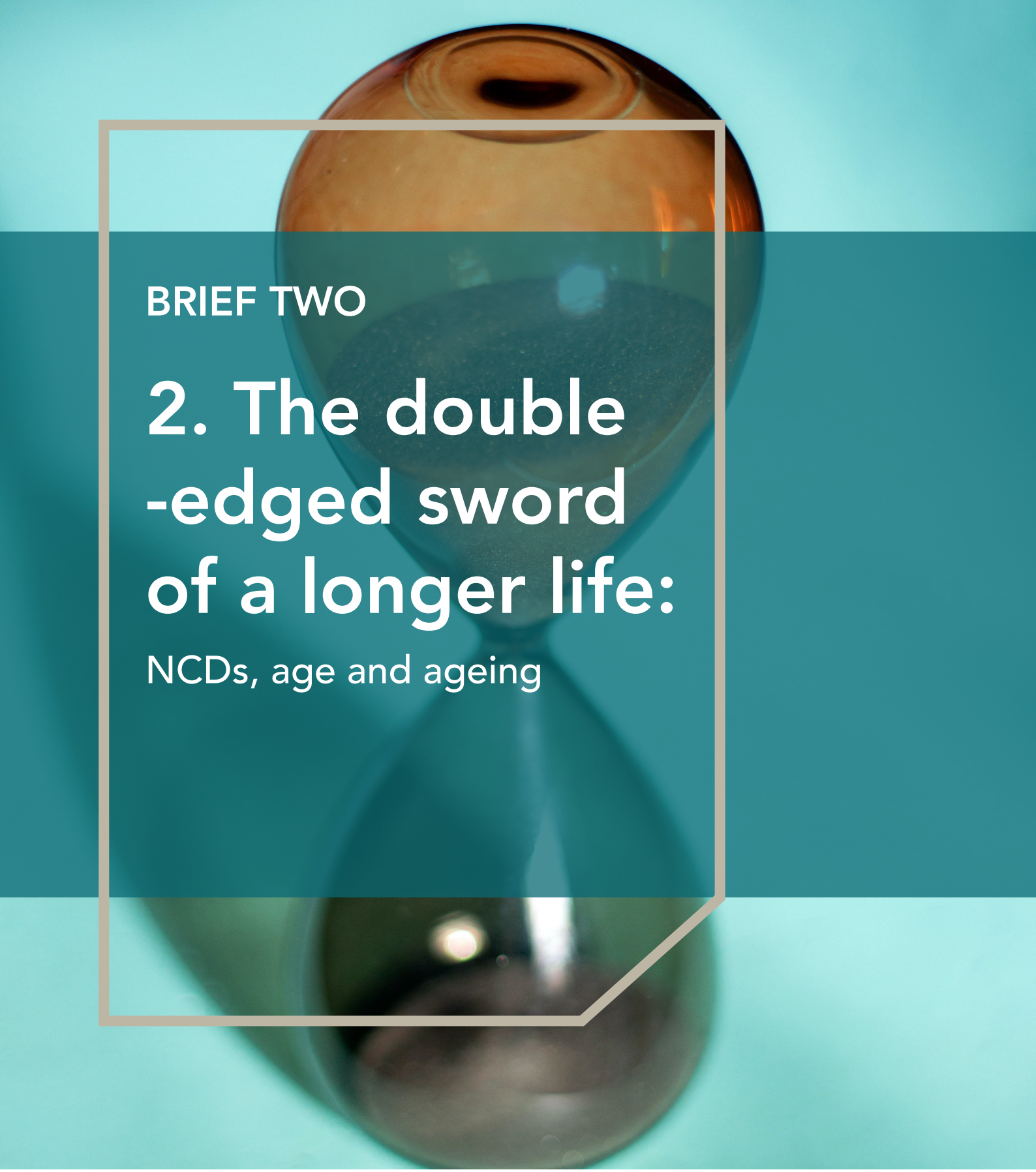


BRIEF TWO

2. The double-edged sword of a longer life:

NCDs, age and ageing

PERCEPT
FUELLED BY EVIDENCE, PROPELLED BY INGENUITY.

Authors: Percept Actuaries & Consultants

15 JANUARY 2022

Research briefs on non-communicable diseases in South Africa

Percept has developed a series of briefs aiming to explain, explore and quantify the burden of non-communicable diseases (NCDs) in South Africa. Throughout the briefs both existing quantitative data as well as emerging qualitative data are drawn together. The primary qualitative data - presented in the form of vignettes - has been collected by Dr. Beth Vale, through in-depth ethnographic research. Given the rising global burden of NCDs, particularly in low- and middle-income countries (LMICs) these briefs are incredibly relevant. Given South Africa's high prevalence of HIV, there's also recently been a focus on the link between HIV and NCDs, as the population living with HIV grows increasingly older with the successful uptake of antiretroviral treatment (ART). As we'll explain in the briefs, an ageing population is more at risk for NCDs. Moving towards universal health coverage (UHC), it's imperative to understand the current needs of our population - and how these may change going forward. We have produced fourteen briefs in this series.

Percept is grateful for the generous funding provided by the following three partners. The views presented are however the authors' own:

- Actuarial Society of South Africa (ASSA): ASSA has an interest in being part of the development of high-quality evidence to support resource allocation and decision-making and the interplay between the supply and demand sides of the health system
- RGA Reinsurance Company of South Africa Ltd (RGA): RGA has an interest in the ways in which life insurance can be responsive to the changing burden of disease and the ways in which we can use data to drive decision-making
- Board of Healthcare Funders (BHF): BHF is a regional representative body of health funders, administrators, and managed-care organisations. It is committed to universal health coverage, value-based healthcare, and accountability for health. Addressing the NCD burden is an important element to achieve some of its objectives.

