HIV and obesity: the global collision of infectious and non-communicable diseases

26 September 2024

WCE
WORLD CONGRESS OF EPIDEMIOLOGY 2024

Speaker Biographies

HIV as model for obesity care
Dr Nomathemba Chandiwana-Ezintsha

HIV & Obesity
Prof Francois Venter- Ezintsha

HIV and Cardiovascular disease
Dr Morné Kahts

Symposium objectives

1. Present strategies for integrating obesity care into existing HIV healthcare systems, drawing from successful HIV program models.
2. Examine how HIV and antiretroviral therapies influence obesity rates and related health risks.
3. Discuss the increased cardiovascular disease risks among people living with HIV, especially in the context of obesity

HIV as a model of care for obesity

Dr Nomathemba Chandiwana
Principal Scientist
Ezintsha, University of the Witwatersrand, South Africa

World Congress of Epidemiology 2024
30 May 2024

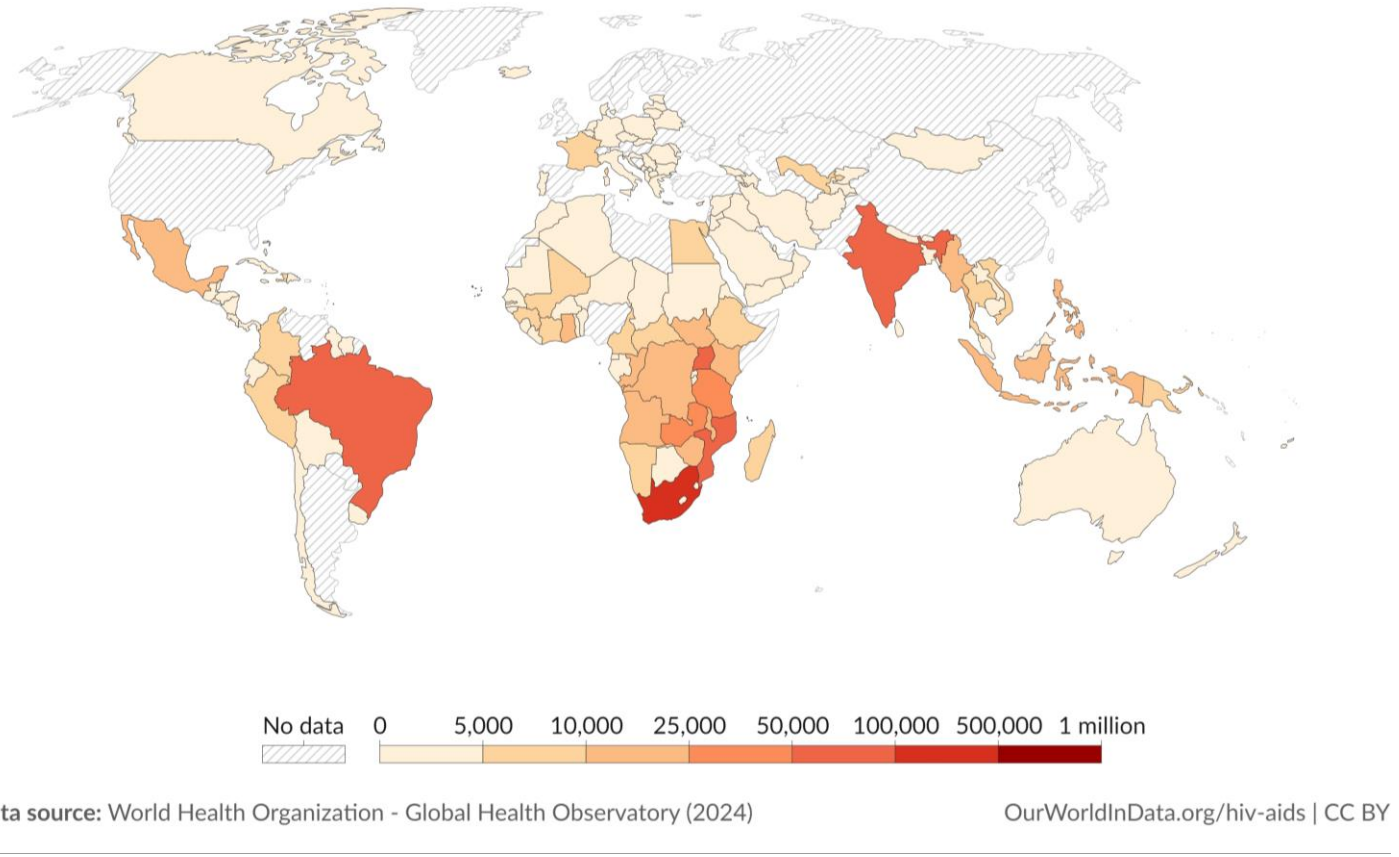
Ezintsha
INVESTIGATE INNOVATE ADVANCE

Disclosure of relationships with commercial interests

