FACULTY OF HEALTH SCIENCES

UNIVERSITY OF CAPE TOWN

GROOTE SCHUUR HOSPITAL

Screening and early detection of cervical cancer in Africa

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Disclosure

- Received honoraria for appearing on various speaker forums on HPV vaccination for GlaxoSmithKline and Merck as well as research funding
- Research grant support from Roche

World Health Statistics 2016*

- 303 000 women die from complications of pregnancy and childbirth
- 5.9 million children die before 5th birthday
- 2 million newly infected with HIV, 9.6 million new TB cases and 214 new malaria cases
- 1.7 billion people need treatment for neglected tropical diseases
- > 10 million die before age 70 due to CVD and cancer
- 800 000 commit suicide

*World Health Statistics 2016, Geneva, Switzerland

World Health Statistics, 2016

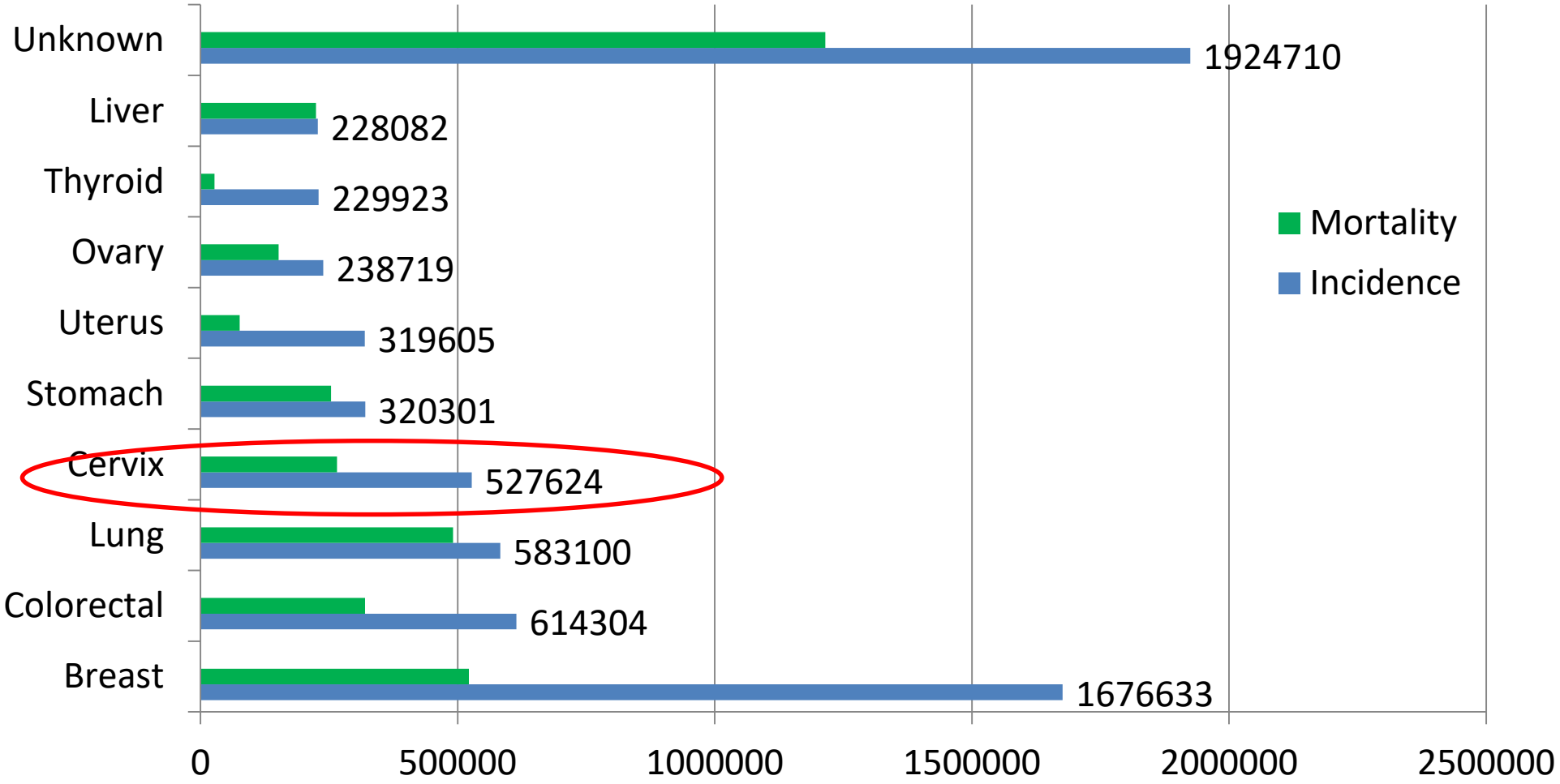
- 1.25 million die road accidents
- 4.3 million die from air pollution (cooking fuels)
- 3 million die from outdoor pollution
- 475 00 murdered (80% men)
- Risk Factors for disease
  - 1.1 billion smoke tobacco
  - 1.8 billion people drink contaminated water
  - 946 million people defecate in the open

Cancer in 2012– global perspective*

- 14.1 million new incident cases of cancer
- 8.2 million deaths
- 32.6 million living with cancer (within 5 years of diagnosis)
- Of these majority occurred in LMICs
  - 8 million new cancers
  - 5.3 million of the deaths from cancer
  - 15.6 million of the 5 year prevalent cases
- Overall ASIR men is 205 and women 165 per 100 000 (25% difference)