Take-home messages

- People living with NCDs are living longer due to the widespread treatment of their conditions. However, they may experience impaired function across the life span of the disease. In fact, often quality of life and morbidity (disability) are the more impactful consequences of NCDs for an individual. Self-reported data indicates that people living with NCDs tend to feel less well than those without them.
- South African homes are often multigenerational. Older persons are relied upon for income and childcare, and social services geared towards elderly care – such as retirement homes or targeted geriatric health services – are limited
- NCDs are more prevalent among the elderly due to several underlying physiological mechanisms that occur with ageing, including chronic inflammation that increases with age, adaption to stress, and stem cell exhaustion.
- Ageing compounds the impact of NCDs, especially through multimorbidity. Elderly patients often face frailty, greater blood pressure variability, and cognitive or functional impairment – which complicates the treatment of NCDs.
- NCDs may also wreak havoc among younger people, with a rise in the prevalence of diabetes and hypertension in medical scheme members as young as 30. However, young people tend to dramatically underestimate their risk for NCDs.

Introduction

Non-communicable diseases (NCDs) collectively account for more than 70% of global deaths, with over half of those deaths among people older than 70.[1] NCDs are also seen as the biggest health issue for those over 60.[2] As more people live to older ages thanks to technological evolution, increased medical knowledge and life-saving medicines, the burden of NCDs is expected to keep rising. It's already showing up in data that documents causes of death in many high-income countries, as well as in some South African provinces.[3]

In this brief, we address **how much of the increase in NCDs can be attributed to people living longer** (age-related diseases), and how much is due to other factors that aren't related to age.

Data and methods

Two broad quantitative data sets were used: household survey data and medical scheme data. Survey data includes General Household Survey (GHS) data, Demographic and Health Surveys (DHS) data and National Income Dynamics Study (NiDS) data. When analysing the quantitative datasets against one another for comparison, we standardised them based on age and sex, given the relationship between age and NCDs (as shown in this brief); and sex and NCDs (see brief 3). This standardisation was done against the 2018 Statistics South Africa (Stats SA) mid-year population estimates for all datasets to achieve fair comparison.

Private-sector data were provided by a large healthcare administrator and managed care services provider. The prevalence of diseases in the medical scheme population is estimated by finding the proportion of beneficiaries who are registered for chronic disease benefits for the relevant disorder. Where relative prevalence ratios are calculated, it refers to the ratio of the prevalence in one subgroup of the medical scheme population compared to another.

We also used qualitative data in this brief, based on primary data collection in one pocket of South Africa to marry the quantitative findings to the reality on the ground.

Why age and ageing are key considerations

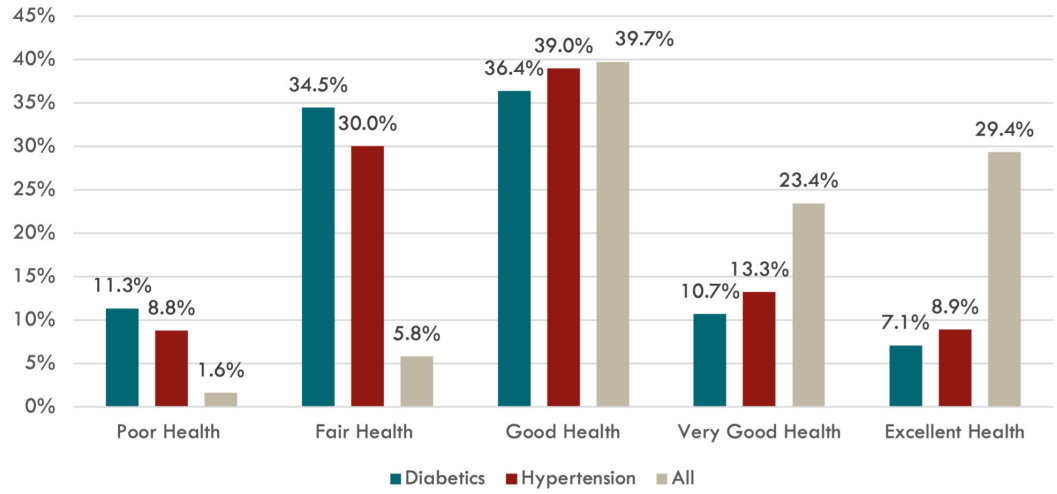
The World Health Organization (WHO) classifies premature deaths as those occurring before the age of 70. It reports that 55% of premature deaths in South Africa are caused by NCDs – a substantial proportion given the quadruple burden of disease in the country, of HIV and TB, maternal and child health, violence and injuries, and NCDs.[4] The UN Sustainable Development Goal 3.4 focuses on reducing the probability of death between the ages of 30 and 70 from cancers, cardiovascular diseases, chronic respiratory diseases, and diabetes with a third by 2030, compared to 2015 levels.[1]

However, NCDs don't only affect those aged 30 and older. There's also growing concern about childhood obesity and adolescent depression.[5] There's also increasing evidence of NCDs among other age groups and this brief looks into those too.