Research funding: Novo Nordisk, Merck, Bill & Melinda Gates Foundation

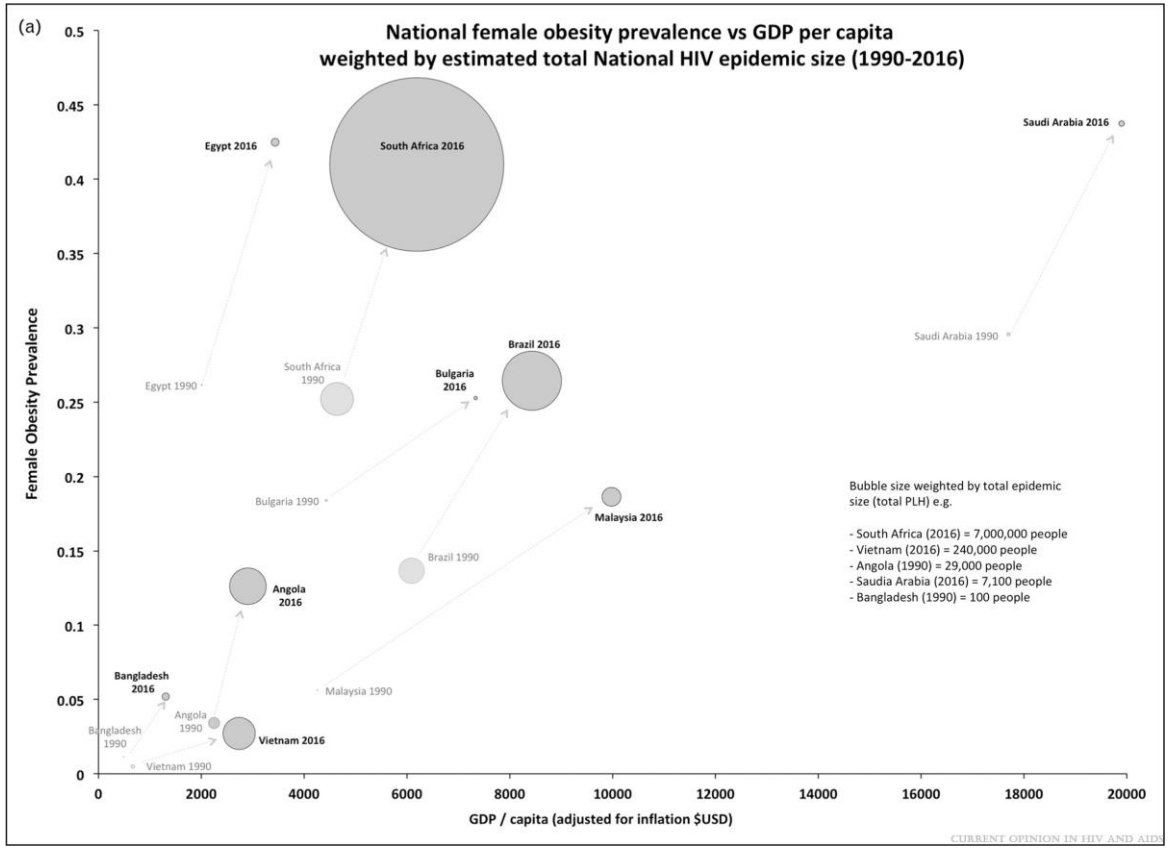
HIV epidemics and obesity rates

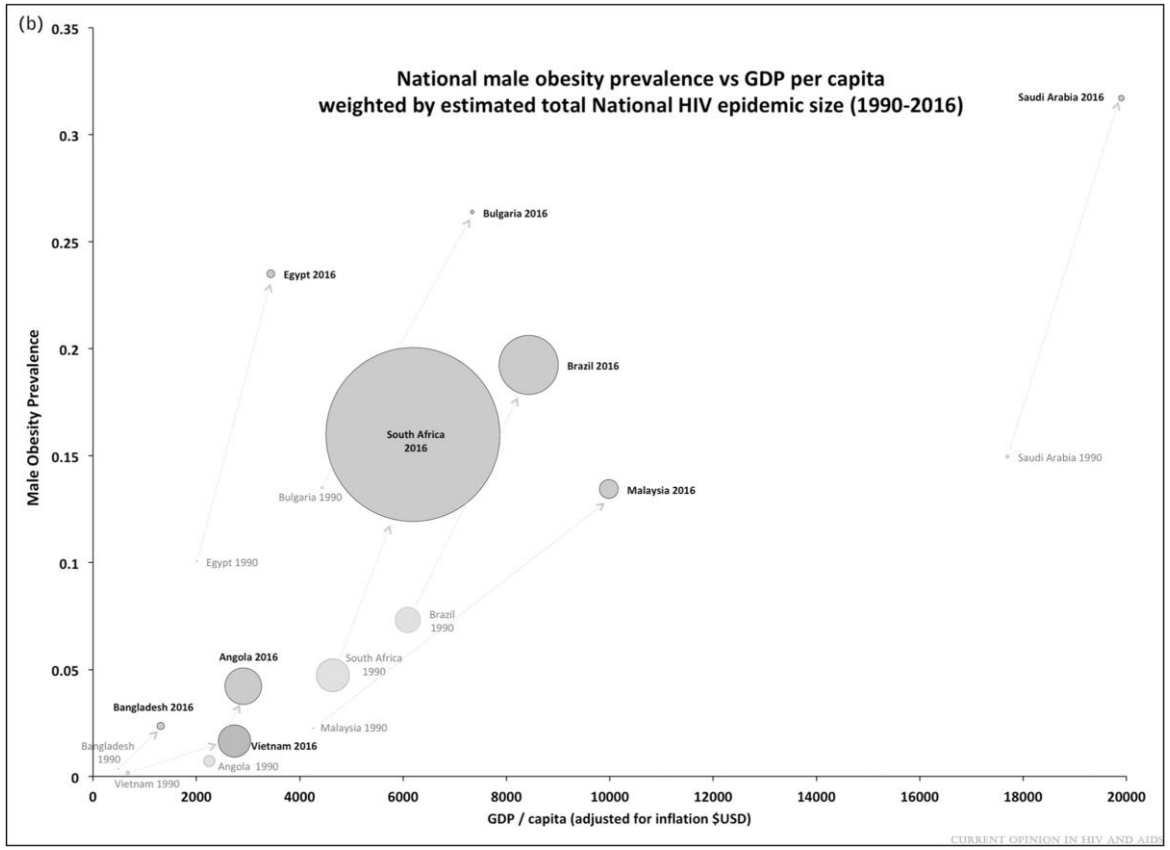
- Growing obesity epidemic in regions with high HIV prevalence
  - HIV epidemics in MICs- South Africa, India, Mexico, and Brazil.
- Weight-related diseases have eclipsed TB and HIV as leading causes of morbidity and mortality
- Annual deaths related to obesity and overweight are now four times more than for HIV globally.



Source: WHO, 2024

GDP and obesity/HIV trends





Levi, 2023

Obesity is a major driver & emerging global health crisis

By 2035, >2/3 of people with obesity will reside in a **middle-income country**

In South Africa and Mexico, **46-47% of all adults** living with obesity

Figure 3.3: A rising proportion of men with obesity live in middle income countries

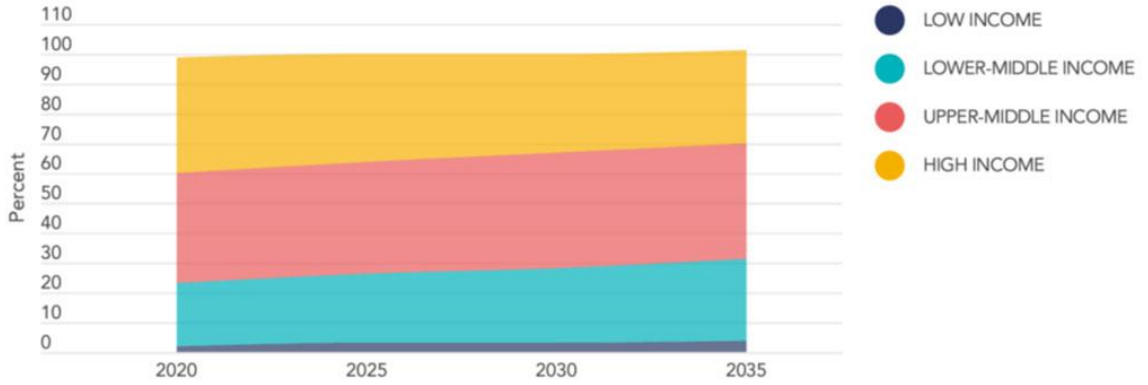
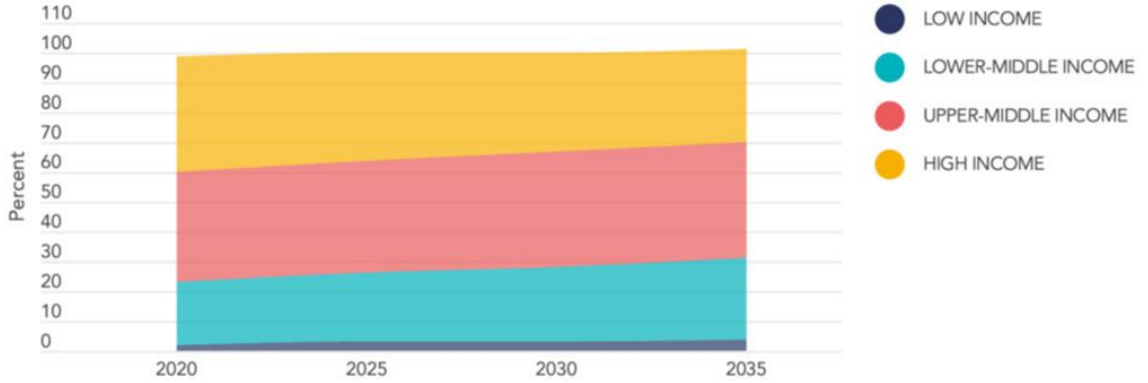
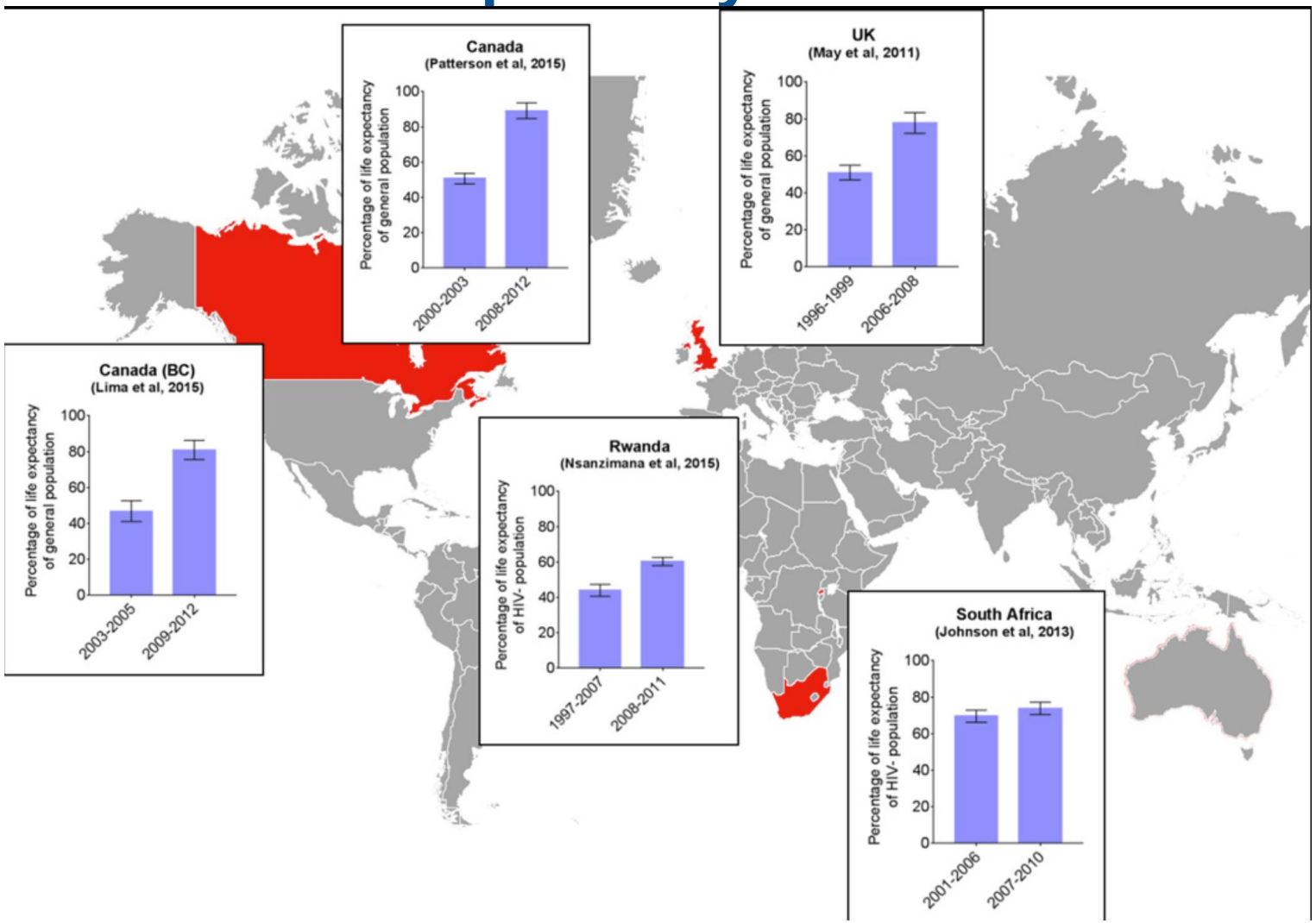


Figure 3.4: A rising proportion of women with obesity live in middle income countries