*www.globocan.iarc.fr/

Top ten cancers in women globally – Globocan data 2012*



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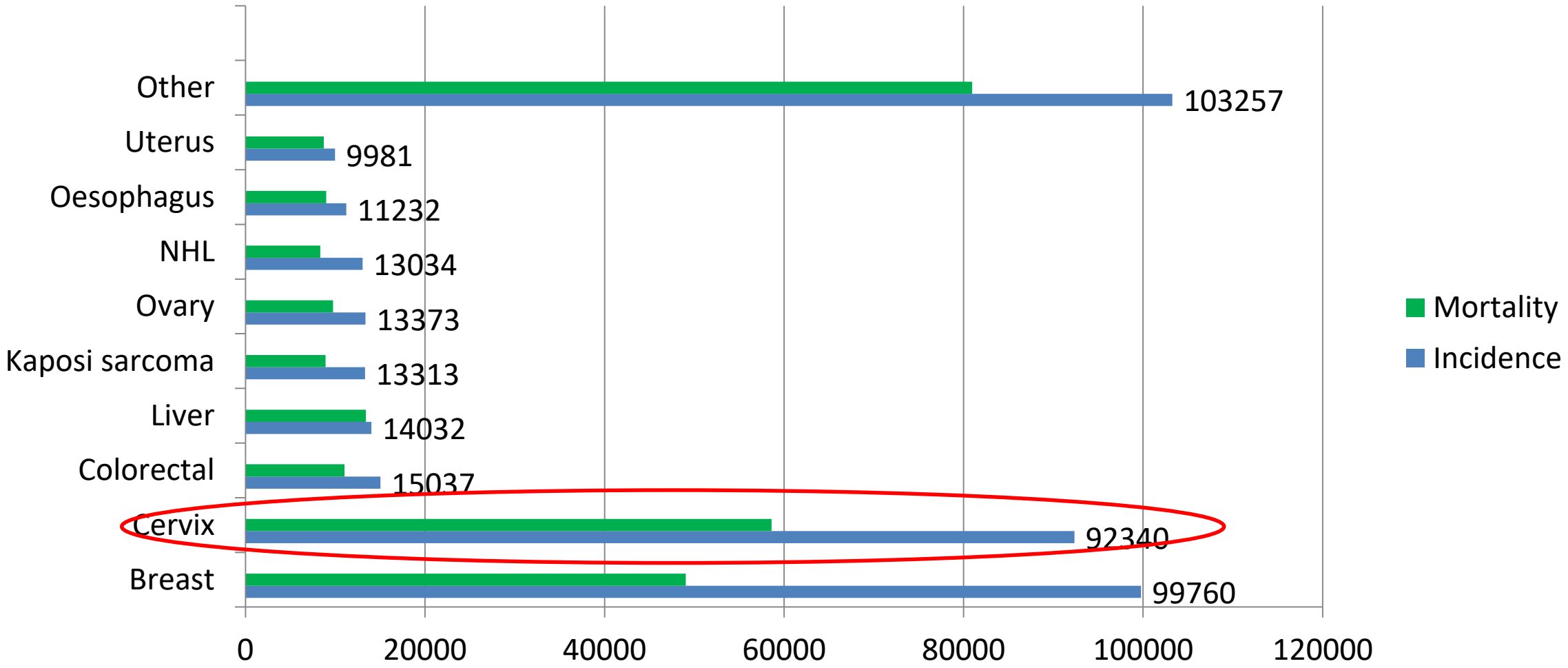
Top ten cancers in women in Africa, Globocan 2012*



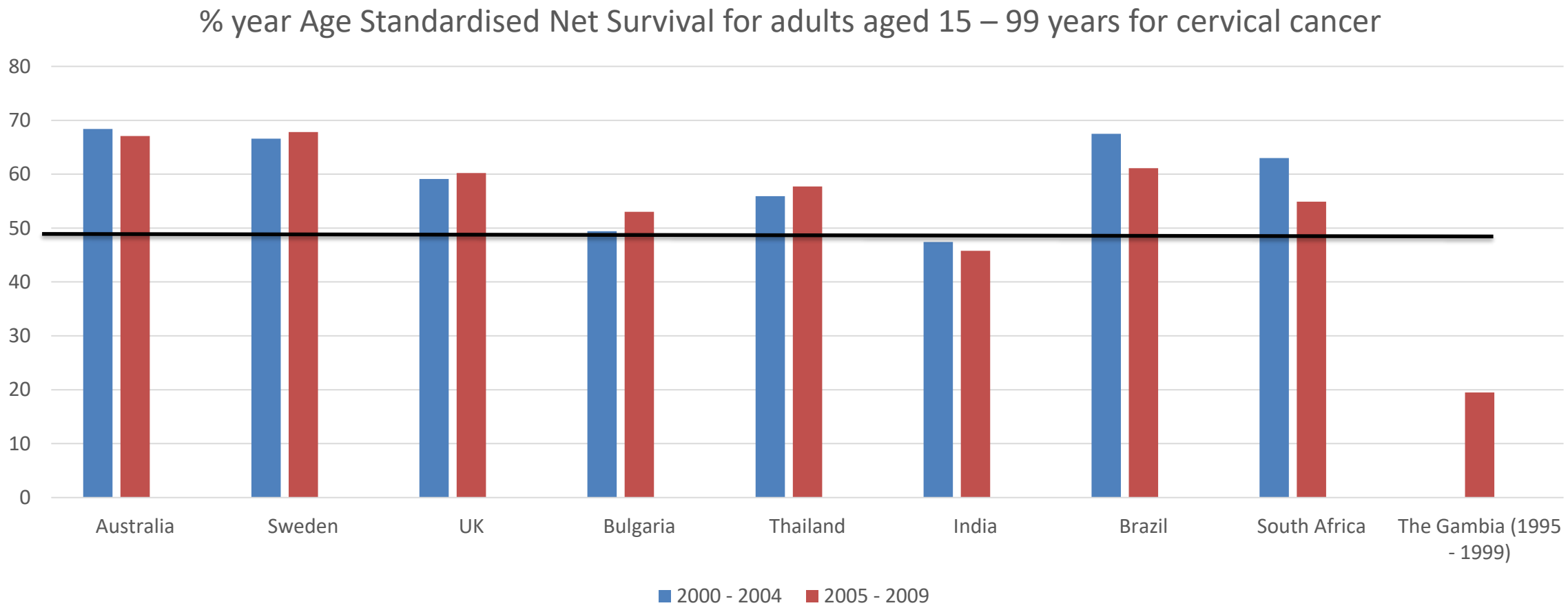
*www,globocan.iarc.fr/

Cancer survival 1995 – 2009: analysis of 25 676 887 million patients*

- 279 population-based cancer registries from 67 countries
- Data for cervical cancer was available for 602 225 women
  - included ***9 countries from Africa (10 registries)***
- Pathological evidence of malignant disease was available for over 23 million patients combined, and from **85.5% of African registries** with a very wide range at national level i.e 15% in the Gambia, 36% in Mongolia and >'er than 99% in Belgium
- Survival for cervical cancer is stable or has increased slightly in many countries:
  - Brazil, Cuba, Ecuador and Puerto Rico in 10 years ASNS increased to 60%
  - Chile increased from 42 – 51%
  - Argentina 46 – 51%
- Global range of survival for cervical cancer is 40 – 70%

* Allemani et al. Lancet November 26, 2014 (Concord -2)

Survival data for cervical cancer per country*



* Allemani et al. Lancet November 26, 2014 (Concord -2)

Survival from Cancer in SSA

- Sankaranarayan et al* evaluated > 300 000 cancer deaths from 1990 – 2001
- Only two registeries in SSA contributed data
  - The Gambia:
    - only 22% of people diagnosed with cancer survived 5 years
  - Uganda:
    - 13% survived 5 years except for breast cancer (46%)

*Lancet Oncol 2010:111; 165 - 173

Cancer case fatality rates by World Bank Income Group*

Cancer site	Low income	Lower middle income	Upper middle income	High income
Breast	56.3	44.0	38.7	23.9
Cervix	68.4	58.6	48.2	32.6
Colorectal	70.5	62.4	60.1	42.4
Lung	91.3	87.1	92.5	82.2
Oral Cavity	55.4	54.2	47.6	27.7