While mortality provides a good indication of the severity of NCDs, it's not necessarily the only appropriate measurement. People living with NCDs may live for many years but experience impaired function across the life span of the disease. Often, quality of life and morbidity (disability) are more impactful consequences of NCDs. Ideally, we would track morbidity through measures such as disability-adjusted life years (DALY), but this data is sparse, especially in South Africa. We'll therefore look at prevalence (the proportion of people living with NCDs) and incidence (the number of newly diagnosed patients) rates of different NCDs by age, and how this changes over time.

Self-reported data helps us to also understand the extent to which people feel well. Given the relationship between NCDs and morbidity, this can be a helpful indicator for understanding the impact of NCDs on a population. Using self-reported data from the National Income Dynamics Survey (NiDS), we see that more people with hypertension and diabetes rate their health as poor or fair, compared to those without these conditions, who self-reported their health as good (either good, very good, or excellent) (Figure 1). This shows that people living with NCDs tend to feel less well than those without them. It's problematic in a situation where most NCDs can be controlled with the right medication and clinical care to the extent that they don't impact daily activities. Therefore, self-reported data provides insight into the extent of unmanaged or poorly managed NCD cases.

Figure 1: Self-reported status of general overall health, compared to those with diabetes and hypertension (NiDS, 2017)[6]



Social context of ageing in South Africa

South Africans older than 60 qualify for an Older Person's Grant, which is intended to help those who are no longer able to work. The grant is means-tested to ensure that those who have sufficient income or assets are excluded.[7]

The country has a complicated history of grandparents having to look after grandchildren due to the legacy of apartheid, which forced people to work far from home; a high prevalence of migrant jobs; as well the burden of HIV/AIDS, which decimated a generation before ARVs were widely available. This reality, coupled with the guaranteed income of the Older Person's Grant brings, has resulted in substantial pressure on older people (especially grandmothers) to assume the breadwinner role, and financially support their adult children while looking after multiple grandchildren as well.[8] In a country where there's very little in the way of private retirement savings or private health insurance coverage, older people mostly make use of the public health sector and are completely reliant on the grant, which is relatively small.

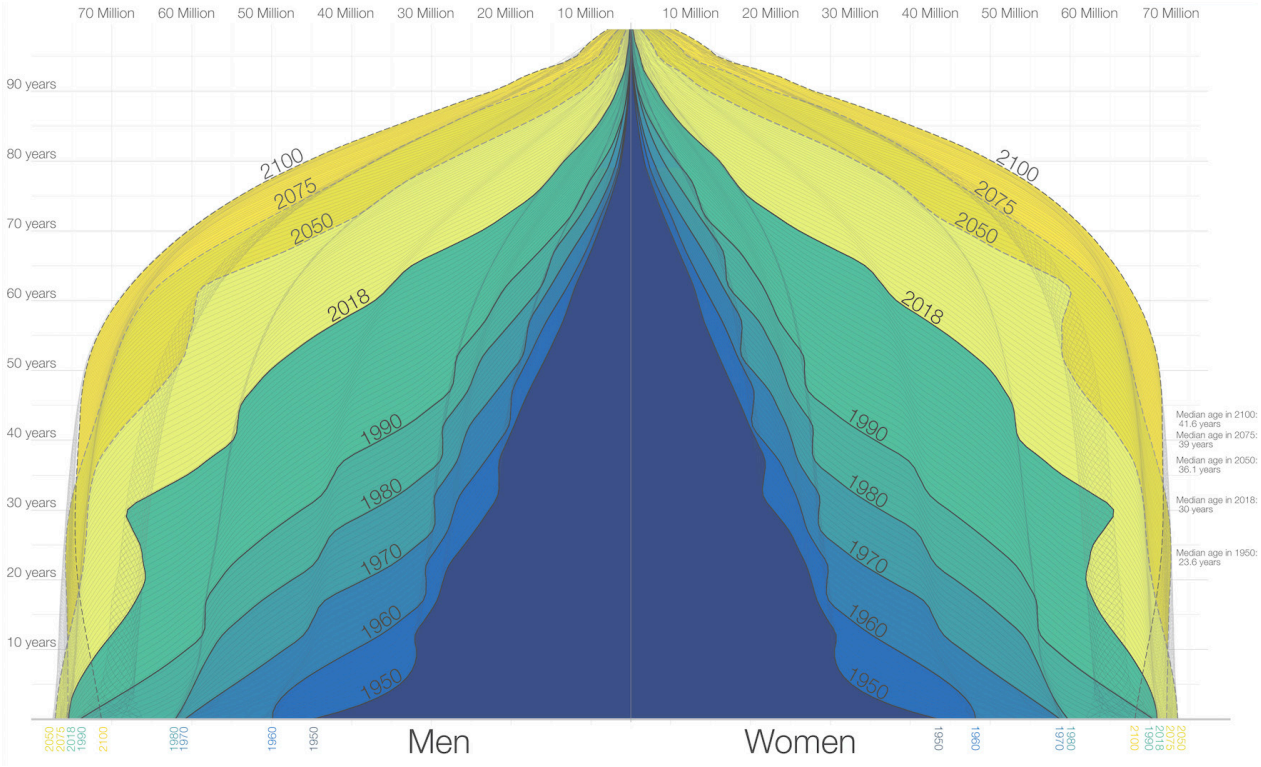
The need to step in as breadwinners comes at a time when their health starts to deteriorate – often with the onset of vision and hearing impairments and when walking long distances may become difficult. Ageing also complicates health-seeking behaviours as older people may find it difficult to read and understand prescriptions, remember to take medication at certain times, or struggle to get to clinics on time for appointments, or by certain times. Therefore, adults who live far from their elderly parents may be forced to leave their jobs to take on a caregiver role, which would have a knock-on economic impact for their family – and wider society.