Source: World Obesity Federation Atlas 2023

HIV and life expectancy



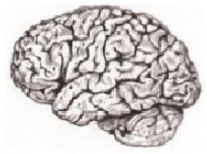
16 fewer years in good health

- Cardiovascular disease.
- Metabolic disease
- Some cancers.
- Osteoporosis
- Kidney disease
- Dementia

Source: Johnson F et al, 2016

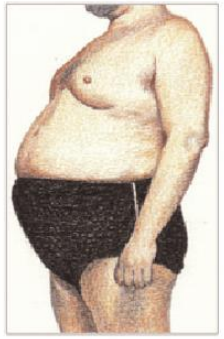
Metabolic complications of HIV

- **Obesity**
- Insulin Resistance and Type Diabetes
- (NAFLD)/Metabolic-dysfunction-associated Steatotic Liver Disease (MASLD)
- Dyslipidaemia
- Lipodystrophy
- Bone Metabolism Disorders
- Hypertension
- **Cardiovascular Disease**



Neurocognitive Disorders
→ GWAS ongoing in HIV+

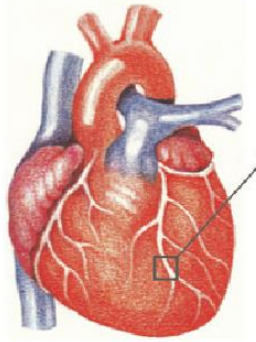
Chronic Liver Disease
Associatation with hepatitis C clearance and response to peg-Interferon+Ribavirin:
✔ GWAS *(IL-28B)*
✔ confirmed in HIV+

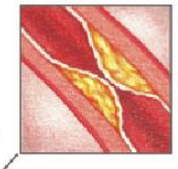


Diabetes Mellitus
✔ GWAS (24 SNPs)
✔ confirmed in HIV+

Obesity, Metabolic Syndrome
✔ GWAS (37 SNPs)
✗ unconfirmed in HIV+

Dyslipidemia
✔ GWAS (33 SNPs)
✔ confirmed in HIV+

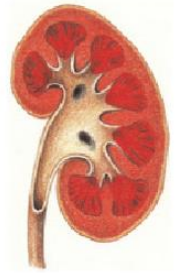




Coronary Artery Disease
✔ GWAS (45 SNPs)
→ confirmation study ongoing in HIV+

Osteoporosis
✔ GWAS (30 SNPs)
✗ unconfirmed in HIV+

Lipoatrophy
? Genetic predisposition



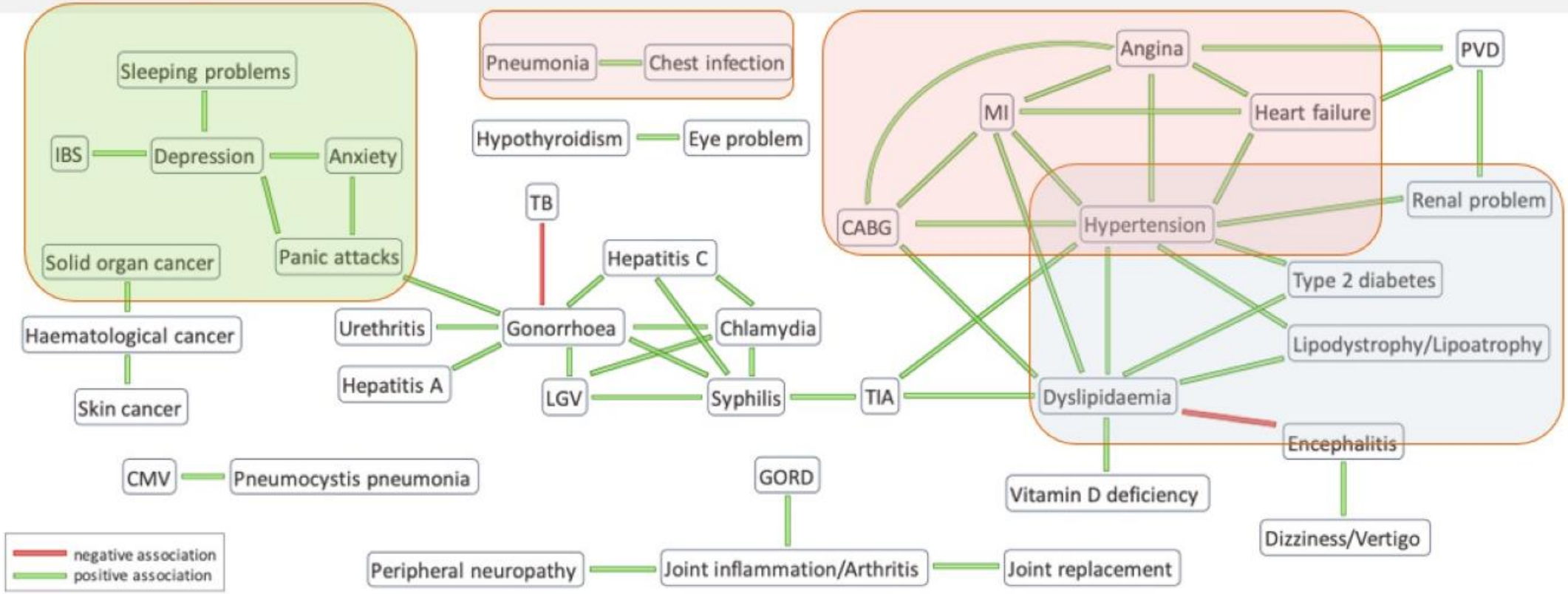
Kidney disease
? Genetic predisposition

Source: Tarr, 2010

NCD in PLWH clinical phenotyping

POPPY Study (N = 1073 people living with HIV)

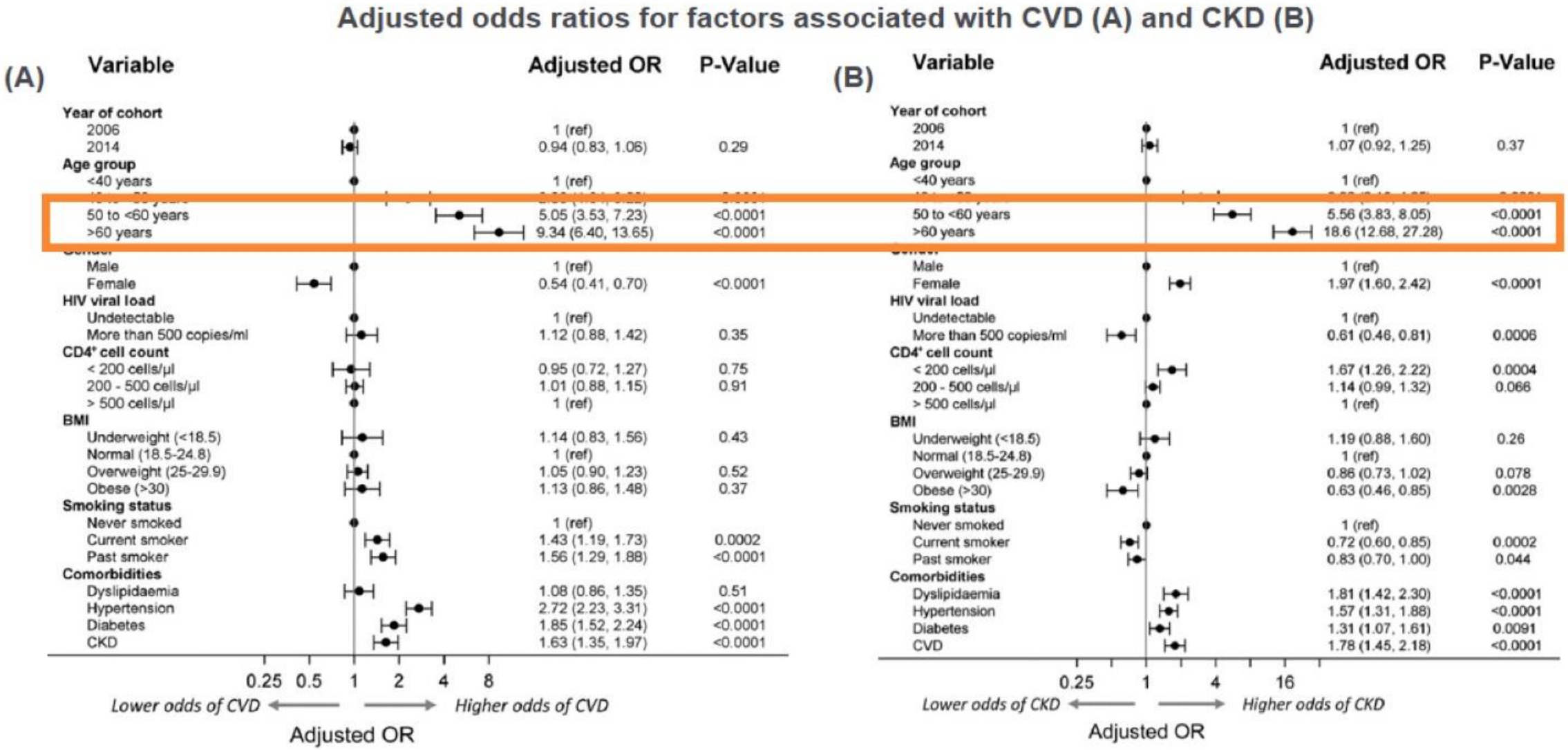
- 85.2% male; median age = 52 [IQR, 47-59] y
- Principal component analysis–6 patterns: CVD, cancers, metabolic, respiratory, STIs, mental health



CABG, coronary artery bypass graft; CMV, cytomegalovirus; GERD, gastroesophageal reflux disease; IBS, irritable bowel syndrome; LGV, lymphogranuloma venereum; MI, myocardial infarction; PVD, peripheral vascular disease; STI, sexually transmitted infection; TB, tuberculosis; TIA, transient ischemic attack.