*Economic Intelligence Unit, 2009

Cost of Cancer Care - USA

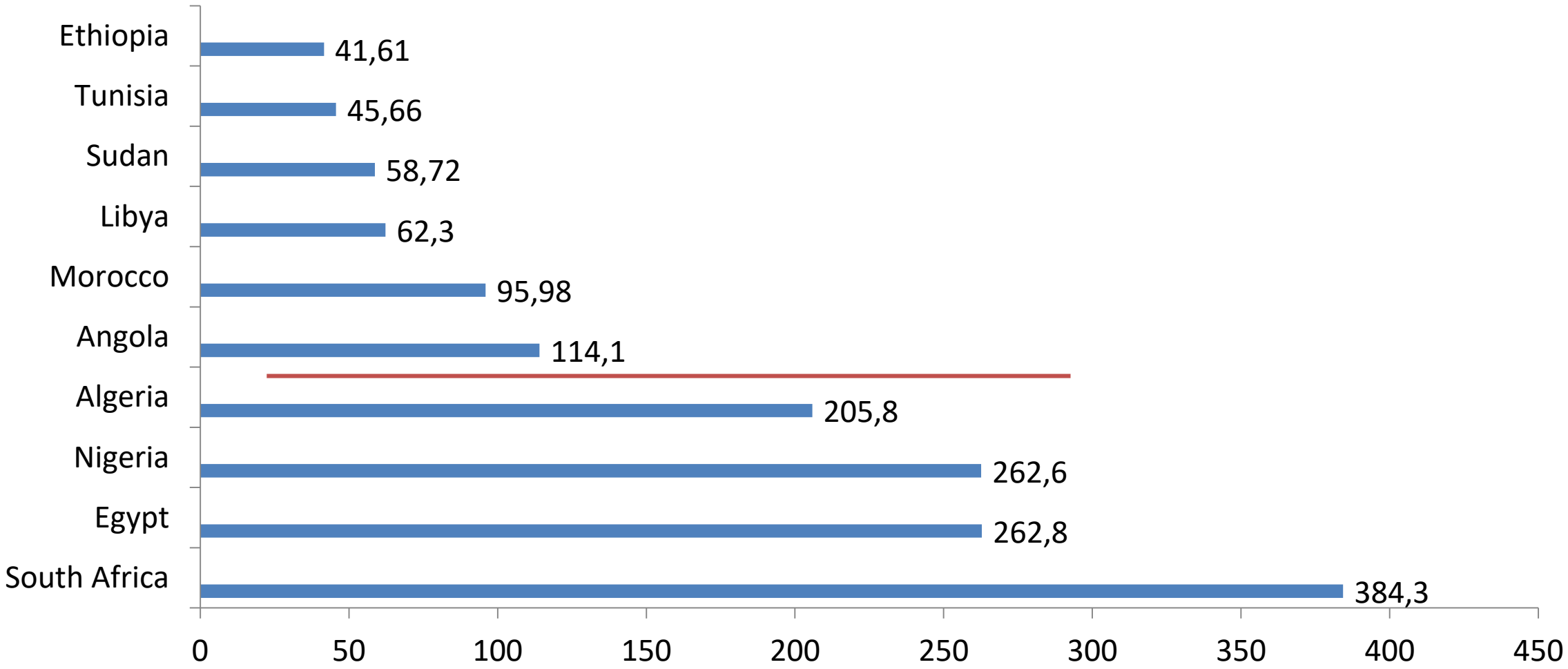
- Cancer cost the USA economy $124 billion in 2010 for 13 tumour sites based on SEER data
- Projected to increase to $173 billion by 2020 (an increase of 39%)
- USA health system characterised by:
  - High out of pocket expenses
  - Strong private and provider sectors
  - Vocal professional and pharmaceutical lobbies
  - Affordability challenges can push some families into bankruptcy or forego essential care

Cost of Cancer Care EU*

- Total economic cost of cancer in EU (17 countries)about €126 billion in 2009
- 66% of all costs accounted for by Germany, France, Italy and UK
- 27% of cancer-related health care costs were drug related
- Across EU population health care costs of cancer were equivalent to €102 per citizen

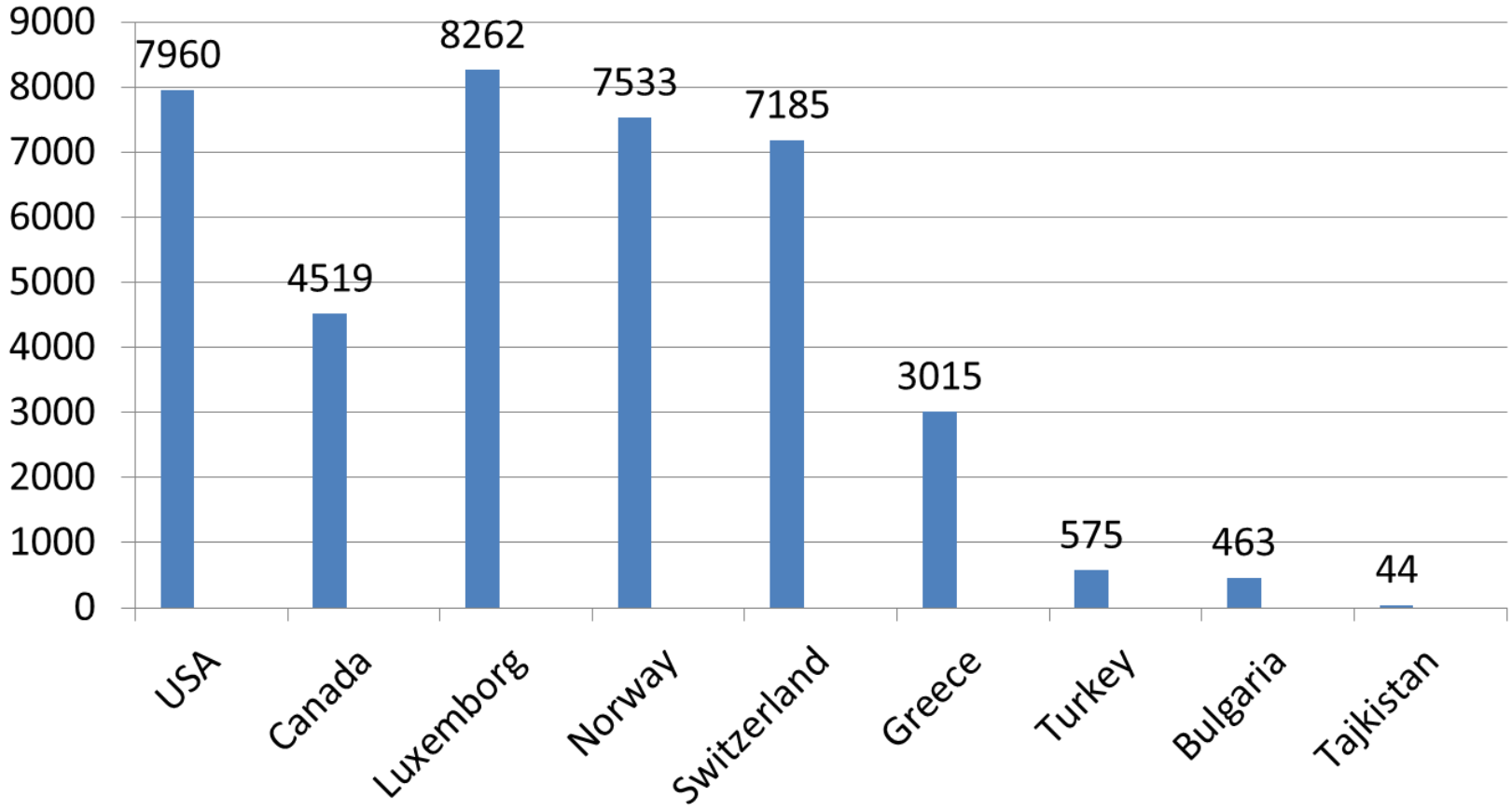
Luengo-Fernandez et al. Lancet 2013; 14:1165 - 74