The social context of ageing in South Africa is clearly complicated. Homes are multigenerational, older persons are relied upon for income and childcare, and there are limited social services geared towards elderly care – such as retirement homes or targeted geriatric health services.

Living longer, getting sicker

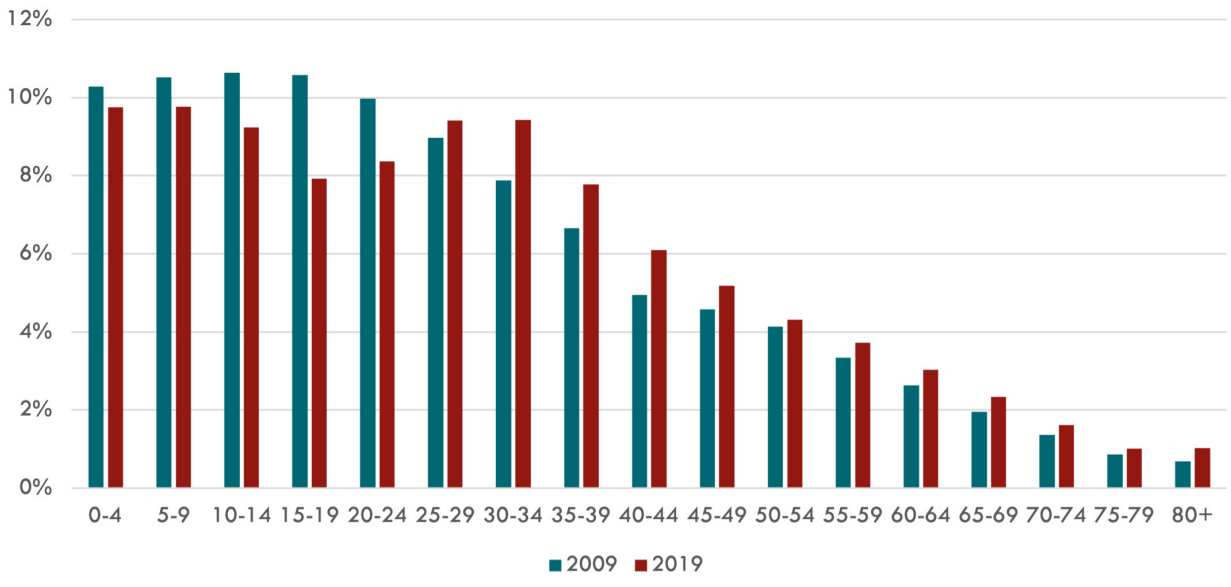
For most of recorded history, a large proportion of people were killed by natural disasters, violence and infectious diseases. Improvements in living standards, education and medicine are now allowing more people to live longer. Coupled with a drop in fertility in developed economies, it has led to an ageing population; a greater proportion of the population being made up by older people and a higher average age for the population.[9] Demographers predict that this trend will continue, which can be seen in the population pyramid below as a widening/rounding toward the top over time, with the median age projected to be 42 years by 2100 – substantially higher than the ~30 years in 2019 (Figure 2).

Figure 2: Global age and sex distribution (United Nations Population Division 2017)[10]



In South Africa, this trend has been muted, with Stats SA estimating that 61% of the population were younger than 40 in 2020.[11] This is partly due to the fertility rate being higher than that of developed countries. However, the age structure has also been limited by higher mortality from infectious (especially HIV-related) diseases. This has shifted given the now widespread and effective use of ARV treatments, which has dramatically increased the life expectancy at birth for both men and women. Figure 3 shows the growth in the population aged 25 and older within the last ten years. We're therefore likely to see significant growth in the 65+ age group.

Figure 3: Changes in South African age structure over the last 10 years (Stats SA, mid-year population estimates 2009 and 2019)[12]



As people with HIV live longer, South Africa faces a complex burden of disease – a collision of infectious and non-infectious diseases (see brief 6). In other countries, this plays out as more of a transition from infectious diseases to NCDs, rather than a dual burden.

Figure 4: Self-reported diabetes prevalence by age and sex, 2010 vs. 2018 (GHS 2010 and 2018)[13]

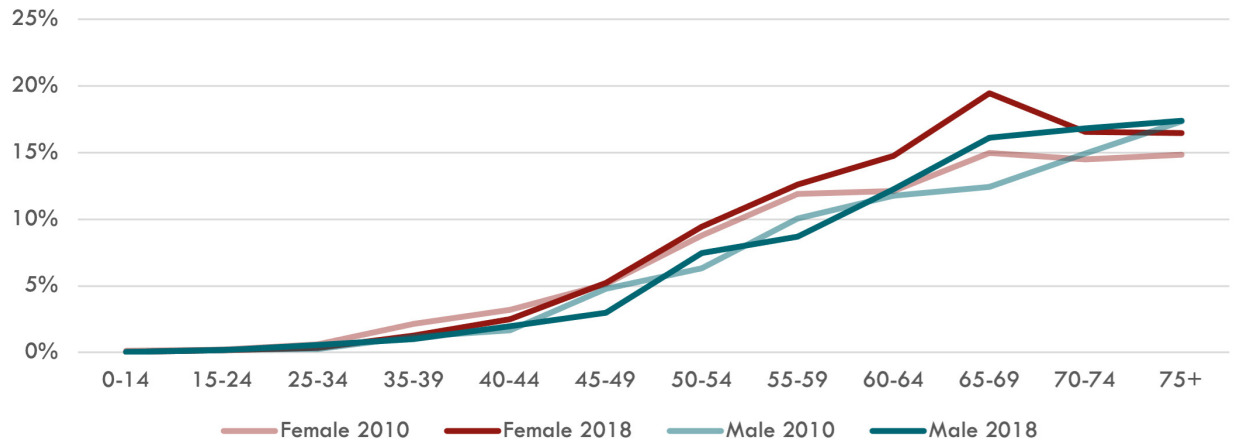


Figure 5: Self-reported NCD prevalence by age (GHS 2018)[13]

