Fragility fractures in Sub-Saharan Africa: The known unknowns!

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Disclosures

Chair of the Royal College of Physicians (RCP) Falls and Fragility Fracture Audit programme (FFFAP) Scientific and Publications committee

Chair of the National Osteoporosis Guideline Group (NOGG), UK
Of the eight regions, only sub-Saharan Africa is projected to sustain rapid population growth through to the end of the century.
Population growth by region, 1950-2020, and projections to 2100

Of the eight regions, only sub-Saharan Africa is projected to sustain rapid population growth through to the end of the century.
Globally, those aged 65+ years make up the fastest-growing age group.

United Nations, Department of Economic and Social Affairs, Population Division
World Population Prospects 2019
By 2100, 13% of all people aged 65+ will be living in sub-Saharan Africa
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The UN and World Bank projections for Population Ageing vs. National Income (2017-2050)

The greatest age growth, disproportionate to income, will be seen in Africa over the next 30 years.
2020-2030: WHO Decade of Health Ageing

“the process of developing and maintaining the functional ability that enables wellbeing in older age.”

https://www.who.int/ageing/decade-of-healthy-ageing
2020-2030: WHO Decade of Health Ageing

“the process of developing and maintaining the functional ability that enables wellbeing in older age.”

Bones
- Fractures
- Osteoporosis

Musculoskeletal Health

Joints
- Arthritis
- Back pain

Muscles
- Falls
- Frailty

Immobility
- Disability
- Pain
- Productivity loss

https://www.who.int/ageing/decade-of-healthy-ageing
Rates of Years Lived with Disability by age in SSA (2016)

Musculoskeletal disorders
- Osteoarthritis
- Back pain
- Neck pain
- Rheumatoid Arthritis
- Gout
- Osteoporotic Fractures

Global Burden of Disease Study 2016
https://vizhub.healthdata.org/gbd-compare/patterns
Lifecourse model of functional capacity in high vs. low-income settings

Acute challenge to health, e.g. a fracture

Functional capacity of organs & systems
(e.g., joints, muscle & bone)

Adapted from Hansen et al. J Physiol. 2016. 594(8): 2147-60
Lifecourse model of functional capacity in high vs. low-income settings

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Age

Acute challenge to health, e.g. a fracture

Adapted from Hansen et al. J Physiol. 2016. 594(8): 2147-60
Bone mass (& skeletal strength) through the course of life

- **Peak bone mass**: The maximum bone mass that can be achieved during growth.
- **Bone loss due to menopause**: The decrease in bone mass after menopause, particularly pronounced in females.
- **Decreasing bone mass with age**: The general decline in bone mass with increasing age.
Bone mass (& skeletal strength) through the course of life

- **Peak bone mass**
  - Male
  - Female

- **Decreasing bone mass with age**

- **Bone growth**

- **Bone loss due to menopause**

- **Window of fracture risk**

Bone mass (& skeletal strength) through the course of life

- Compromised Peak Bone Mass

Bone mass (& skeletal strength) through the course of life

A 10% increase in PBM (~1SD) predicts ~50% reduction in fracture risk later in female life

SAMSON; the Sub-Saharan African Musculoskeletal Network

A network across West, East and Southern Africa which aims to:

1. **Build sustainable capacity** in Musculoskeletal Health Research by creating a collaborative research platform to share learning
2. **Inform** health policy, promote training, knowledge transfer and public engagement
3. **Provide guidance** to standardise methods for Musculoskeletal assessment across SSA

SDG3: Ensure healthy lives and promote well-being for all at all ages
FRAGILITY FRACTURES IN SUB-SAHARAN AFRICA: THE KNOWNS AND UNKNOWNs

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Disclosures

- Received speaker fees from Abbot Nutrition, Pfizer Healthcare
- Associate Editor of JBMR
Low hip fracture incidence in SSA?
What evidence do we have?
Ethnic- and gender-specific incidence rates for hip fractures in South Africa