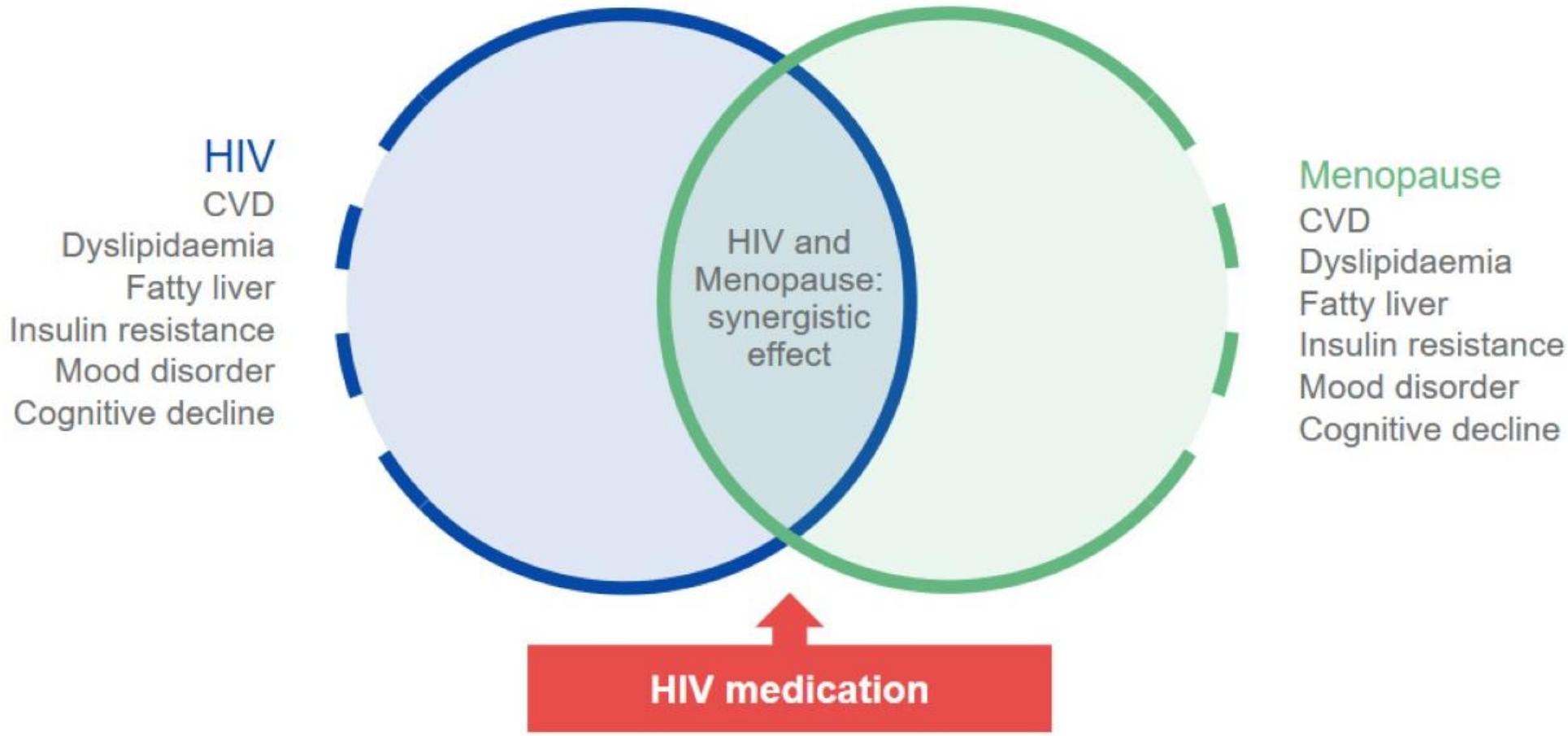
De Francesco D, et al. Open Forum Infect Dis. 2018;5:ofy272.

Age is the most important risk factor



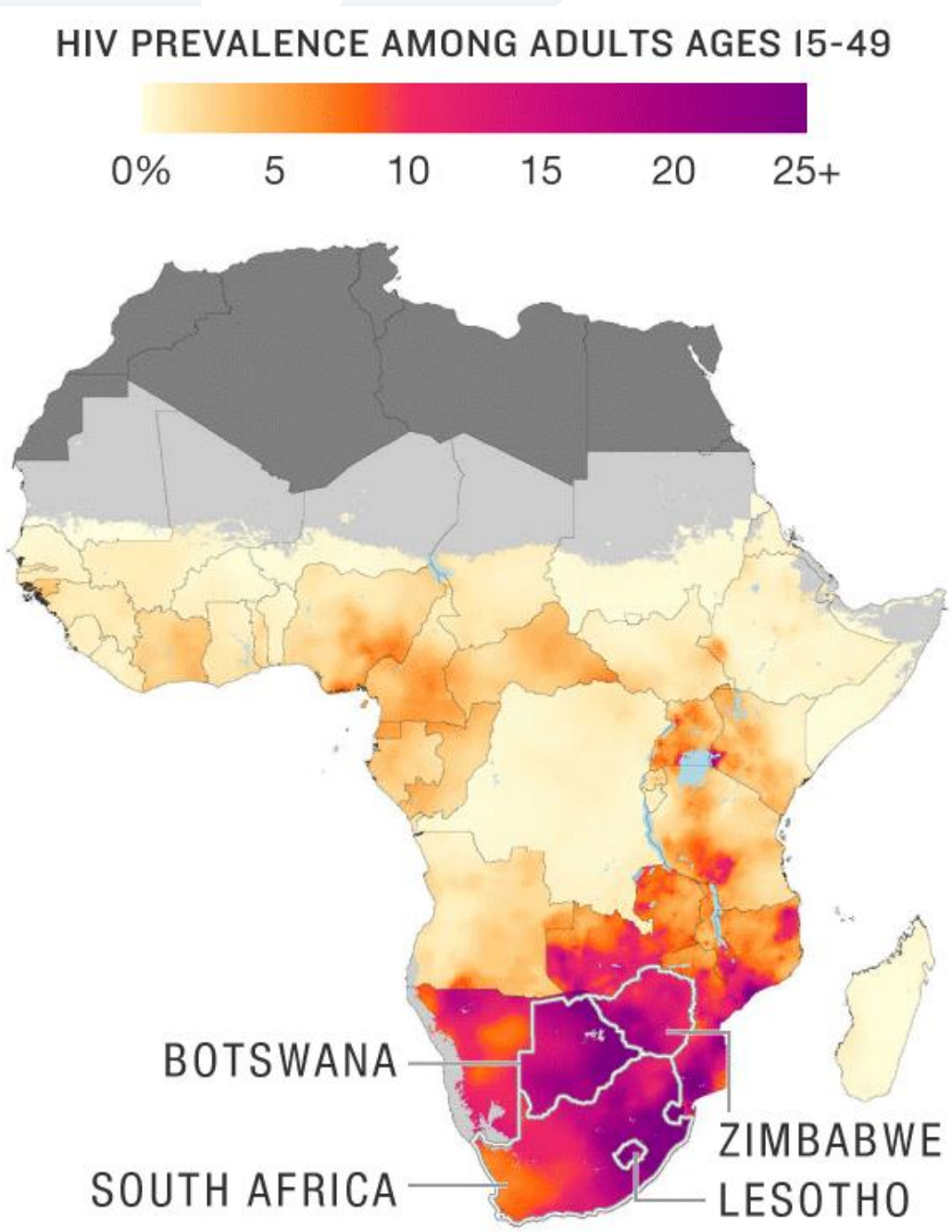
BMI, body mass index; CD, cluster of differentiation; CKD, chronic kidney disease; OR, odds ratio.
Pelchen-Matthews A et al. AIDS. 2018;32:2405-2416.

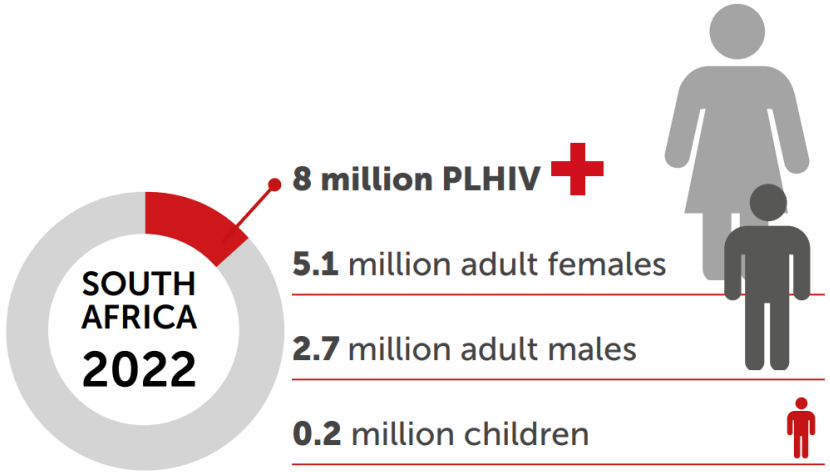
Menopause the cardiometabolic transition



CVD, cardiovascular disease.
Image courtesy of Shema Tariq, FRCP PhD.