GDP of richest countries in Africa in billions, 2012*



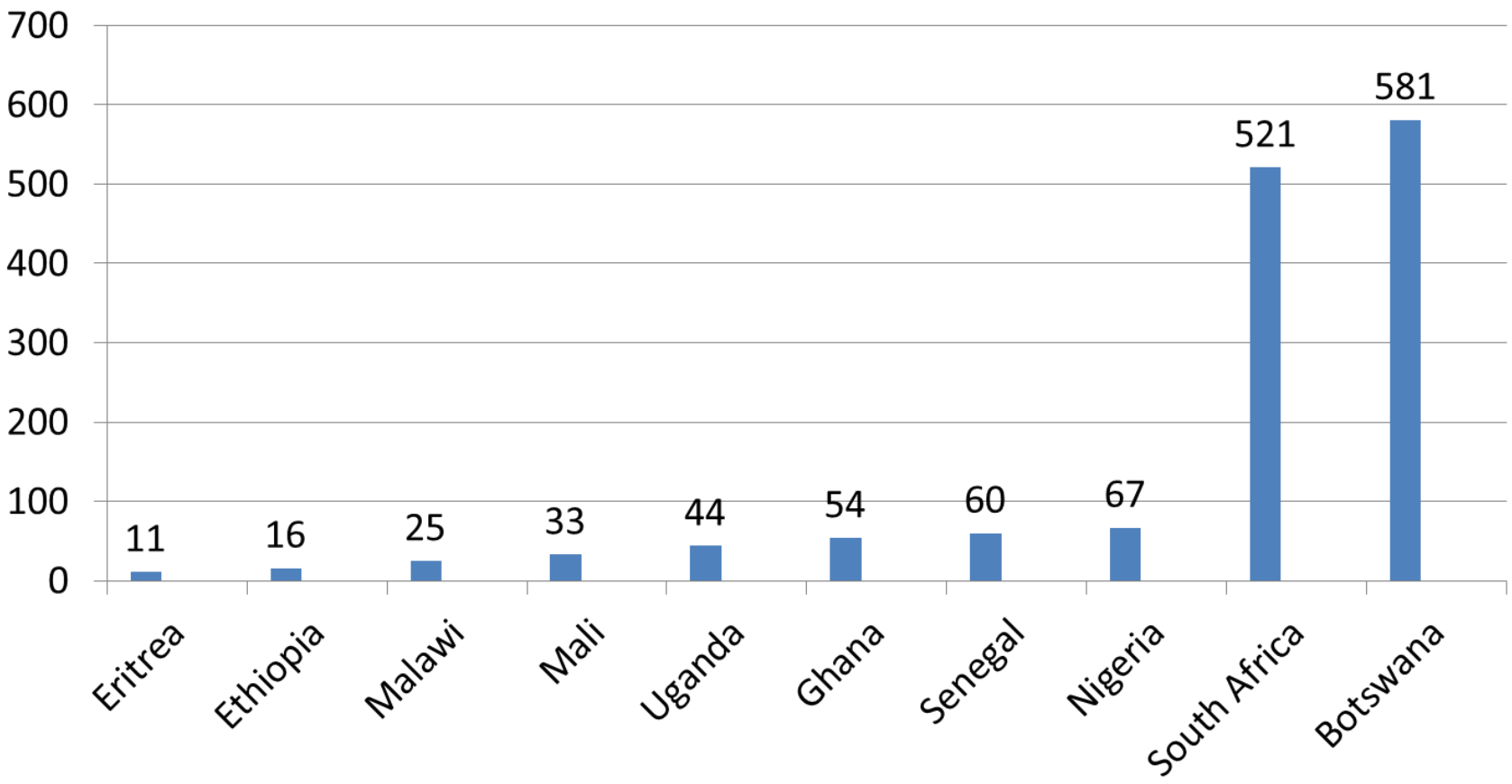
*www.worldbank.org

Total Health Expenditure per Capita ($), 2009*



*World Health Statistics, 2012

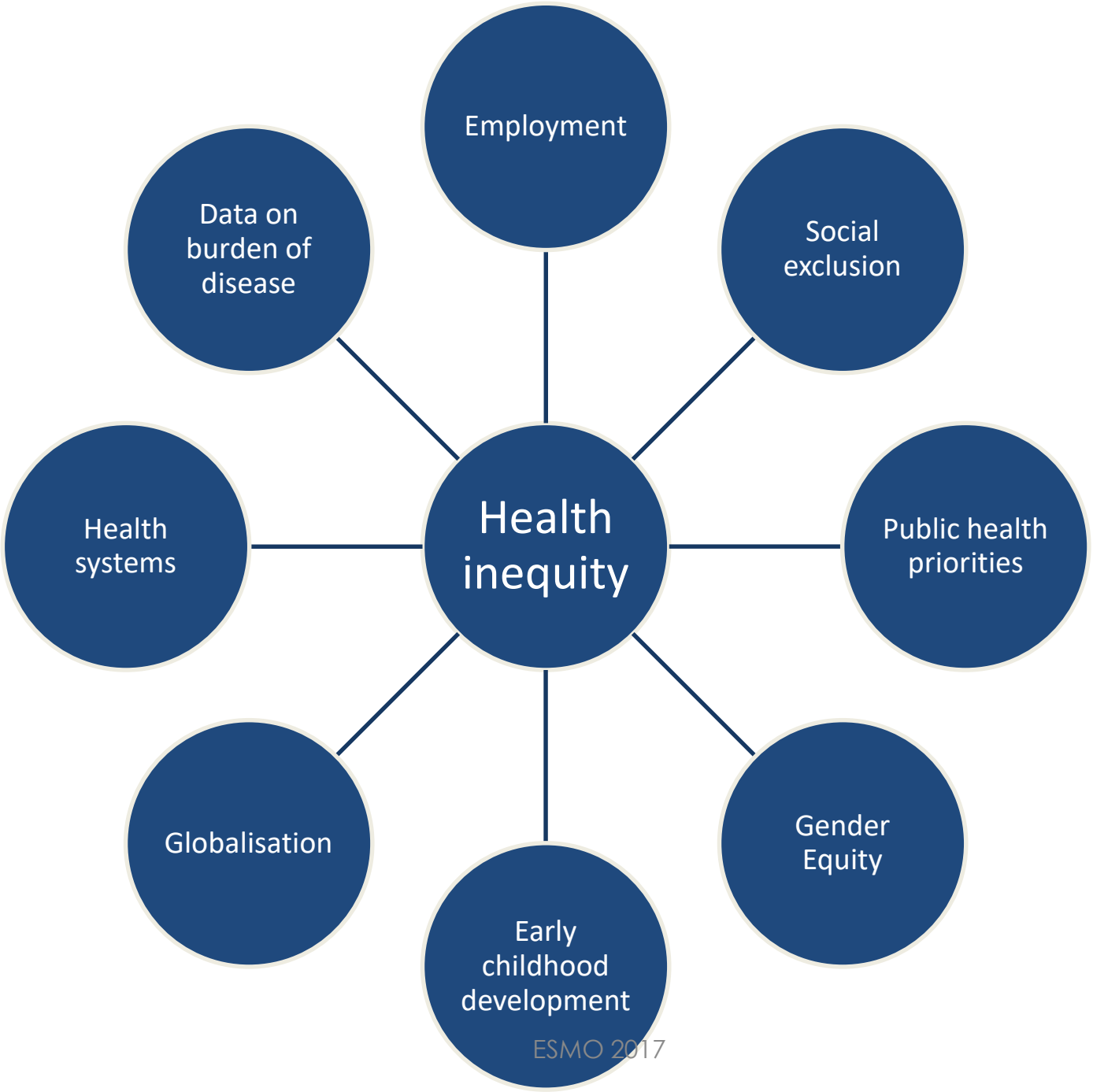
Total Health Expenditure per Capita ($) 2009 in various African countries*