- South Africa multi-ethnic population >50million
  - 79.2% African
  - 8.92 Coloured
  - 8.86 White
  - 2.49% Indian

- Gauteng, Western Cape, KwaZuluNatal

- Prospective observational study in 94 hospitals, 25 public, 69 Private sector

- Subjects aged 40years and above with a fragility fracture of the hip, neck of femur or trochanter

- 2767 subjects enrolled
  - 66.3% enrolled in public sector
Ethnic- and gender-specific incidence rates for hip fractures in South Africa

- Findings similar to other multi-ethnic populations
- Higher in women than men, except at lower ages
- IR in SA White 129.9 per 100,000 cf. UK 349 Netherlands 246 per 100,000
- IR in Africans 43.6 per 100,000 (W), 31.1 per 100,000(M) Africans, despite lowest rate of Fx, second highest # Fx in absolute terms
- >> Solomon et al. in 1960’s, 4.3 and 6.9 per 100,000 W, M
- Rates in Indian population similar to those in North India, lower than Singapore Indian
Hip fracture incidence in South Africa: an update

Women:
- White 176.0 per 100,000
- Indian 147.7 per 100,000
- Coloured 73.2 per 100,000
- African 43.6 per 100,000

Men:
- White 76.5 per 100,000
- Indian 69.2 per 100,000
- Coloured 39.7 per 100,000
- African 31.1 per 100,000
30-day and 1-year mortality in South Africa

- eThekwini, 5 public sector hospitals
- 200 patients, mean age 74.3y, 72% female
- 30 day mortality 13%; 1 year 33.5%, by contrast in UK 6.9%, 30% respectively
- 1y M24(41.1%) vs W 42 (30.6%) HR 0.58 (95% CI 0.27,1.29)
- 1y A 27(40.9%) vs I 33(30.0%) HR 11.5 (95% CI 1.51,2.57)
- Delays to surgery predicted death (HR 1.02, 1.00-1.05)
- Elevated serum creatinine (HR 2.43, 95%CI 1.02-5.76) and CRP (5.78, 95% CI 1.97-16.91) predicted death at 1-year
Vertebral fracture prevalence in South Africa and The Gambia

South Africa\(^1\): (n=189, \(\geq 40\)y, W)
- 9.1\% African; 5.0\% white
- \(~60\%\) classified as mild
- Low trauma Fx 18\% (A), 11\% (W)

The Gambia\(^2\): (n=488, \(\geq 40\)y, M,W)
- All African
- Grade 2/3 = 9\%
- Hip Fx (self report) 3\% W, 0.4\% M

Conradie et al., Arch Osteo 2015; 10
Zengin et al., Ward, Front Endocrinol 2017
Gambian Bone Ageing Study (GamBAS)

- Prospective study, M&F, 8, 5yr age range bands - 40 to 75+. Stratified by age band and gender, randomised follow-up 1.5 to 2 years. 240 per gender, ~30 per age band
- DXA (+LVA), pQCT, jumping mechanography and grip strength. Fasting bloods, 2hr & 24hr urine, lifestyle and medical history
- Baseline; n=488 (227M, 262F); Follow-up 1; n= 386 (468); FU2 – 270
- GamBAS Urban pilot, 60-80y olds n=101 (51F), plus knee radiographs

- Fractures in 9% LVA scans, osteophytes 14%
- Sarcopenia prevalence 45% women: 20% men. Needs new definition
- NCD comorbidity: Sex differences in markers of poorer cardiovascular health and lower BMD, present in women but not men
- Peripheral vascular calcification associated with lower BMD in women
- Bone loss similar magnitude to HIC’s
Sarcopenia in older Gambian adults: *new definitions required*

- FNIH ALM had best sensitivity and specificity to predict poor grip and lower limb function; in women ~70% .
- FNIH ALM in men 40% sensitivity, 90% specificity
- FNIH: 45% (68%) women: 20% (81%) men

- EWGSOP: 10% (85%) women: 19% (82%) men
- Sensitivity poor, 20-40%; specificity 90%.