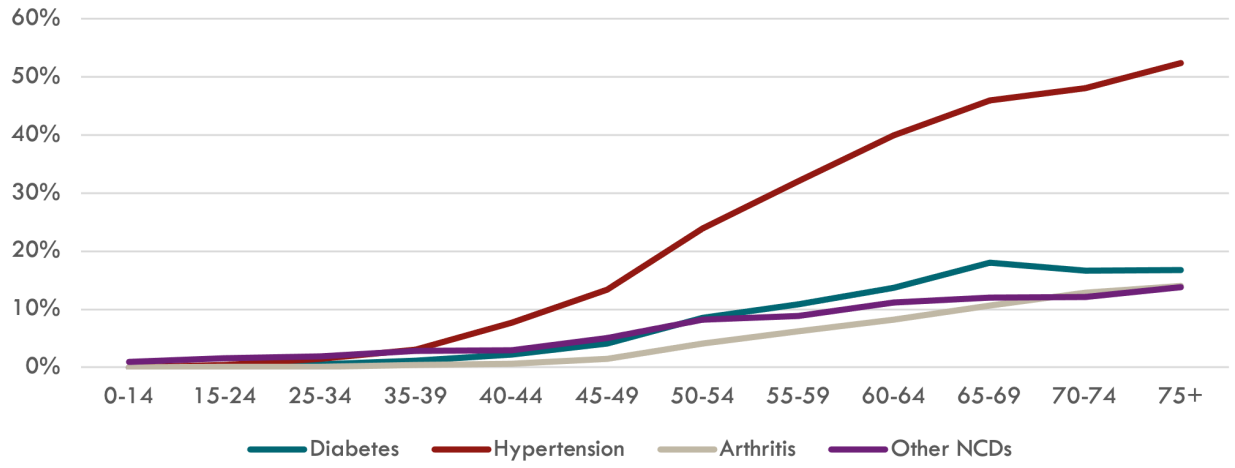


Figure 4 and Figure 5 show, respectively, self-reported diabetes prevalence by age and self-reported 'other NCD conditions' by age. These graphs illustrate that older people are more likely to experience (or perceive to experience) NCDs.

NCDs share several underlying physiological mechanisms with ageing. Historically, old age was considered a disease in itself, until medical advances identified that most old people didn't die because of the weaknesses of age or senility, but rather due to the cumulative mutual effect of age-related diseases.[14] Chronic inflammatory diseases like diabetes, cardiovascular disease, cancer and dementia have shown that the physiological link to ageing is strong enough to have led to the term "inflammageing" – the chronic, low-grade (subclinical) inflammation that is observed in older persons.[14] The physiological mechanisms underlying each disease are discussed more in briefs 7-9.

Ageing and NCDs have several common physiological mechanisms, such as adaptation to stress, stem cell exhaustion, and inflammation.

Ageing compounds the impact of NCDs, especially through multimorbidity (having more than one NCD or chronic disease at the same time). For example, older adults with diabetes also face a higher risk of cardiovascular and cancer mortality.[15] Multimorbidity, especially overlap with the biggest infectious diseases, is discussed in brief 11. Elderly patients also often face frailty, greater blood pressure variability, and cognitive or functional impairment16 – which complicates the treatment of NCDs. Ironically, these complications often lead to this population group being excluded from clinical studies and trials.[16] Older persons are therefore substantially impacted by disease but seldom studied.

Age should be used as a standardising factor when comparing statistics between groups. For example, we may see a greater prevalence of diabetes in an area, but that area could simply have a greater proportion of older people. Therefore, comparisons need to be age-standardised as much as possible.

NCDs can also accelerate and compound a person's experience of ageing, especially when they're dealing with more than one illness at a time or in a household. For example, hypertension and the consequent blood pressure variability could increase dizziness, resulting in an increased risk of falls in the elderly.[17] Falls are a leading cause of the decline and eventual mortality for older persons.[18]

In Vignette 1 below, we tie all of the sections above together (why ageing is an important consideration, the social context of ageing, and the implications of living longer) through qualitative data from the field.

Vignette 1: NCDs and the social realities of ageing

NCDs are often classed as city problems, but urbanisation has wreaked havoc in rural areas too, as I've seen in the Karoo Heartland. Many young people leave for larger towns and cities in search of jobs, or serve as migrant workers, returning intermittently. Meanwhile, the elderly stay. These older caregivers, who often shouldered caregiving responsibilities during the peak of the HIV/AIDs epidemic, now find themselves especially vulnerable to NCDs.

"Some of them live alone," the local Hospice Association told me, "or without sufficient care. They cannot walk to the clinic for medication and rarely get proper check-ups. That's where we try to step in." Not long after this, I observed a clinic consultation between a local doctor and a patient in her 60s suffering from high blood pressure. She was among those who lived alone. "If you get a stroke, who will look after you?" the doctor asked.