South Africa at the epicenter of HIV epidemic





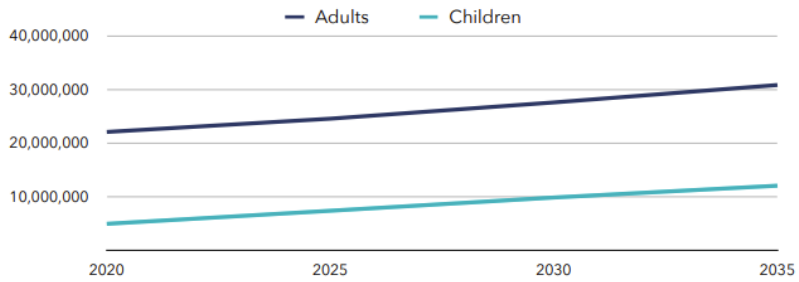
Ezintsha

South Africa

2.3%
Annual growth rate in the projected numbers of adults with high BMI 2020–2035

6.2%
Annual growth rate in the projected numbers of children with high BMI 2020–2035[1]

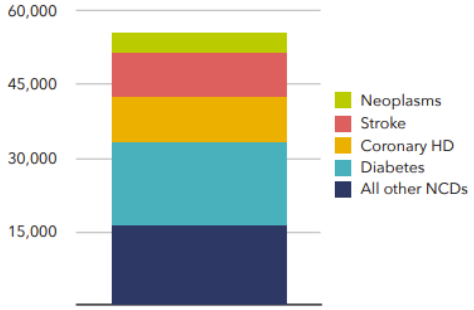
Projected numbers of adults and children with high Body Mass Index (BMI)



Non-communicable diseases (NCDs) in adults attributed to high BMI, 2019

	Person-years lost (DALYs) to NCDs due to high BMI in 2019	Deaths from NCDs due to high BMI in 2019
All non-communicable diseases	**1,681,895**	**55,358**
of which diabetes mellitus	589,315	16,879
of which coronary (ischaemic) heart disease	231,532	8,987
of which stroke	286,014	9,030
of which cancers (neoplasms)	105,257	4,194

Deaths from NCDs due to high BMI in adults 2019



Early signs of NCDs in children aged 5–19 years, 2020 and 2035[1][2]

	2020	2035
Prevalence of children with high BMI	**31%**	**71%**
Numbers of children with high BMI	**4,877,371**	**12,008,292**
of which, children with high blood pressure attributable to high BMI	464,734	1,463,899
of which, children with hyperglycaemia attributable to high BMI	172,937	449,029
of which, children with low HDL cholesterol attributable to high BMI	495,676	1,354,070

Prevalence and Projections

- 2020: 31% of the population with high BMI.
- 2035: Projected increase to 71%.

Children Affected by High BMI:

- 2020: Approximately 4.9 million children.
- 2035: Expected to rise to over 12 million.

Health Consequences

- Increases in high blood pressure, hyperglycaemia, and low HDL cholesterol due to high BMI.

Environmental and Lifestyle Factors:

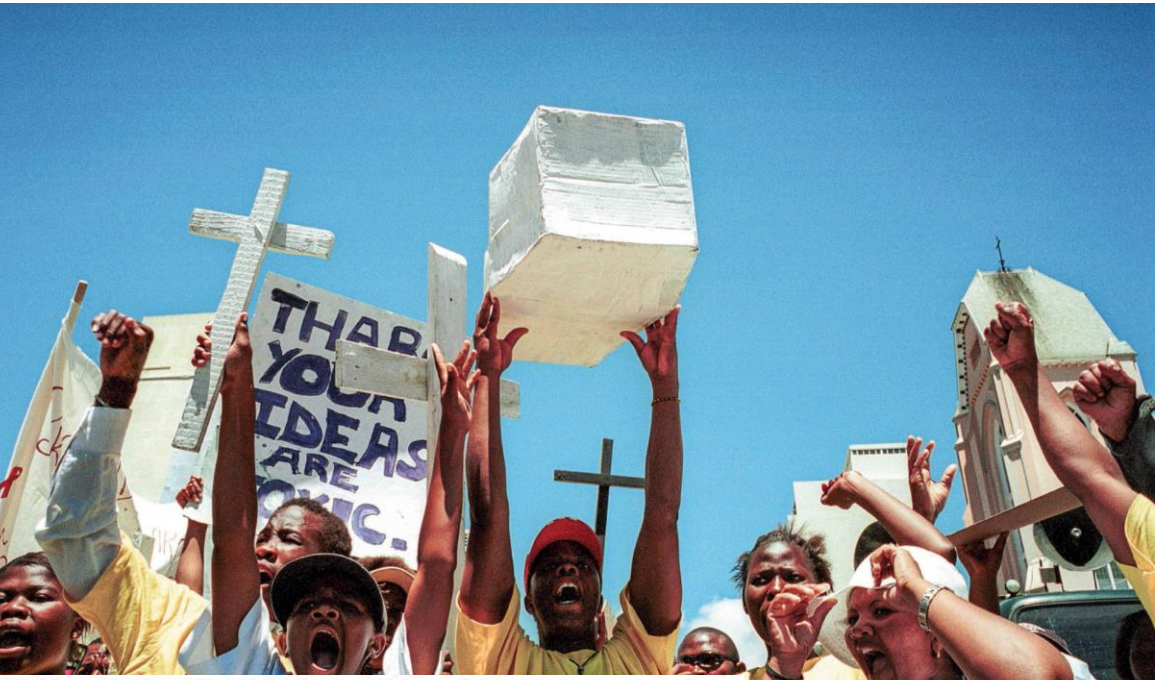
- Urbanization, low physical activity, high consumption of animal proteins and sugars.

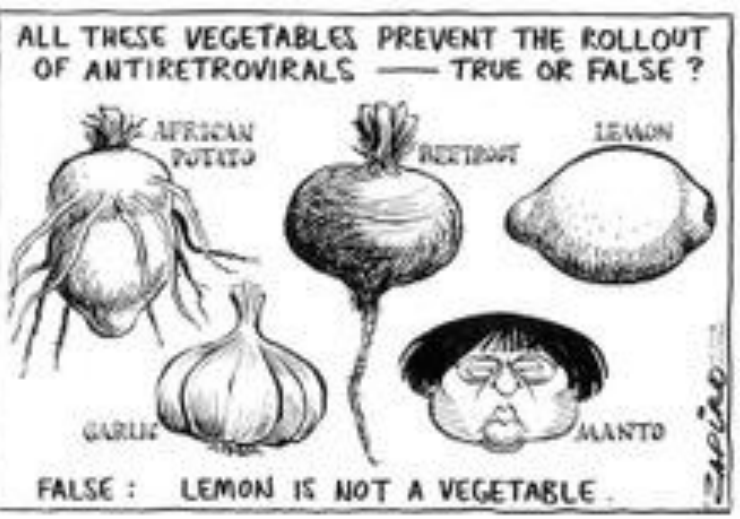
Parallels between HIV and obesity

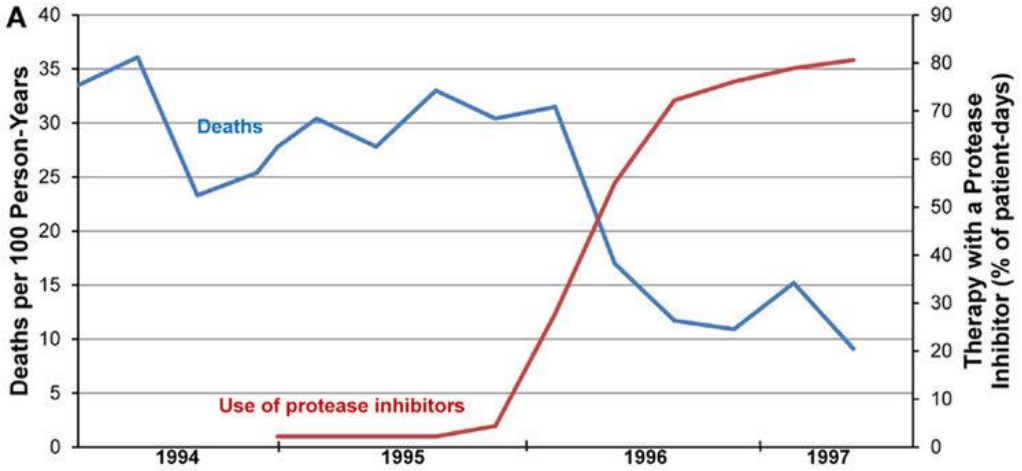
Source: Image, AIDS map, 2023

- Similar threats to public health
- Available but underutilized interventions
- Stigma and medical community challenges
- Structural and environmental drivers of obesity