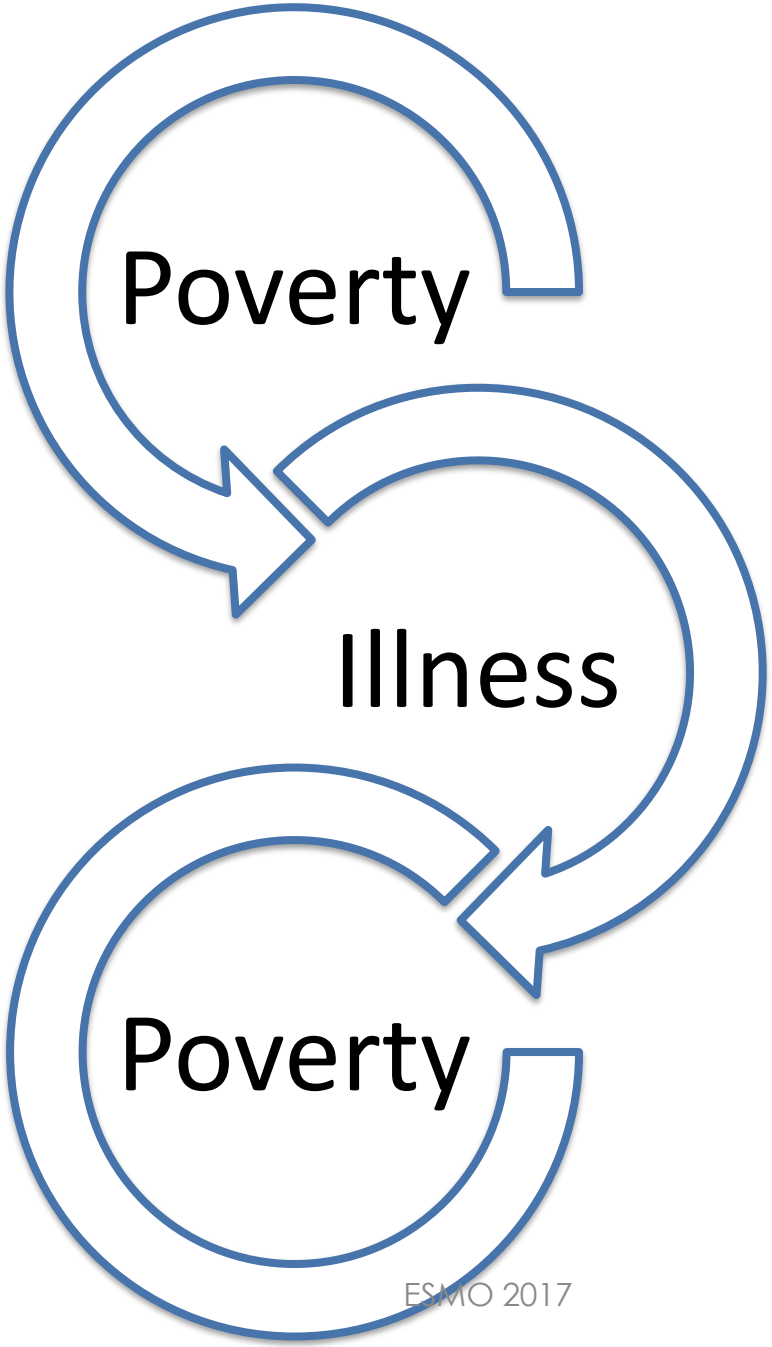
*World Health Statistics, Geneva, 2012

Health Inequity

- Health inequities are defined as 'avoidable inequalities in health between people within and between countries…'
- Obvious examples:
  - Infant mortality rate (number of live births surviving first year of life)
    - 2 /1000 Iceland
    - 120/ 1000 in Mozambique
  - Lifetime risk of maternal death
    - 1 in 17 400 in Sweden
    - 1 in 8 in Afghanistan
- The poorest of the poor have the worst health


Employment
Data on burden of disease
Social exclusion
Health systems
Health inequity
Public health priorities
Globalisation
Gender Equity
Early childhood development

ESMO 2017


Poverty
Illness
Poverty

Problems with statistics in Africa and other developing countries

- Population of Africa in 2008
  - 812 million
  - 404 m men, 408 m women
- 7.2% of population covered by medically certified causes of death
- 8.3% covered by population-based registeries
- In 2008
  - 667 000 incident cancers/518 000 deaths
  - ***78% of all people with cancer died***

Out of pocket expenditure

- User fees for health care were suggested by World Bank in 1980s – precondition for financial loans
- Extent of financial catastrophe and impoverishment due to direct out-of-pocket payments for health impacts at least 10% of population
- Estimated 150 million people pushed over poverty line by being forced to pay for health care out of own pockets
- Highest proportion paid in poorest countries
  - Nigeria 62% of total health expenditure
  - USA 12%, Netherlands 6%, UK 10 %
- Main impact, major reduction in use of health care