But there are also many older caregivers who aren't alone. Instead, they're caring for their grandchildren, often assisted by an Older Person's Grant. These childcare responsibilities can have implications for their own health-seeking. In another consultation, I observed a woman in her 50s who received treatment for HIV and hypertension, and was diagnosed with alarmingly high blood pressure. "I'm worried you're going to have a stroke," the doctor said. "I'm going to send you to the hospital right away." "But I can't," the patient protested, "I have grandchildren in the house."

Sometimes grandparents support their grandchildren as well as their own children, who've been unable to find work. Grief, trauma and financial stress can seep into the body, exacerbating NCDs among the elderly. The anthropologist Betsey Brada (2018) recently studied connections between adolescents with HIV and hypertension among their caregivers (who were often also their grandparents) in Botswana.

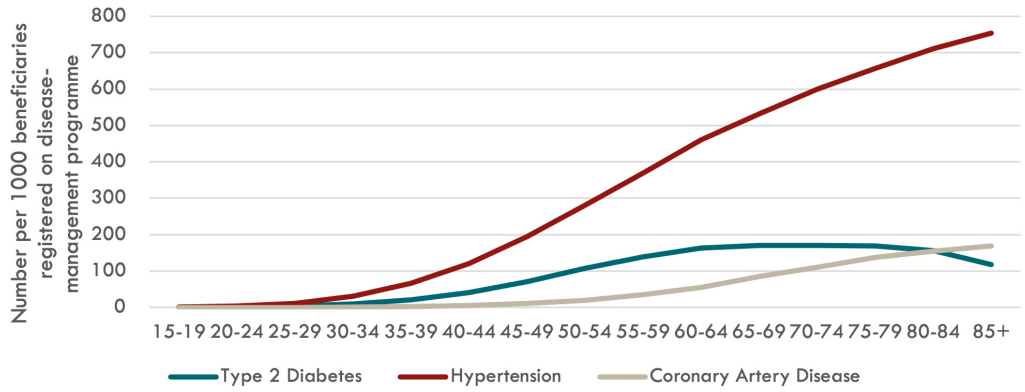
Middle-aged caregivers who haven't yet reached retirement age also contend with stressors, which undoubtedly speeds up biological ageing. Some must carry the dual burden of caring for both their elderly parents and their children or grandchildren, often with child support grants as their only income.

All of these realities characterise the vulnerabilities of ageing and extend well beyond biological factors.

NCDs among all Age Groups

The relationship between age and NCDs is complicated. While there used to be a perception that only older age groups were at risk, it's becoming apparent that certain NCDs may wreak havoc in younger ages too. Figure 6 shows the increased prevalence of diabetes and hypertension from ages as young as 30 in medical scheme members.

Figure 6: Number per 1,000 beneficiaries registered on a disease-management programme in 2017 (Council of Medical Schemes (CMS) Annual Report 2017-2018)[19]



Ageing is understood within the context of the body's damage-repair cycles – an individual experiences physiological stresses throughout life to the extent that these stresses overcome the body's ability to repair itself. If the intensity of the stress is low and/or the individual's lifestyle facilitates recovery, they can overcome the damage and perhaps even experience protective effects that decelerate ageing.[14] This is one way in which biological age can differ from chronological/actual age. For very fit and healthy people, their chronological age may be a few years younger than their biological age. This essentially allows them to live longer.[20] However, biological age is still a good indicator to determine those at a higher overall risk.

The age-related weakening of body functions also suggests that, when an NCD does manifest at a younger age, it may be driven by a different mechanism. For example, the elderly experience an age-related decline in pancreatic function which impairs insulin secretion, whereas younger diabetics may have normal insulin secretion, but have developed insulin resistance. Therefore, the same disease could develop in both the young and old, but with a different primary physiological driver.16 This suggests that screening and health-promotion messaging should differ for various age groups, as well as treatment protocols.

Some of the apparent increases in the incidence of NCDs can be attributed to greater awareness and health-seeking behaviour, as well as better/earlier screening. For example, there was a 52% increase in colorectal cancer rates within the Discovery Health Medical Scheme (DHMS) population between 2011 (75/100K population) and 2017 (113/100K population)[a]. However, it doesn't seem as if the underlying risk factors for colorectal cancer have changed drastically.

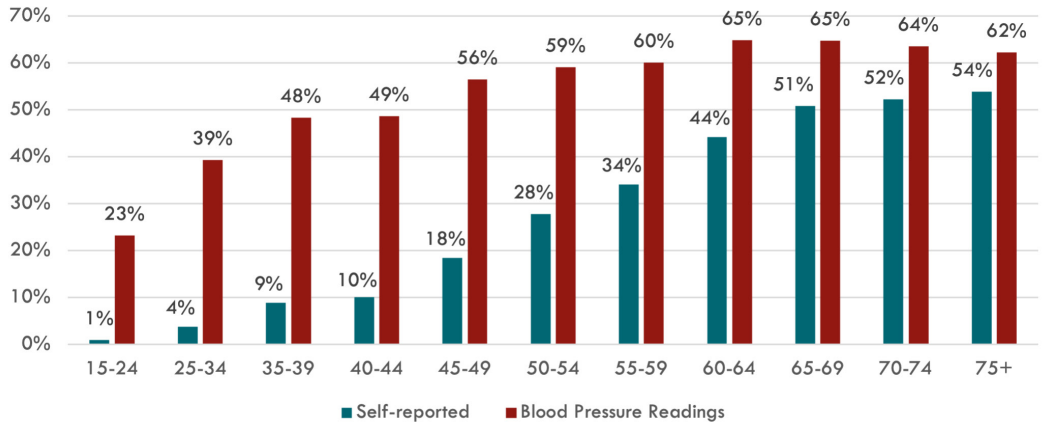
[a] www.discovery.co.za/assets/discoverycoza/medical-aid/find-a-document/guides/healthcare-claims-tracker-oncology-claims.pdf

While this could be a sudden emergence of latent disease, it's more likely due to public campaigns around testing for colorectal cancer. This is especially apparent in medical scheme environments where a funder can incentivise screening activities by paying for them, or rewarding screening.