Lesson 1: Cost of inaction







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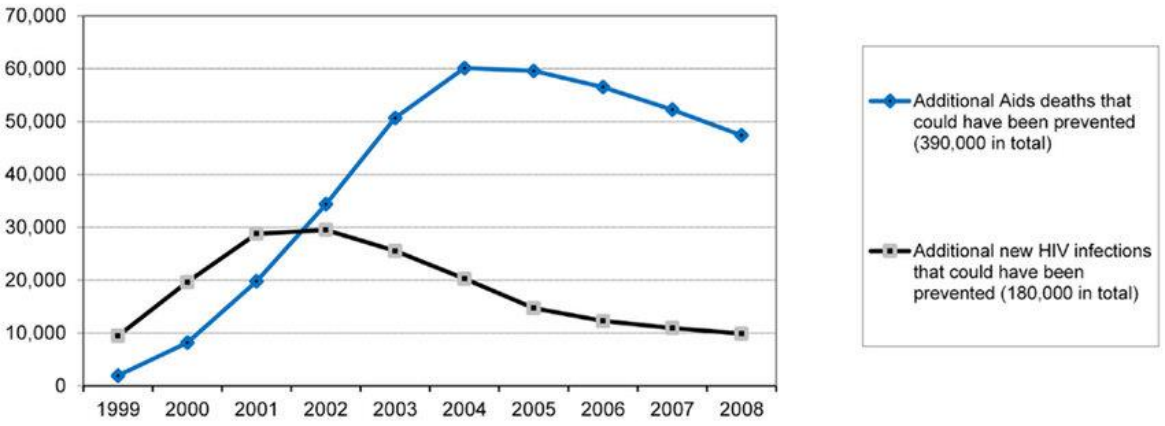
The Human Cost of Mbeki's Presidency: Lives saved and HIV infections prevented if HAART had been rollled out nationally at the same rate as in the Western Cape Province and if a National MTCTP Program had been Introduced in 1999

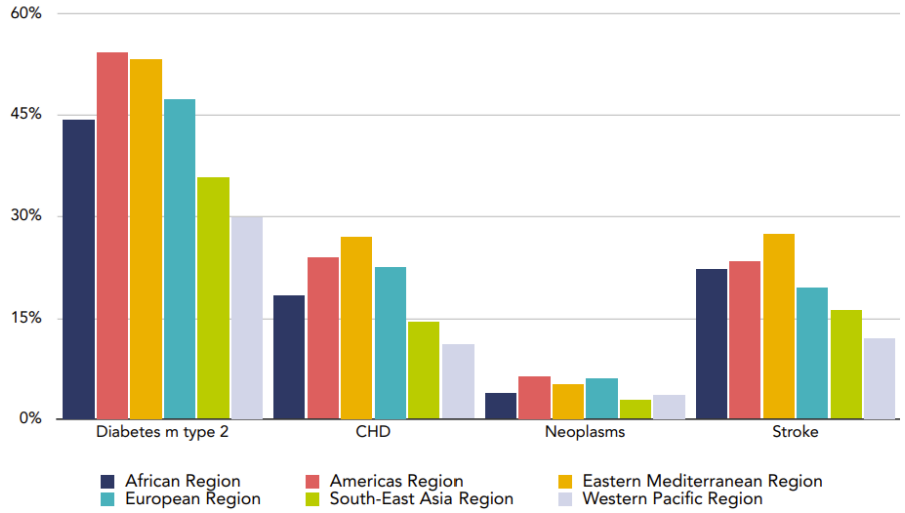


Cost of inaction

Table 2.1 Adult overweight and obesity 2020-2035, WHO regions

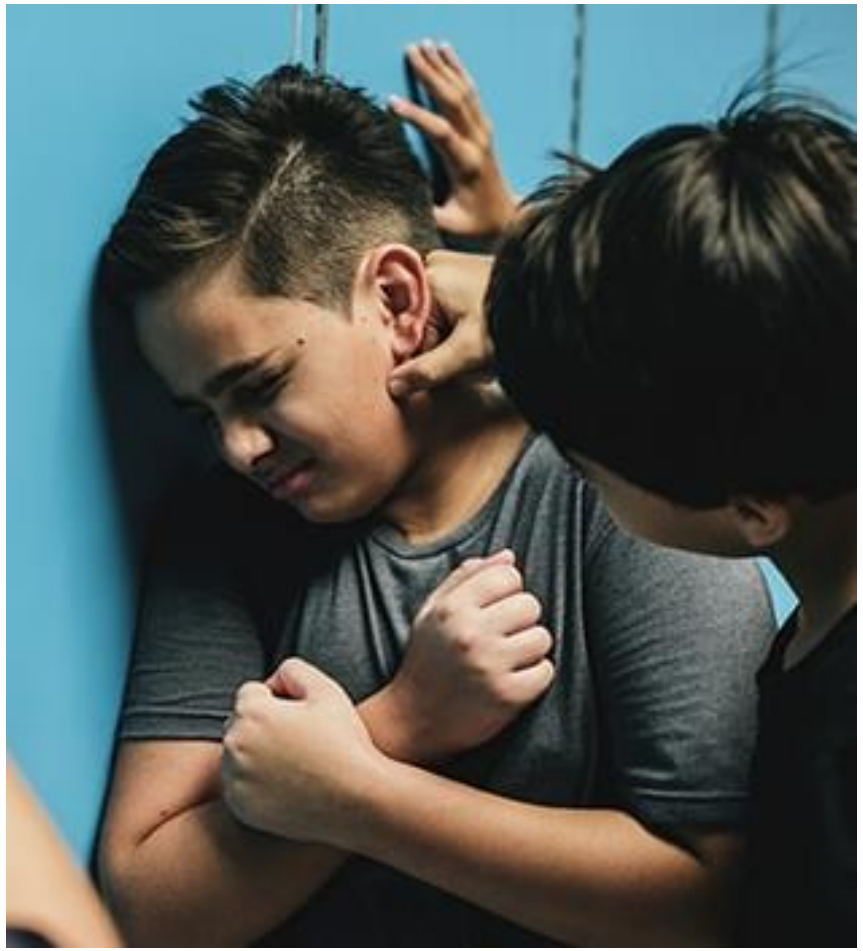
		2020	2025	2030	2035
African region (AFRO)	Adults with overweight (millions)	118.28	143.51	172.80	204.43
	Adults with obesity (millions)	68.39	94.72	131.78	182.00
	Prevalence of overweight and obesity (high BMI)	35%	39%	43%	47%

Figure 2.1: Proportion (%) of deaths from leading NCDs attributable to high BMI



Source: IHME, 2024

Lesson 2: Reducing Stigma



HIV

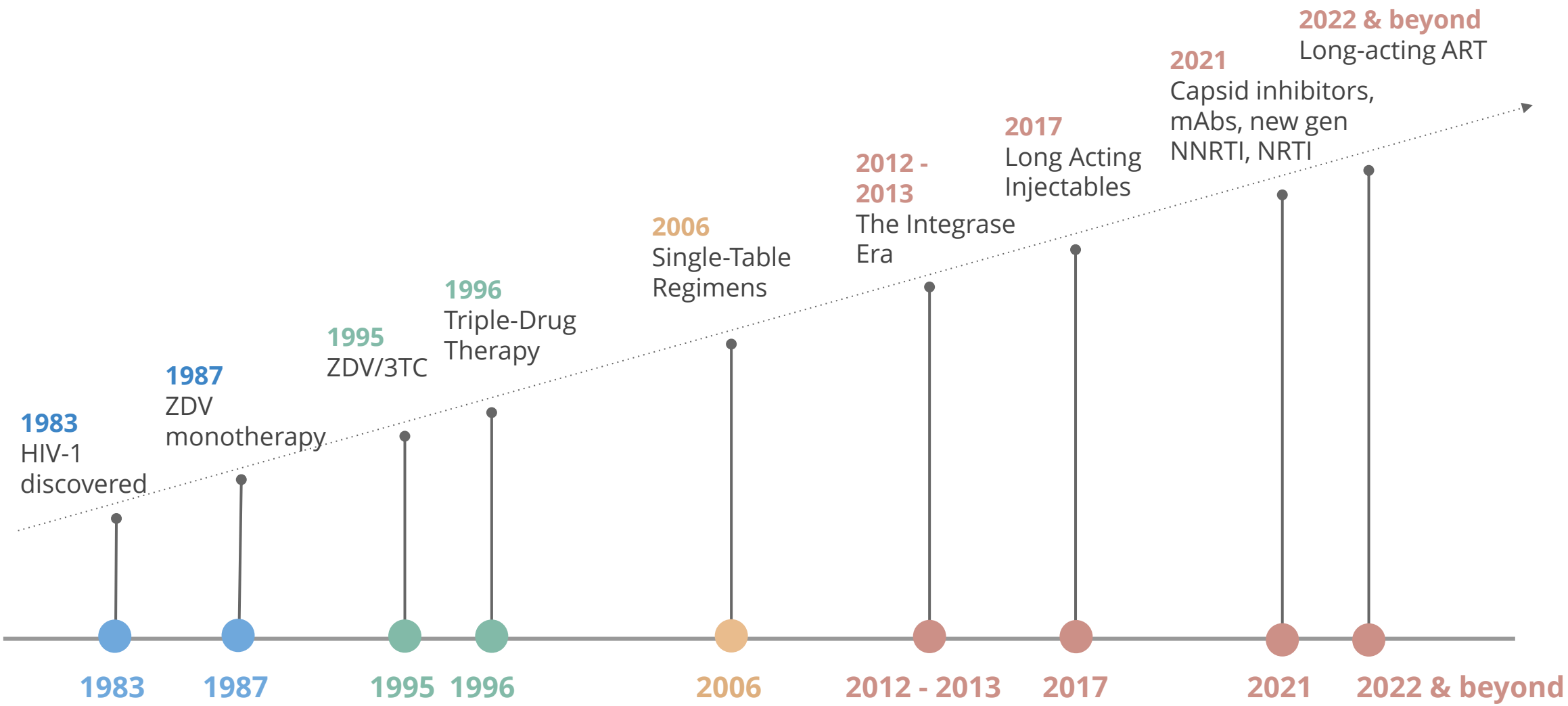
- In 25 of 36 countries with recent data, >50% of people ages 15–49 years hold discriminatory attitudes toward people living with HIV
- 21% of people living with HIV reported being denied health care in the past 12 months

Obesity

- 71% of children with obesity report being bullied at school, and increases with BMI percentile
- Internalised weight bias exacerbates **more** teasing from peers and lower self esteem
- Lower expectations and assessment scores of kids with obesity

Source: Puhl RM, 2013.