- Associations between muscle force and bone outcomes

- Highlights importance of not applying definitions across diverse populations

Zengin et al., Ward, J Cachex Sarc Musc 2018
Non communicable disease of ageing: Cardiac workload, BMD & body composition in Gambian adults

- Rate pressure product (myocardial oxygen consumption) and pulse pressure (arterial stiffness)
- Sex differences in the associations between cardiac workload and aBMD
- Higher RPP, lower aBMD in women, similar results with PP
- Women but not men with PVC had lower aBMD
- With rising CVD in ageing populations, need to identify common preventative strategies

Advancing age was the main predictor of skeletal change in this population – the magnitude of which was in keeping with data from high-income countries.

In women, CTX and P1NP were strongly associated with decreases in trabecular vBMD.

Better muscle function was associated with less change in bone, and hence better bone health with ageing, though no consistent patterns found.
Environment, pubertal timing and future bone health

- Timing of puberty a known risk factor for future fracture risk
- Age at peak velocity: M Ca 14.4, P 14.8 y; F Ca 13.3, Pl 13.2y
- There were transient increases in BMC after Ca supplementation in a population accustomed to low calcium intake
- In boys, puberty was consistently earlier in the calcium group compared to the placebo group; Ca boys were shorter at the end of the growth
- No supplement effect on puberty in girls
- No persisting effect of calcium supplementation on BMD in boys or in girls who are accustomed to low dietary calcium intakes.
Environment, pubertal timing and future bone health

High fracture risk

Peak bone mass
Ageing
Menopause
Maintenance
Puberty
Bone mass
Fetal
Maternal

Age
0 10 20 30 40 50 60 70 80

Dibba AJCN 2000;71;
Dibba AJCN 2002;76;
Prentice AJCN 2012;96;
Ward JCEM 2014
Ward JBMR S1, 2014
Schoenbuchner PhD University of Cambridge 2016
Children living with HIV in Zimbabwe have impaired bone architecture, despite treatment with anti-retroviral therapy: a cross-sectional study

**The IMVASK pQCT Study**

- Harare, Zimbabwe
- HIV+ and HIV- Children and Adolescence
- 8 to 16 years old,
- Established on ART (>2y)
- From Parirenyatwa and Harare Hospital clinics (HIV+); from schools within the same catchment area (HIV-)
- Frequency matched for age and sex
- 273 (HIV+) and 298 (HIV-)

**Aim:** To compare the bone density, bone size and predicted bone strength parameters of trabecular and cortical bone in children and adolescents living with and without HIV in Harare, Zimbabwe

- There are deficits in bone size in both boys and girls living with HIV who in the later stages of puberty
- There are deficits in predicted bone strength in children with HIV infection who are in the later stages of puberty
- This study population is currently in follow-up; longitudinal data will show us whether or not deficits attenuate with age
- Cynthia Kahari, PHD student, NIH Fogerty Fellow
Changes in Bone Mineral Density During and After Lactation in Ugandan Women With HIV on Tenofovir-Based Antiretroviral Therapy

- Pregnancy and lactation associated with loss of BMD
- Women newly diagnosed with HIV and initiated on ART
- 426 pregnant women (210 WWH; 216 REF)
- Consistent decreases in aBMD in first 6mo
- TH and WBBMD did not return to L2 levels when women were NPNL
- LS aBMD losses similar in WWH and REF, and recovered in both groups.
- Accentuated bone loss evident in WWH, with only partial recovery in the hip and whole body
HIV, treatment and BMD in South Africa

Assessed for eligibility
n = 311

- Did not meet inclusion criteria n = 16
- Declined to participate n = 16
- Other reasons n = 34

Enrolled and measured at baseline
n = 247

Nief HIV-negative
Reference group
n = 98

- Lost to follow-up n = 39
- Excluded n = 20
- Pregnant or lactating n = 13
- Tumor syndrome n = 1
- Seroconverted n = 5