When comparing South Africa to other countries, it's important to first assess the guidelines around screening. For example, US & UK guidelines encourage routine screening after middle age even in the absence of other risk factors.[16] In South Africa, where resources are limited in the public sector, screening targets those at risk.[21] However, screening rates are still relatively low, as is evident in high rates of undiagnosed hypertension in the country.[22] According to policy guidelines, the blood pressure of all individuals presenting at primary care facilities should be measured, but a randomised control trial of primary care clinics in South Africa found that blood pressure machines were often broken due to heavy use, and that blood pressure readings were often ignored.[23]

Figure 7 illustrates how young people, in particular, tend to dramatically underestimate their risk for NCDs. This is problematic because they may not present for clinical screening if their perception of risk is low. Screening campaigns should therefore be widely accessible, to ensure that it's not only those who are worried/experiencing negative symptoms who show up for screening.

Figure 7: Self-reported vs. objective measures of hypertension by age (NiDS, 2017)[6]



As the world has become more globalised, we've also seen an increase in the incidence of NCDs which can't be ascribed to increased screening alone. Globalisation has changed what is readily accessible and also what people may aspire to. For example, the growing role of supermarkets and processed foods may contribute to obesity among consumers in LMICs countries, given the available and affordable options, as well as the advertising pushed on consumers.[24] It illustrates the complexity of NCDs, and how mixing genetics and environmental factors create a 'perfect storm' – even for those who are young and who should in theory be less affected by NCDs.

Mental illness in particular is associated with socio-economic adversity and isolation, which can lead to depression, anxiety, substance abuse and suicide. There is growing concern about the prevalence in young people; globally, one in five adolescents experience a mental health condition, while suicide is the third leading cause of death in those aged 15–19.[5] The intersection of technology with social structures has given rise to new experiences of social isolation, such as cyberbullying, which require novel health interventions.

"Epigenetics" is a term used to describe how our DNA changes and in that changing, certain genes may be switched 'on' or 'off'. All this means is that a gene that previously was able to stop the body from growing a tumour, for example, could be 'switched off' through the changing of our DNA.

Our DNA can change for many reasons and this is a part of natural life, however, sometimes these changes can be harmful. Schalkwyk and Mill have suggested that the current NCD epidemic may be fundamentally changing our DNA, which in turn is then passed onto the next generation - increasing susceptibility to NCDs even at a young age. [20]

As a result, we are seeing how changes happening in a mother's body may actually be 'passed down' to her child in utero, influencing that child's susceptibility to NCDs and other illnesses. This has been widely investigated by the 'first 1,000 days' body of research, with substantial evidence showing the relationship between the mother's health and her child's, both while in utero and after birth.[26] For example, maternal gestational diabetes is associated with increased risk of childhood obesity and, later, of diabetes.[25] The prevalence of obesity in children in South Africa increased from 10.6% in 2005 to 13.3% in 2016 - more than twice the global prevalence of 5.6%, providing evidence for thisargument.[5] Vignette 2 illustrates the way in which NCDs accumulate over time.

Vignette 2: The accumulation of NCDs-risk over a life course

13 March 2019
Notes from a Primary Healthcare Clinic in the Karoo Heartland

The patient, who I will call Kobus, was taking daily medication for hypertension and cholesterol, and had previously suffered a stroke. He looked as though he was in his early 50s. Dressed in a tracksuit, he walked unevenly into the consultation room, using a single crutch for support. This was because one side of his body was partially lame. Kobus had incurred this disability after suffering a brain injury. He had been hit on the head more than fifteen years earlier. Interpersonal violence is the leading cause of death among young men (aged 15-24) in this municipal district.[1]

Kobus is no longer a young man, but his encounters with interpersonal violence had rippled into his later life. As a consequence of his brain injury, he now had epilepsy. Although his was the result of injury, nurses at the local hospital told me that epilepsy was in fact not an uncommon comorbidity. They had observed a particular linkage between epilepsy and diabetes, which is also reported in clinical literature[2] but remains poorly understood. People taking insulin or other diabetic medication have been shown to be at greater risk of hyperglycaemia, and therefore epilepsy.

While I don't know the order in which each of his conditions were diagnosed, I do know that **by the time he turned fifty, Kobus was grappling with three lifelong illnesses, each of which demanded daily medication.** Every morning, he took pills for high blood pressure, and every evening, pills for epilepsy and cholesterol. While the term chronic is often associated with long-term, slow-burning symptoms, Kobus had in fact experienced some highly acute episodes, including epileptic fits and a stroke.

