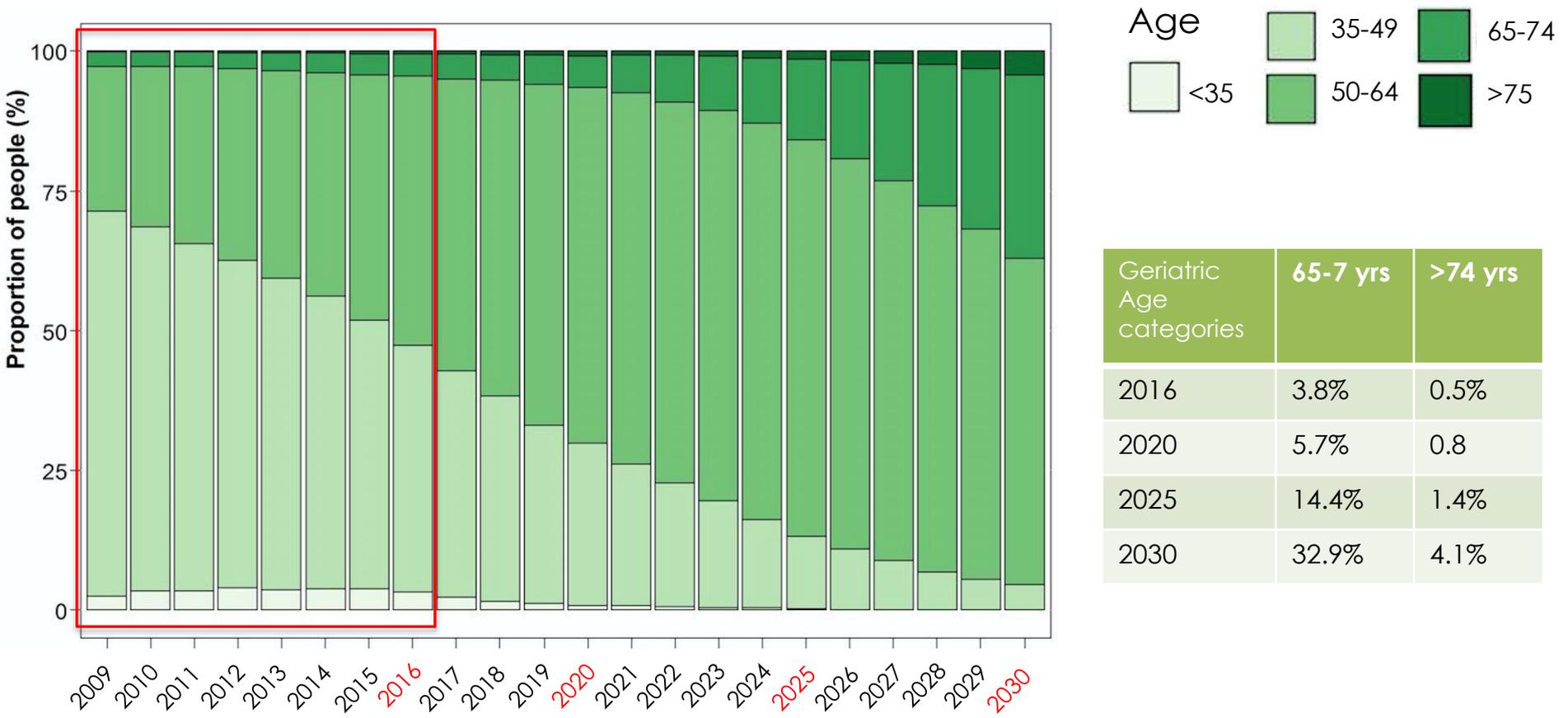
Geriatric Age categories	65-7 yrs	>74 yrs
2016	3.8%	0.5%
2020	5.7%	0.8