Barriers to secondary prevention of cervical cancer in developing countries

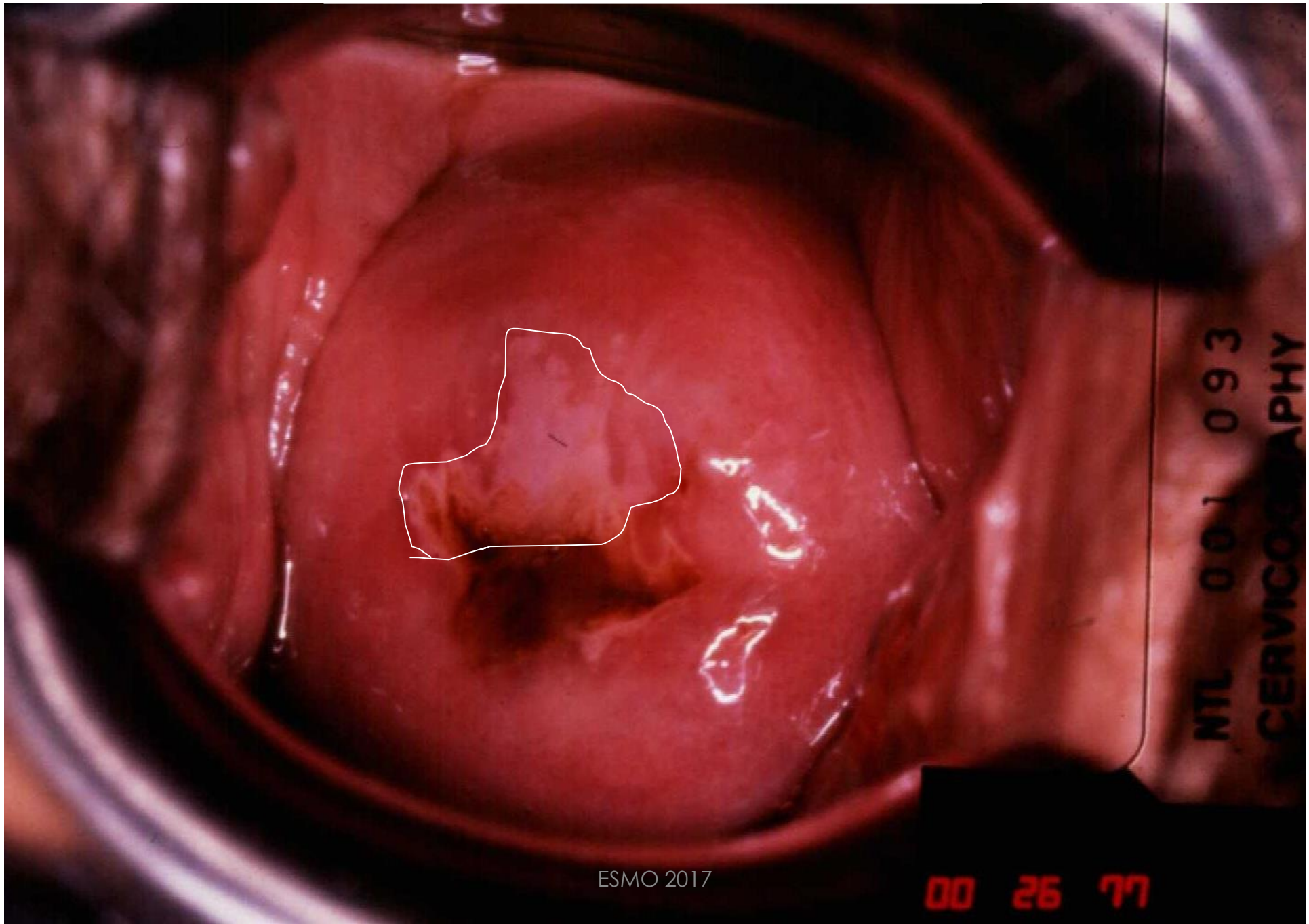
- Competing health needs
- Limited financial, human and capital resources
- Poor health care infrastructure
- Endemic civil strife, war, environmental instability and widespread poverty
- Poor governance, colonisation, exploitation from developed world
- The traditional screening process itself

Alternative strategies for cervical cancer prevention

- Visual Inspection with Acetic Acid (VIA)
  - Cross sectional studies showed promising sensitivity and specificity
  - Meta-analysis of 26 studies* in which VIA was performed on asymptomatic women who underwent confirmatory testing with a disease threshold of CIN 2 plus reported:
    - Sensitivity of 80% (range 79 – 82%)
    - Specificity of 92% (range 91 – 92%)
    - PPV of 10%
  - Two large RCT showed significantly poorer performance of VIA compared to HPV DNA testing (Denny et al and Sanakaranarayanan et al)
  - IS VIA better than nothing at all? Or is this a case of Third Rate for the Third World?

*Sauveget et al, Int J Gynecol Obs, 2011

Courtesy Dr Sankararyanan, IARC



Courtesy Dr Sankararyanan, IARC

WHO Demonstration Project

- WHO Demonstration Project in six African countries* showed:
  - Of 19 579 women screened
    - 326 (1.65%) were suspicious for cancer
  - Of these 326 women
    - Only 96 (29.4%) were investigated and 79/326 (24.2%) had confirmed cancer of the cervix
    - **There was no information on 230 women (70.5%)**
    - HIV positive women were receiving free ARVs but had to pay for consultations and cervical biopsies
    - The majority of women with cancer were treated with radiation

*Prevention of cervical cancer through screening using VIA and treatment with Cryotherapy. WHO 2012, Geneva, Switzerland

WHO Demonstration Project

- Target population women aged 30 – 50 years
- Coverage rates were very low: range 0.4% Zambia to 7.1% in Madagascar

Results

- 1980/19 665 (10.1%) were VIA positive
- 1731 (87.4%) were eligible for cryotherapy
- 1058/1731 (60.9%) received cryotherapy
  - **601 (34.6%) were lost to follow up**
  - 39.1% of women had treatment day of screening
  - 24.3% within 6 days
  - 18% within 30 days

RCT of VIA in Mumbai*

- Cluster randomised trial initiated in Mumbai in 1998
- Four rounds of cancer education with VIA screening at 24 month intervals in the screening group
- Cancer education offered only at beginning of study in the control group
- After 12 years of follow-up, screening group showed a 31% reduction in cervical cancer mortality (RR = 0.69; 95% CI = 0.54 – 0.88, p = .003)

Shastri et al. JNCI February 2014

HPV screening for Cervical Cancer in Rural India*

- Cluster randomised trial
- 131 746 well women aged 30 – 59
- 4 groups:
  - HPV testing
  - Cytologic testing
  - VIA
  - Standard of care (no screening)
  - Screening January 2000 – April 2003
  - 88% of women with positive results had colposcopy

Sankaranarayanan et al. N Engl J Med 2009;360:1385- 94

Incidence of cervical cancer and rates of death in different groups in Indian Trial

	HPV test	Cytologic	VIA	Control
Incidence all ca cx	**127**	152	157	118
Stage 2 Cancer or >	**HR: 0.47 (0.32-0.69)**	HR: 0 .75 (0.51 – 1.10)	HR 1.04 (0.72 – 0.49)	1.00
Death	**HR:0.52 (0.33 – 0.83)**	HR:0.89 (0.62 – 1.27)	HR:0.86 (0.60 – 1.25)	1.00