Lesson 3: Access to treatment



Lesson 4: Community mobilization

Lesson 5: Public awareness and messaging

UNAIDS, 2022

HIV a b**lueprint for tackling obesity**

- [x] Use of key policy levers
- [x] Systems/demand creation
- [x] Strong activist movement

Obesity is South Africa's new HIV epidemic

Articles Opinion

Stigma, inaction and cost: Will SA t
lessons learned from

By **Nomathemba Chandiwana** and **Francois Venter** — March 4,

y Day is on 4 March 2024, and our nation needs to pay
with the HIV epidemic in the 1990s, we are facing a
eat to the health of the population that has been ignored
Weight-related diseases have eclipsed tuberculosis (TB)
eading causes of morbidity and mortality. Over two-
h African (SA) women are overweight or are living
For example, type 2 diabetes, stroke and heart disease,
directly linked to the disease of obesity, account for
p four causes of death nationally and incur massive
costs.[2,3] Moreover, excess weight gain has deleterious
ond cardiovascular disease risk, with evidence strongly
poor pregnancy outcomes, cancer, liver and kidney
l illness, and sleep disorders.[4,5]
V in the early 2000s, tools to prevent and treat obesity
but too often are being ignored or obfuscated through
naction, industry interests, and societal inertia. Also, as
has waited too long to convert effective interventions
public health strategy. Instead, we remain trapped in a
y while blaming and stigmatising those affected.
al establishment has not always been an ally in
e obesity health emergency.[6] A poor understanding
ogy of the disease, the endocrinological complexity of
l the contribution of diet and exercise to weight gain
ıcare providers to preach the common refrain of 'eat
e more'. This serves to further perpetuate shame and
se with the disease, even as it is now well understood
ve alone for most of those affected.[7] Unsuitable weight
ntributes to confusion and anxiety for individuals with
n turn allows a *diet, exercise and supplement industrial*
rive with minimal regulation.[8]
t too late for SA to implement an effective response to
d disease crisis. There are two important next steps.
the lessons from the HIV epidemic to reduce obesity-
and facilitate widespread access to novel anti-obesity
g a public health approach; and second, to establish

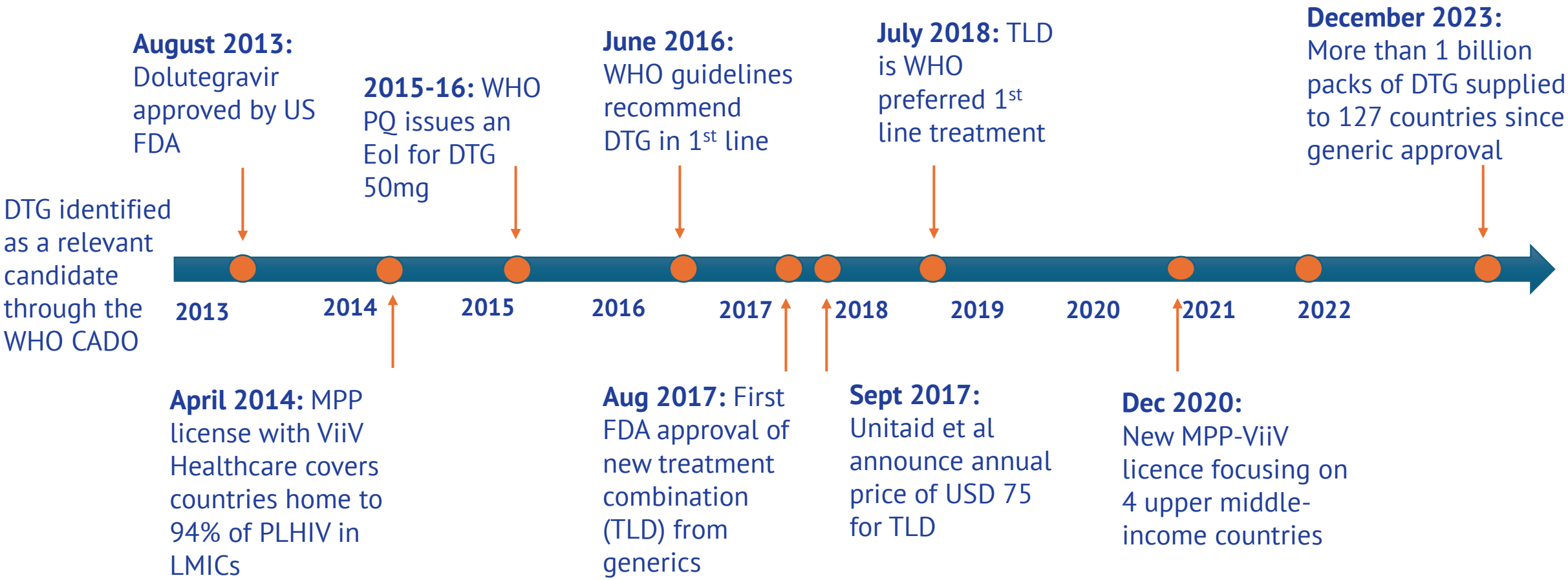
Obesity science is also teachin
unlikely to be sufficient to tack
environment – structural socie
system and our built environ
rise in obesity levels in the pa
For example, the introduction
processed food and sugar-swee
and spaza shops accompanied
at children, alongside a built
physical activity, are major dri
supply, facilitating access to a diversity of affordable fresh, healthy, unprocessed food and the means to prepare it, and ensuring that the public is aware of the dangers of highly processed and ultra-processed food, is a necessary step.[17] It is highly unlikely that these systematic changes will be possible without firm government and regulatory intervention. Profit margins on heavily processed goods are far higher than on their less packaged counterparts, and powerfully resourced industries oppose such action, including opposition to even the most tentative steps around regulating sugary drinks and, more recently, promotion of food labelling.[12,18-20] One chilling difference from HIV is that the viral vector did not have a massive unregulated marketing machine behind it. Distressingly, there has been little sign of urgency on the part of government to take up the issue of food advertising, quality and affordability, and some of these industries clearly have the ear of senior officials, as in other countries.[18]

Debates on where to focus resources, programming, and attention on the prevention or treatment of clinical obesity are also reminiscent of the early HIV epidemic. Then, many prevention advocates regarded people with HIV as sad casualties of failed prevention programmes, too expensive and complex to treat. The language 'medicalising a social problem' has similarly started to creep into the discourse about obesity and its management, occasionally with a moral touch of 'they brought it on themselves.'[7] Allowing this language to persist would be a dreadful mistake. To destigmatise obesity, and effectively combat the obesity epidemic, it will be important to maximise the

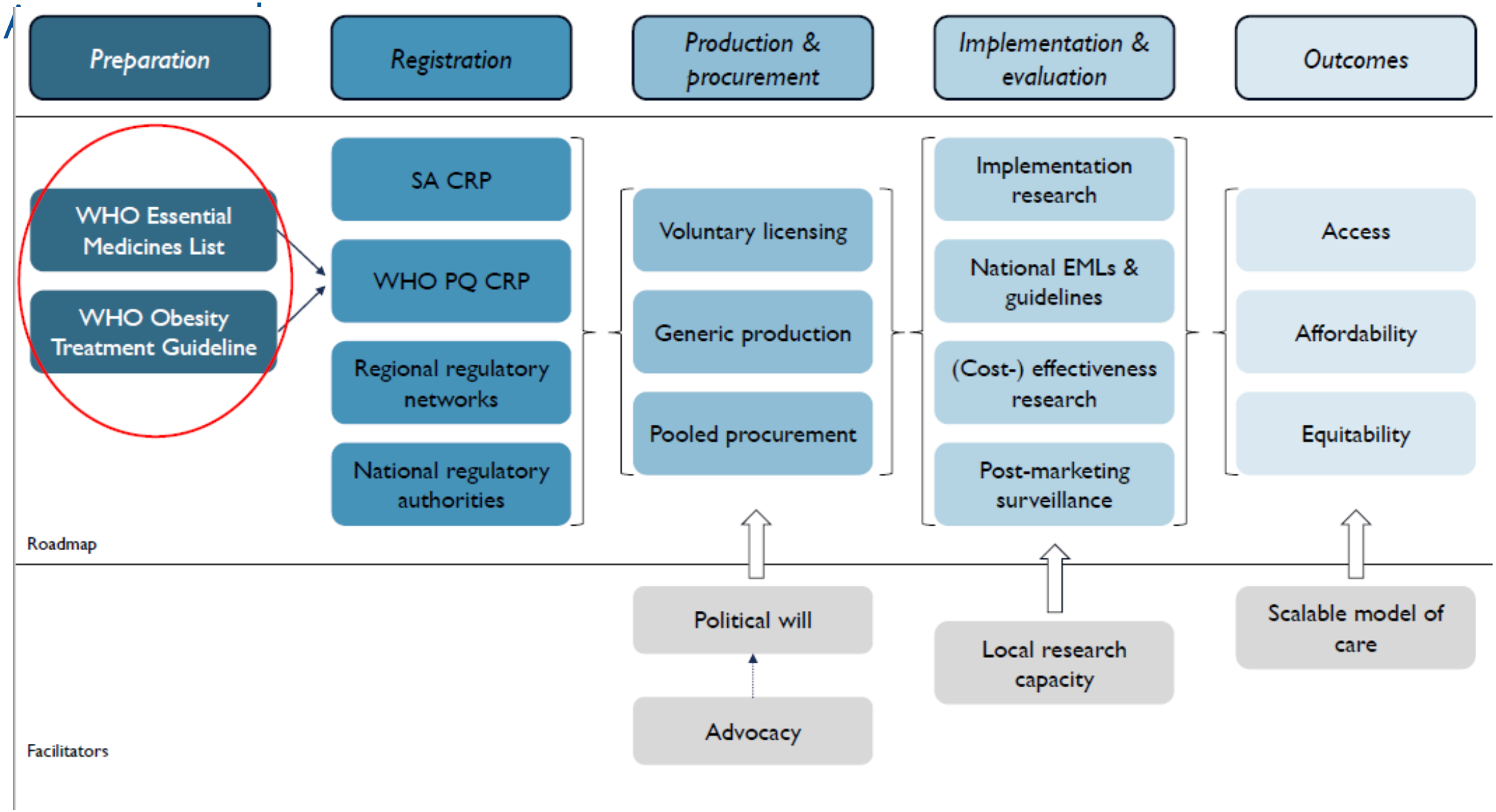
Public health strategies from HIV for obesity