PPres HIV-positive
Preserved CD4 count
n = 74

- Lost to follow-up n = 15
- Excluded n = 26
- Pregnant or lactating n = 13
- Started ART after 12m n = 13
- Stopped ART before 24m n = 0

Flow HIV-positive
Low CD4 count
n = 75

- Lost to follow-up n = 25
- Excluded n = 12
- Pregnant or lactating n = 6
- Started ART after 12m n = 3
- Stopped ART before 24m n = 3

Nief HIV-negative
n = 39

ART N
HIV-positive, ART-Never
n = 28

ART Y
HIV-positive, ART-Yes
n = 43

Hamill et al. J Bone Miner Res, 2017; 32
Hamill et al. JBMR Plus, 2020;
Fractures in sub-Saharan Africa: Epidemiology, economic impact and ethnography

- Rapid population ageing
- High HIV prevalence
- Increasing multi-morbidity
- Under and over nutrition
- High Trauma Rates
- Chronic under resourced healthcare services
- Medical pluralism

The International Osteoporosis Foundation Fracture Risk Map of the World

https://www.iofbonehealth.org/facts-and-statistics/frax-map

There is a need to investigate musculoskeletal ageing, including fractures, in older populations in West, Southeast and Southern Africa.

Adapted from Hansen et al. J Physiol. 2016. 594(8): 2147-60
Fractures in sub-Saharan Africa: Epidemiology, economic impact and ethnography (E³)

The International Osteoporosis Foundation Fracture Risk Map of the World

Rapid population ageing
High HIV prevalence
Increasing multi-morbidity
Under and over nutrition
High Trauma Rates
Chronic under resourced healthcare services
Medical pluralism

Hip and Vertebral Fractures
- Pain
- Disability
- Quality of Life
- Death
- High demands on health care services
- High health care costs


https://www.iofbonehealth.org/facts-and-statistics/frax-map
Fractures-E³: Five workpackages over 5 years (2020-25)

**South Africa**
Prof Bilkish Cassim

**Zimbabwe**
Prof Rashida Ferrand

**The Gambia**
Dr Landing Jarjou & Prof Kate Ward

**Orthopaedic Trauma Lead:** Prof Matt Costa

**WP1: Vertebral Fracture Prevalence**
Prof Kate Ward

Prevalence of fractures, OA, sarcopenia, multi-morbidity etc
Risk factors for fracture

**WP2: Hip Fracture Incidence**
Dr Celia Gregson

Risk factors for fracture
Fracture management
Clinical outcomes over 1 year

**WP3: Health Economics**
Dr Sian Noble

Quantify direct health costs of hip fracture & model future fracture burdens

**WP4: Hip Fracture Service Survey**
Dr Celia Gregson

Quantifying hip fracture service availability and readiness

**WP5: Ethnographic Study**
Prof Rachael Gooberman-Hill

Understand fracture care pathways and factors influencing access to services
The Fractures-E³ country team leads

**South Africa**
Prof Bilkish Cassim
Head of the Department Geriatrics, University of Kwazulu-Natal

**Zimbabwe**
Prof Rashida Ferrand
Professor of International Health, Biomedical Research and Training Institute

**The Gambia**
Dr Landing Jarjou
Head of Calcium, Vitamin D & Bone Health at MRC Unit
The Gambia
1. Calibration of fracture risk assessment tool (FRAX) for use in Africa (with clinical guidelines)

2. Develop fracture registries for use across SSA

3. Evidence to support inclusion of osteoporosis treatment as WHO Essential Medicines

4. Multidisciplinary research capacity development

5. Understanding of current fracture service provision, current and projected musculoskeletal burdens to inform the planning of future health service provision
Conclusions
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https://www.bristol.ac.uk/translational-health-sciences/research/musculoskeletal/rheumatology/research/global-musculoskeletal-health/

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