Critical findings

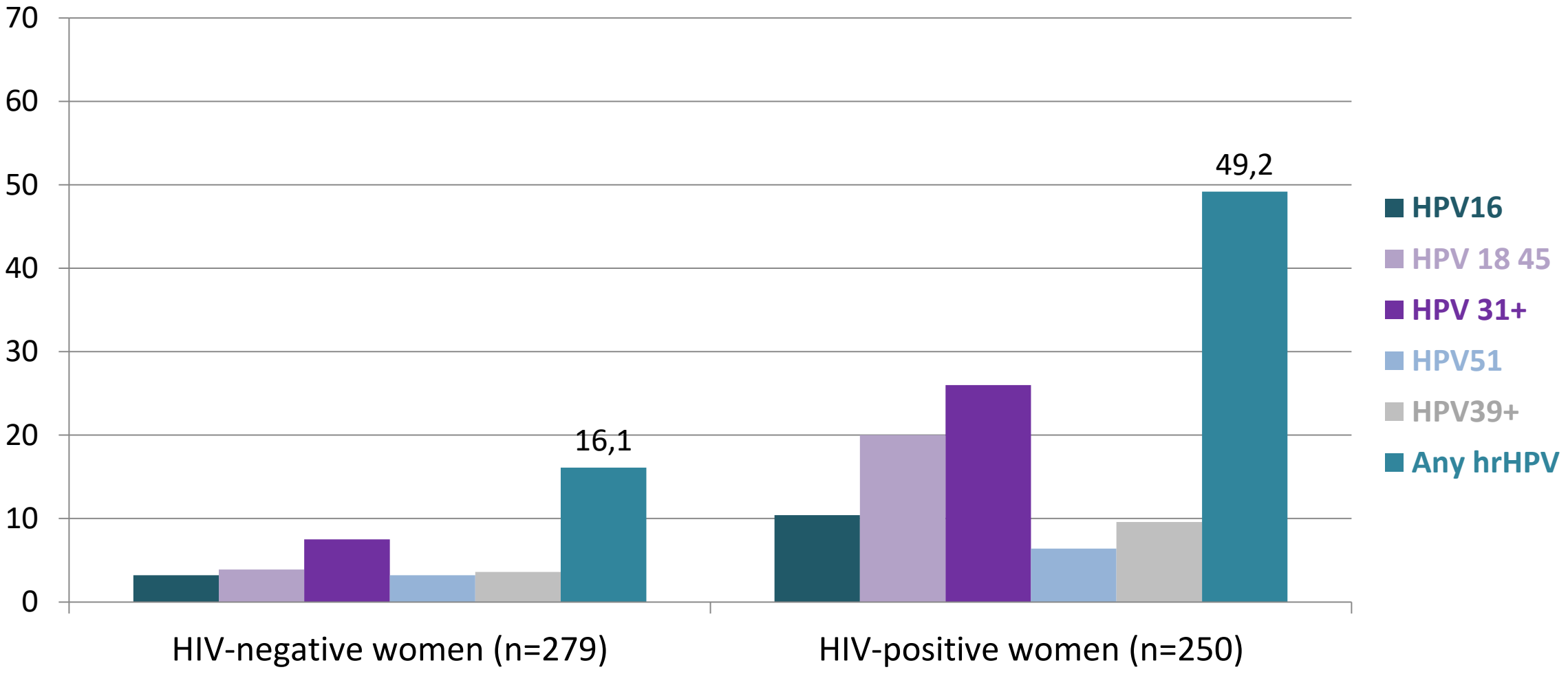
- Single round of HPV testing and treatment of positives associated with significant decline in rate of advanced cervical cancer and deaths
- No significant reduction in rate of death in either the cytologic or VIA groups
- ASIR of invasive cancer in women with negative cyotology and VIA tests were four times the rate among HPV negative women, supporting the very high NPV of HPV testing.

*Sankaranarayanan et al. N Engl J Med 2009;360:1385- 94

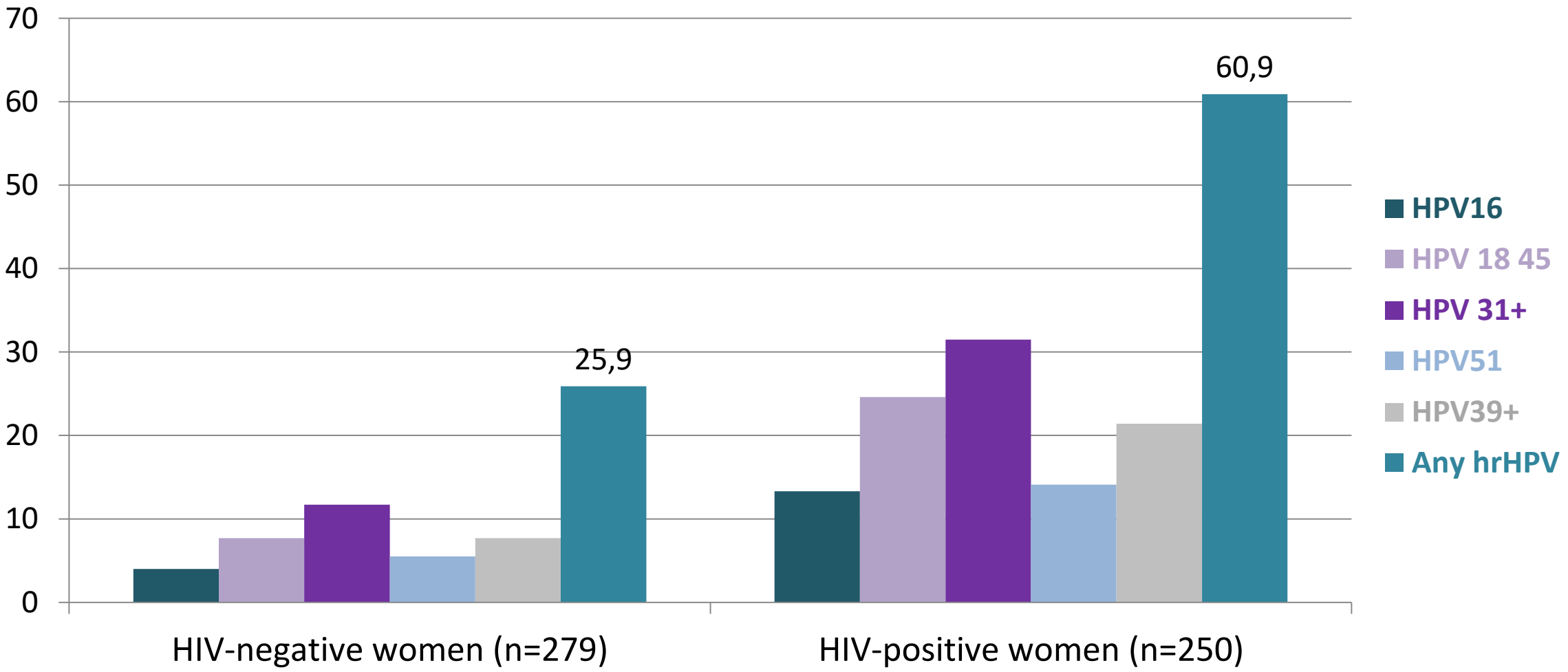
Point of Care Testing – HPV Xpert (Cepheid)

- Recruit 1000 women (500 HIV-pos, 500 HIV-neg) from women's health services in Cape Town, South Africa.
- Age 30-65 years
- Clinician-collected cervical samples
- Self-collected vaginal samples
- HPV Xpert testing of both samples
- mRNA biomarker testing **CDKN2A, TOP2A and MKI67**
- Colposcopy and histological sampling for all women to determine CIN2+ (adjudicated pathology review)

Prevalence of HPV on clinician-collected cervical samples in screening population