Observed (red area) and projected age distribution of HIV-infected patients



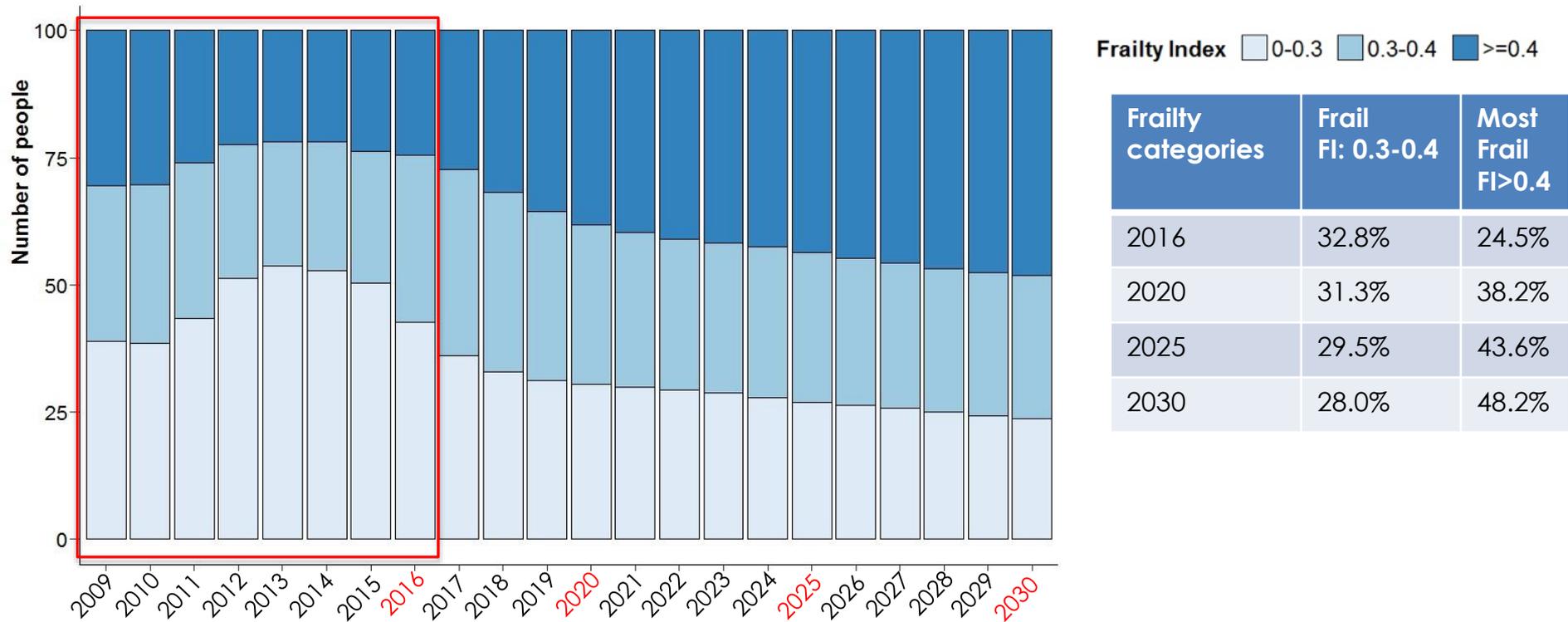
Geriatric Age categories	65-7 yrs	>74 yrs
2016	3.8%	0.5%
2020	5.7%	0.8
2025	14.4%	1.4%