Conclusion

The ageing population in South Africa implies a rise in NCD prevalence over time. While NCDs are seen as an inevitable consequence of ageing, there is a large and growing number of younger people affected by these diseases as well. In South Africa, NCDs account for 55% of premature deaths and the country's children are some of the most obese in the world. Adolescent depression continues to rise, as do depression-related suicides. This has far-reaching consequences for societies.

There seems to be a polarisation of health and disease at each age, with individuals developing habits at very young ages that set them up for a lifetime of disease. It suggests a need for screening and health promotion interventions to be tailored for different age groups, with a high payoff for earlier intervention.

Nevertheless, a focus on NCDs in the ageing population remains a key focus area, where the NCD coupled with the effects of ageing shows faster, more dire consequences than what we see at younger ages. Therefore, as a country, SA needs an approach that envelops young and old as well as screening, prevention and treatment. Given the current reality of NCDs in the country, screening alone is insufficient and will result in many untimely and avoidable deaths.

References

1. Bennett JE, Stevens GA, Mathers CD, et al. NCD Countdown 2030: worldwide trends in non-communicable disease mortality and progress towards Sustainable Development Goal target 3.4. *Lancet*. 2018;392(10152):1072-1088. doi:10.1016/S0140-6736(18)31992-5
2. World Health Organization. *Preparing for an Ageing Population.*; 2019
3. Statistics South Africa. *Mortality and Causes of Death in South Africa*, 2016: *Findings from Death Notification.*; 2018
4. World Health Organization. Premature NCD deaths. Global Health Observatory Dat.
5. Shung-King M, Lake L, Sanders D, Hendricks M. *Child and Adolescent Health: Leave No One Behind. Children's Institute*, University of Cape Town; 2019
6. The University of Cape Town. National Income Dynamics Study. Published 2017. Accessed April 26, 2021. www.datafirst uct.ac.za/dataportal/index.php/catalog/712
7. South African Government. Old age pension; Social benefits
8. Yancura L (Lori). Context Matters: Grandmothers in South Africa and the United States. *Gerontologist.* 2016;56(1):164 167. doi:10.1093/geront/gnv679
9. Ritchie H, Roser M. Our World in Data: Age Structure. 2020
10. United Nations Population Division. Our World in Data. Published 2017. Accessed April 26, 2021. https://ourworldindata.org/
11. Statistics South Africa. STATISTICAL RELEASE Mid-Year Population Estimates 2019.; 2019 [should 2019 be repeated here?]
12. Statistics South Africa. Mid-Year Population Estimates.; 2019. Accessed April 26, 2021. www.statssa.gov.za, info@statssa.gov.za, Tel: +27 12 310 8911
13. Statistics South Africa. General Household Survey 2019.; 2020. Accessed March 12, 2021. www.statssa.gov.za, info@statssa.gov.za, Tel: +27 12 310 8911
14. Franceschi C, Garagnani P, Morsiani C, et al. The Continuum of Aging and Age-Related Diseases: Common Mechanisms but Different Rates. *Front Med.* 2018;5(MAR). doi:10.3389/fmed.2018.00061

References

15. Kalyani RR, Golden SH, Cefalu WT. Diabetes and Aging: Unique Considerations and Goals of Care. *Diabetes Care*. 2017;40(4):440-443. doi:10.2337/dci17-0005

16. Selvin E, Parrinello CM. Age-related differences in glycaemic control in diabetes. *Diabetologia*. 2013;56(12):2549-2551. doi:10.1007/s00125-013-3078-7

17. Buford TW. Hypertension and Aging. *HHS Public Access*. 2016;26:96-111. doi:10.1016/j.arr.2016.01.007.Hypertension

18. World Health Organization. *Falls*.; 2018

19. Council for Medical Schemes. CMS Annual Report 2017-2018: Annexures

20. Schalkwyk L, Mill J. Ageing: how our "epigenetic clocks" slow down as we get older

21. Department of Health Republic of South Africa. *Strategic Plan for the Prevention and Control of Non-Communicable Diseases* 2013.; 2013

22. Berry KM, Parker WA, McHiza ZJ, et al. Quantifying unmet need for hypertension care in South Africa through a care cascade: evidence from the SANHANES, 2011-2012. *BMJ Glob Heal*. 2017;2(3):2011-2012. doi:10.1136/bmjgh-2017-000348

23. Thorogood M, Goudge J, Kabudula CW, Limbani F, Roseleur J, Gómez-Olivé FX. Time to review policy on screening for, and managing, hypertension in South Africa: Evidence from primary care. *PLoS* One. 2019;14(1):1-13. doi:10.1371/journal.pone.0208983

24. Qaim M. Conference on 'Sustainable food consumption' Globalisation of agrifood systems and sustainable nutrition. Proc Nutr Soc. 2017;76(1):12-21. doi:10.1017/S0029665116000598

25. Barouki R, Gluckman PD, Grandjean P, Hanson M, Heindel JJ. Developmental origins of non-communicable disease: Implications for research and public health. *Environ Heal A Glob Access Sci Source*. 2012;11(1):1-9. doi:10.1186/1476-069X-11-42

26. Cusick S, Georgieff MK. *The First 1,000 Days of Life: The Brain's Window of Opportunity*

27. Massyn N, Padarath A, Peer N, Day C. District Health Barometer 2016/17. Published online 2017

28. Lu CL, Chang YH, Sun Y, Li CY. A population-based study of epilepsy incidence in association with type 2 diabetes and severe hypoglycaemia. Diabetes Res Clin Pract. 2018;140:97-106. doi:10.1016/j.diabres.2018.03.020