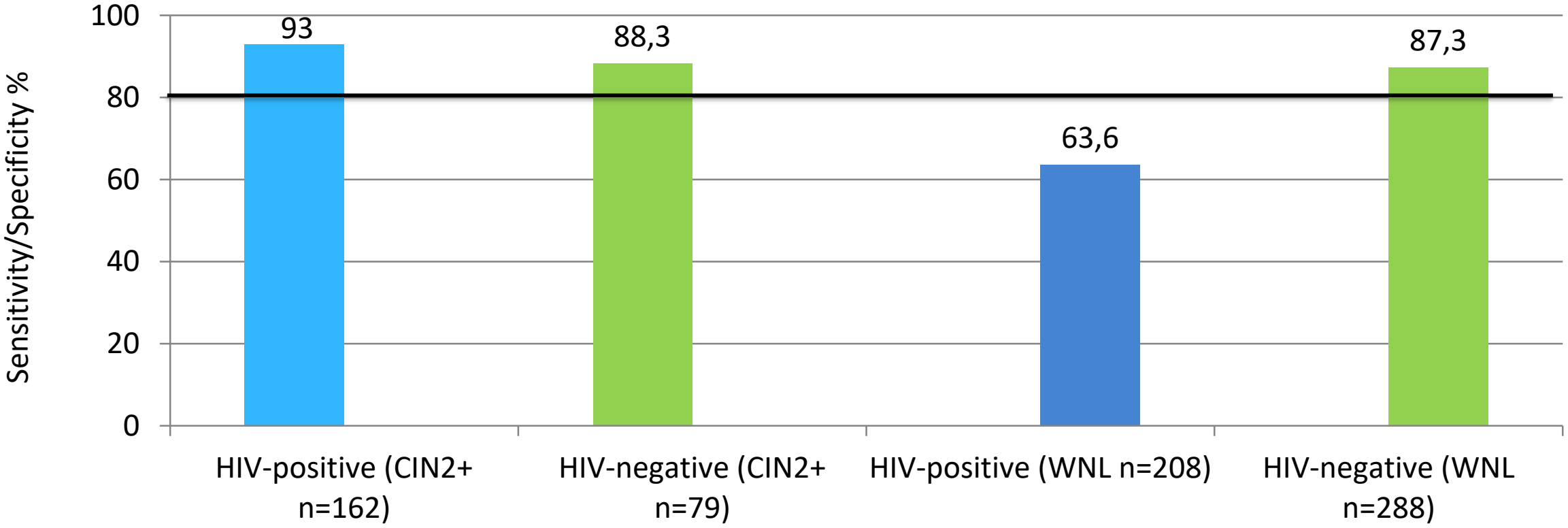


HPV Prevalence on self-collected vaginal samples in screening population



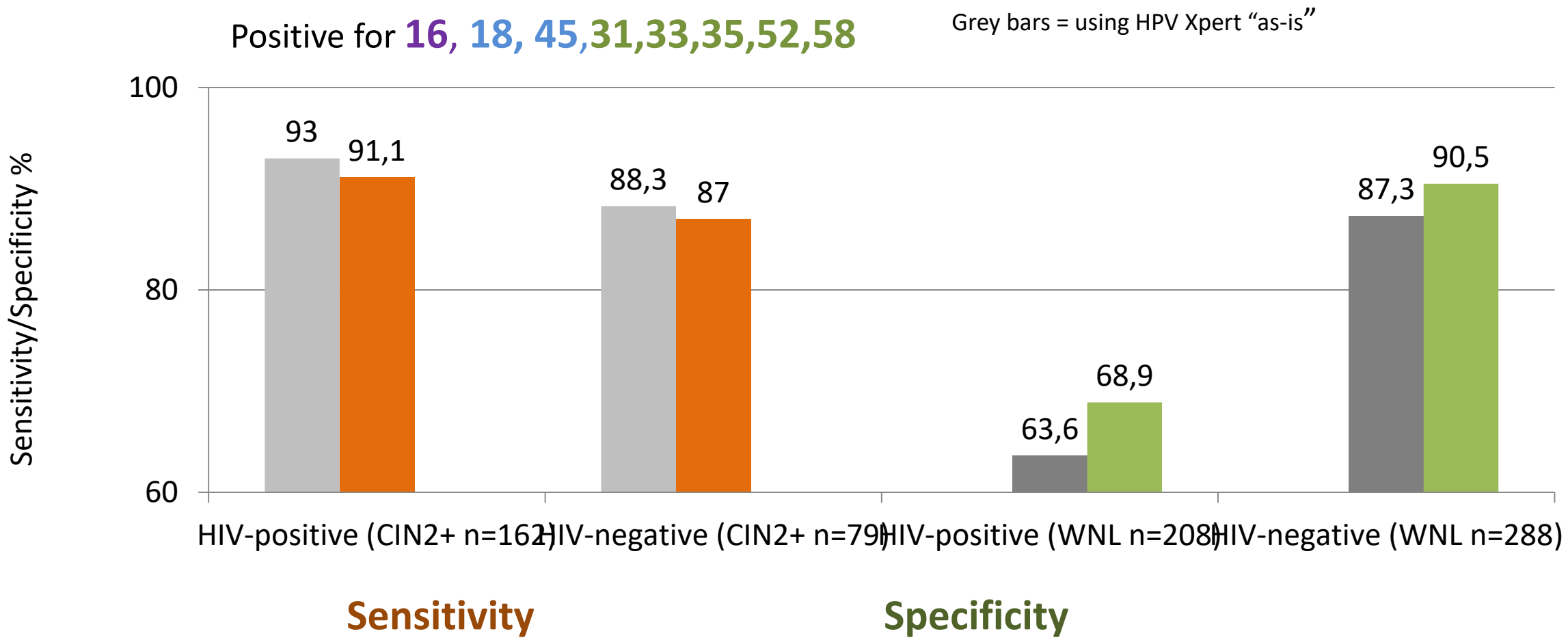
Develop Screen and Treat algorithms to detect CIN2+

Positive for any of 16,18,45,31,33,35,52,58,51,59,39,56,66,68



Sensitivity **Specificity**

Improve algorithm by restricting to select types



Conclusions

- Focus of most health care services is on provision of curative services
- Health systems are largely dysfunctional and too weak to support the most basic care
- Cytology based screening programmes are too complex and too expensive to either initiate or sustain in poor countries
- Even VIA was problematic as women with suspected cancer could not afford basic diagnostic tests

Conclusions

- Cancer is not recognised as a significant health problem
- Afflicts older women who do not prioritise their own health and are often breadwinners and heads of households
- User fees may be crippling
- Lack of health care professionals and training
- Lack of investment by many African Governments in the health of their people

Conclusions

- Health and wealth are strongly correlated
- Cancer care in developing countries is abysmal and not recognised as a public health problem
- Health systems in poor countries are too weak to support the most basic care, let alone cancer with its complexity and expense
- Incidence to mortality ratio for cancers in Africa is around 80% compared to 36% in wealthy nations

Conclusions

- Prevention is the only feasible option for intervention at this point in time
  - Tobacco control
  - Decent water and sanitation
  - Avoidance of western style diet
  - Screening
  - Vaccination
  - Control of environmental toxicity