Observed (red area) and projected age distribution of HIV-infected patients



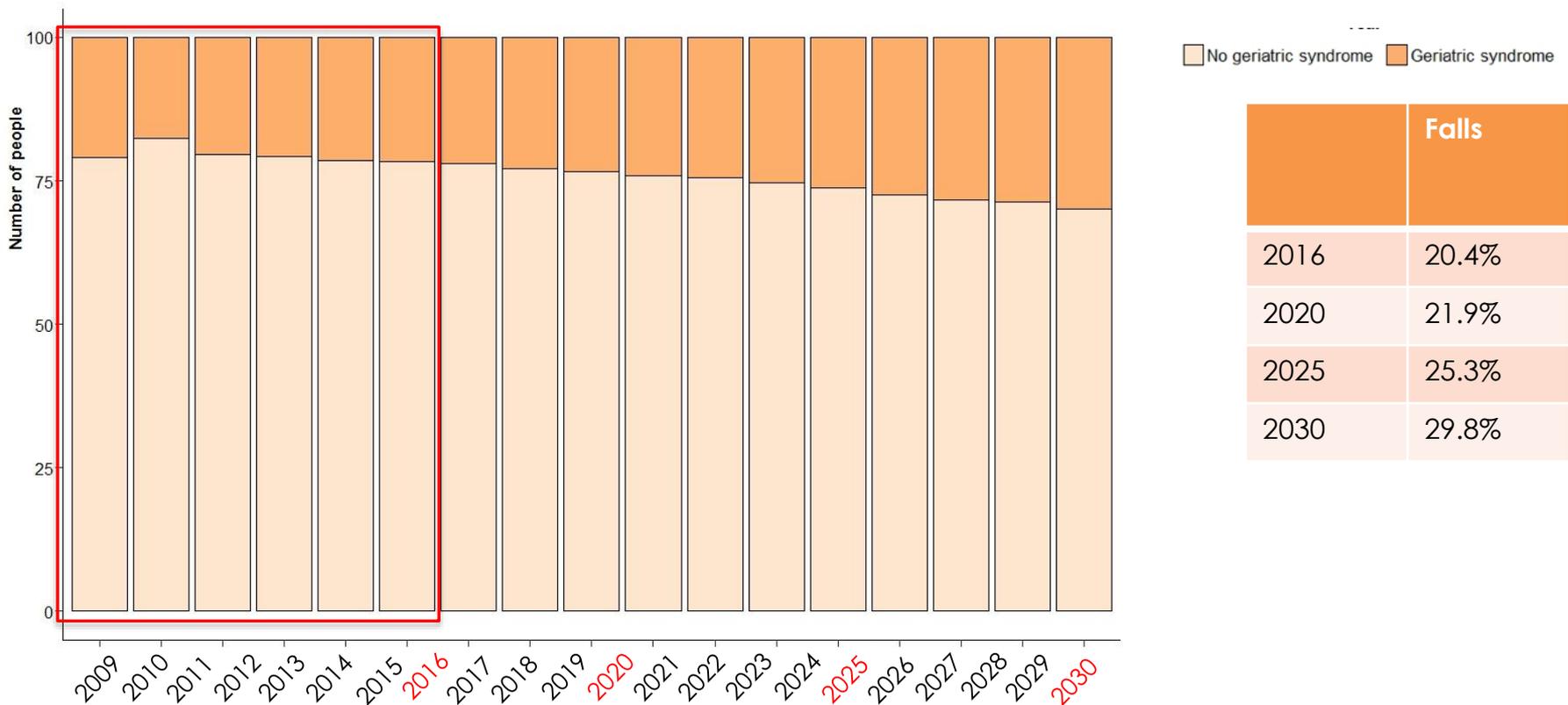
In 15 years time the HIV geriatric population will increase from 4% to 37%

Observed (red area) and predicted burden of Frailty in HIV-infected patients between 2009 and 2030 as simulated by the model



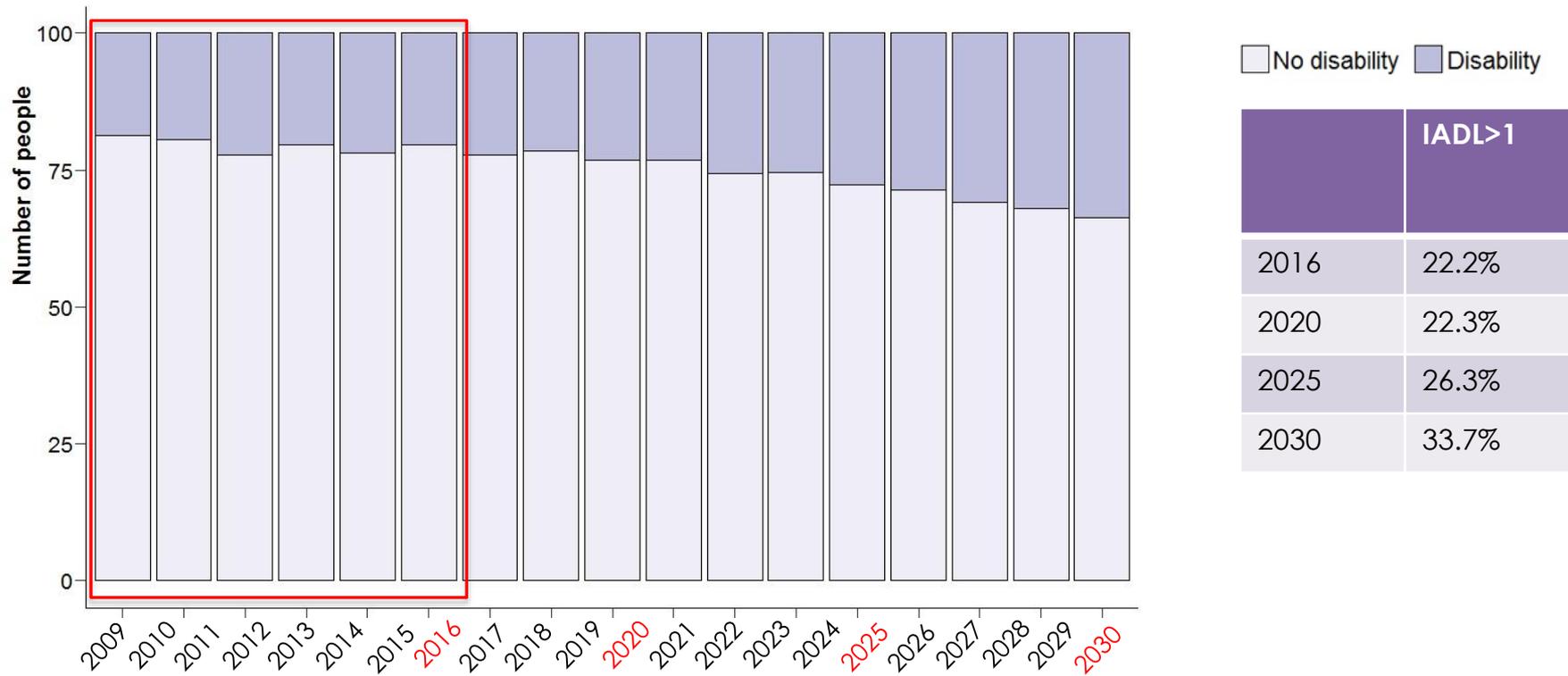
In 15 years time the most frail HIV population will increase from 24% to 48%