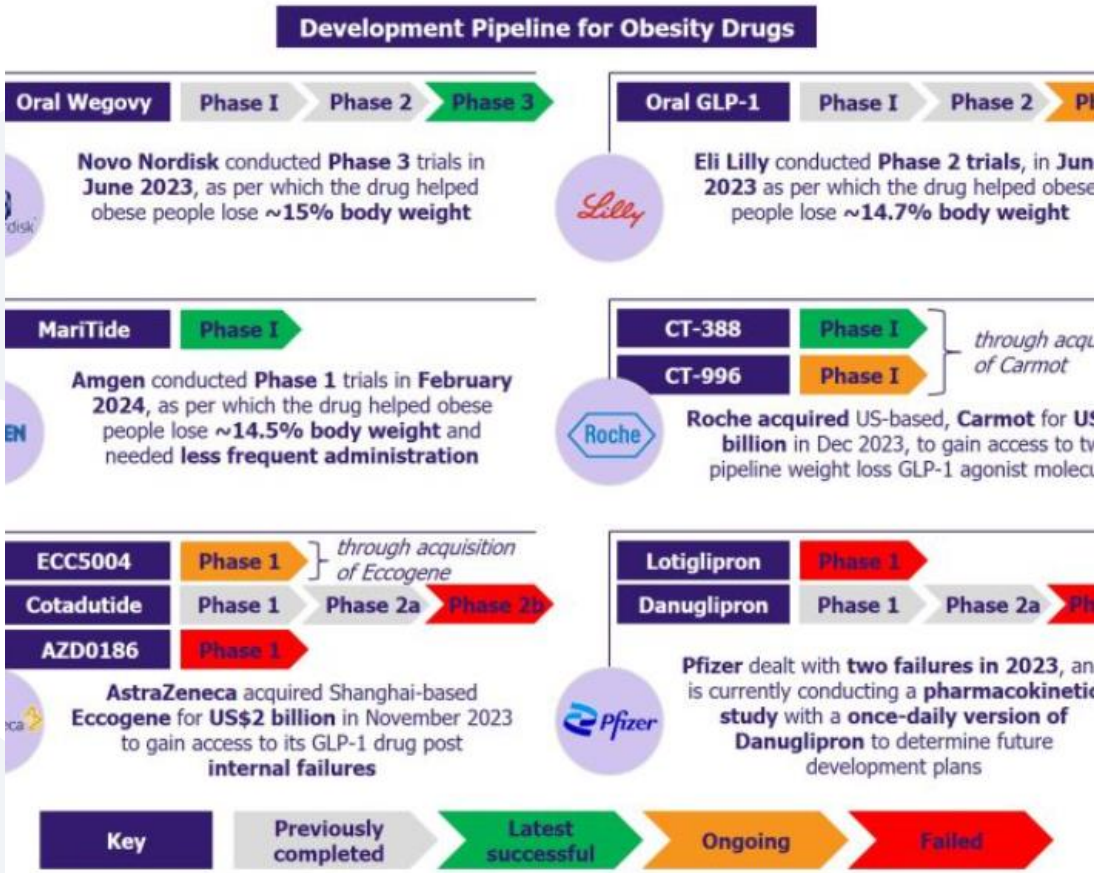
- Comprehensive Testing and Diagnosis
- Community engagement & Stigma Reduction
- Antiretroviral Therapy - scaled up access and adherence support- **AOMs**
- Pre-Exposure Prophylaxis (PrEP)- **Increasing physical activity, Improving sleep**
- Early Treatment of Comorbidities- **type 2 diabetes, MASLD, mental health**
- Integration of Services
- Targeted Interventions for Youth
- Political will and Government Commitment

The dolutegravir story



MPP, 2023 (Courtesy of Giulia Segafredo)


Preparation
Registration
Production & procurement
Implementation & evaluation
Outcomes
WHO Essential Medicines List
WHO Obesity Treatment Guideline
SA CRP
WHO PQ CRP
Regional regulatory networks
National regulatory authorities
Voluntary licensing
Generic production
Pooled procurement
Implementation research
National EMLs & guidelines
(Cost-) effectiveness research
Post-marketing surveillance
Access
Affordability
Equitability
Roadmap
Political will
Advocacy
Local research capacity
Scalable model of care
Facilitators



Source: Chandiwana, 2024

Novel anti-obesity drugs for people with HIV

Obesity is a global health crisis. People with obesity have increased risks of type 2 diabetes, cardiovascular disease, and death from any cause; people with HIV are not exempt from this epidemic. Weight gain with modern antiretroviral therapy, especially with guideline-recommended dolutegravir and tenofovir alafenamide, has been extensively documented and disproportionately affects women and Black populations, although not in all studies.[1,2] Possible explanations for antiretroviral therapy-associated weight gain include immune recovery in people with advanced HIV disease, older age, transitioning from older weight-suppressing drugs to newer ones, genetic factors, and lifestyle factors.[1,3] Even before this era, people with HIV had greater risk of cardiovascular-disease events than did those without HIV and, without urgent action, obesity and its cardiometabolic complications are likely to become major causes of premature death and disability for tens of millions of people with HIV in the coming decade.

Except for bariatric surgery, persistently effective interventions to address obesity have been absent. Lifestyle interventions, such as diet and exercise, remain important components of cardiovascular-disease risk reduction but are rarely successful at effecting meaningful weight loss alone.[4] Transitioning between classes of antiretroviral therapy has not been effective either;[3] however, solutions could finally be in sight. The field of obesity medicine is experiencing an innovation boom that offers promising developments. Anti-obesity medications, such as GLP-1 receptor agonists and disease-protective drugs (eg, statins), and safety of novel anti-obesity medications in people with HIV. Preliminary data have suggested that people with HIV and people without HIV might respond differently to GLP-1 receptor agonists.[7] This difference could be attributed to persistent gut dysfunction, chronic inflammation, and increased cardiovascular risk in people with HIV.[3,7] Moreover, little is known about their safety with extended use, including their effects on HIV viral suppression. Additionally, some concerning adverse effects of GLP-1 receptor agonists, such as lean muscle loss and lipoatrophy, require further study.[7] The results of the REPRIEVE trial, which showed large reductions in major cardiovascular events with pitavastatin use in people with HIV at low-to-moderate cardiovascular-disease risk, further motivate the need to evaluate these promising drugs in the context of treated HIV infection and alongside other recommended agents.[8]

Second, implementation evaluation is needed to assess the feasibility and acceptability of these drugs among people with HIV and to define optimal approaches for integration into routine HIV care. From the perspective of people with HIV, assessing the acceptability of various delivery options (eg, injectable *vs* oral) and their associated side-effects will be important.[9] There could be a unique opportunity to assess these factors alongside increasing interest in injectable antiretroviral therapy. Many antiretroviral-therapy programmes have well functioning, rigorous clinical-management algorithms that do not include use of anti-obesity medications or management of cardiometabolic

Lancet H

Proposed approaches for novel AOMs

Opportunities

- Include appropriate AOMs in the national formulary
- Propose and regularly update evidence-based guidelines for obesity/NCD management
- Specify an appropriate mix of medical and surgical interventions for public/private sectors in guidelines
- Promote generic manufacture of AOMs at scale
- Simplify AOM access requirements

Challenges

- Cost
- Cold chain requirements
- Training / upskilling HCPs
- Conflicts with differentiated service delivery models
- HCP attitudes
- Patient concerns

Take-aways

- Obesity, like HIV in the past, is a significant and growing threat to public health that requires urgent attention and action.
- Stigma surrounding both HIV and obesity hinders effective prevention and treatment efforts.
- Both HIV and obesity have effective prevention and treatment tools available.
- Government policies and advocacy are essential to create environments that support healthy lifestyles and make effective treatments accessible and affordable.
- The success of HIV programmes in South Africa, including community engagement, health activism, and science-based policy, can provide a blueprint for tackling obesity
- Continued research and innovation are essential to develop and refine effective obesity interventions, much like the advancements made in HIV treatment over the years.

Thank you to my [awesome] mentors/collaborators:
Jennifer Manne-Goehler
Francois Venter
Nzama Mbalati
Yvette Raphael
Sylvia Kehlenbrink
Giulia Segafredo