Observed (red area) and predicted burden of Falls in HIV-infected patients between 2009 and 2030 as simulated by the model



In 15 years time 30% of PLWH will experience a geriatric syndrome

Observed (red area) and predicted burden of IADL in HIV-infected patients between 2009 and 2030 as simulated by the model



In 15 years time 34% of PLWH will be disable

Discussion

- HIV and ageing epidemic is far beyond than a simple age shift or an increase prevalence in age-related comorbidities.
- The increasing numbers of older patients with frailty, falls and disability depict an “**geriatric -HIV**” scenario.
- When Multi-morbidity is the norm, **frailty and disability** turn to be relevant clinical outcomes and allows patient risk stratification and tailored clinical interventions
- We believe that our results can be generalised to other high-income countries with mature epidemics and good access to HIV care.

Study limitations

- The relationship between age and gender, falls and disability, was postulated to constant over time
- The model does not simulate the heterogeneity of lifestyle factors (eg, diet, smoking, and exercise) or effect of individual antiretroviral drug use on the development of Frailty
- Falls and Disability were modeled on the basis of age projection and not (yet) stratified by FI categories

The Geriatric-HIV model

Clinical Implications

- Geriatricians and occupational therapist must be part of the interdisciplinary team taking care of HIV patients
- The Comprehensive Geriatric Assessment may introduce in HIV care a Multi-dimensional approach which include patients related outcomes, QoL, neurocognitive impairment, physical function, geriatric syndromes.
- Patient visit diversification must be built in an individualised management plan focused on quality of life and prevention of disability

The Geriatric-HIV model

Research Implications

- ✓ Lack of disability should be used to compare “healthy life-expectancy” in HIV cohorts in comparison to the general population.
- ✓ HIV-infected population has been largely ignored, with most Randomised trials of ART have ignored older patients or excluding people with multimorbidity.
 - ✓ Physical function (SPPB) cognitive function (MoCA) and frailty (FI and Frailty Phenotype) can be used in RCT to stratify patient characteristics.
 - ✓ QoL, geriatric syndromes and disability may be used as clinical end points in HIC clinical trials



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

16 December 2015
EMA/CHMP/778709/2015
Committee for Medicinal Products for Human Use (CHMP)

Points to consider on frailty: Evaluation instruments for baseline characterisation of clinical trial populations
Draft

Draft agreed by Frailty PtC drafting Group	March 2015
Draft agreed by Working parties	May 2015
Draft agreed by Guidelines Consistency Group	November 2015
Adopted by CHMP for release for consultation	16 December 2015
Start of public consultation	21 December 2015
End of consultation (deadline for comments)	31 May 2016
Adoption by CHMP	
Date for coming into effect	

The Geriatric-HIV model

INTERPRETATION

To our knowledge, this is the first model that has quantified burden of disease.

In addition to demographic projections for a developed country with an ageing epidemic the model captures the key factors affecting clinical care of HIV-infected patients, including Frailty, geriatric syndrome and disability providing evidence for the development of new clinical and research intervention for PLWH.

The new target

90-90-90-90-90

90% diagnosed

90% on treatment

90% virally suppressed

90% fit at 90 years



Thank you....
...and stay fit!