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Title: **A sex-disaggregated analysis of mortality consequences of a priority package of services for universal health coverage**

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1. Introduction

The importance of including sex in study design and data analysis has gained traction in the biomedical research community. Biological differences between males and females coupled with the recognition that women have historically been underrepresented in clinical trials (Beery and Zucker 2011; Curno and others 2016; Jagsi and others 2009) added momentum to existing efforts to consider sex in research trials (2010; Avery and Clark 2016). A similar movement is underway in the global health community (Heidari and Bachelet 2018; Ovseiko and others 2016; WGH 2018), inspired in part by the integral role of gender in pursuing the Sustainable Development Goals (United Nations 2018).

Disease Control Priorities, 3rd edition (*DCP3*), represents one of the most comprehensive efforts to-date to review the effectiveness, cost-effectiveness, and feasibility of health-related interventions in low- and middle-income countries (LMICs) (Disease Control Priorities 2018). This multiyear effort of over 400 researchers, policymakers, and technical experts culminated in an evidence-based set of recommended services to be included in Essential Universal Health Coverage (EUHC) benefits packages in LMICs (Jamison, Gelband, and others 2018). As part of the original presentation of EUHC, *DCP3* included a modeled estimate of the impact potential of scaling up EUHC on mortality in low- and lower-middle-income countries. Like many of its contemporary global health publications, *DCP3* did not present the results of this modelling in a

sex-disaggregated way. This paper aims at addressing this limitation in *DCP3*'s analysis of EUHC.

1.1 Sex-Specific Considerations from Global Mortality Estimates

One area of global health where sex-specific data is routinely reported is in estimates of disease burden. The leading producers of morbidity and mortality estimates, the World Health Organization and Institute for Health Metrics and Evaluation, consistently report data for both males and females as part of the Global Health Estimates and Global Burden of Disease Study, respectively (2017; WHO 2017).

According to the GBD study, mortality rates decreased dramatically in both men and women from 1970 to 2016 – from 1,400 to 690 per 100,000 in women and from 1,700 to 1,000 per 100,000 in men (2017). A closer look at the sex-specific findings on causes of death from the WHO's GHE is informative for understanding the sex-disaggregated impact of EUHC in *DCP3*. Notable differences persist between males and females in both overall and cause-specific mortality burden. In 2016, the World Health Organization estimated there were 22.1 million deaths in LMICs, just over half – 54% – in males. Mortality among men outnumbers women in all three major cause categories (communicable, noncommunicable, and injuries) (WHO 2017).

Males and females account for a roughly equal share of deaths due to communicable, neonatal, and nutritional diseases, despite the ongoing (downward) trend of maternal mortality in LMICs. Infectious disease prevalence is higher in males, driven primarily by disparities in tuberculosis (TB) and HIV/AIDS cases. The high incidence of HIV/AIDS in men who have sex with men as well as HIV-TB co-infection drives this disparity (WHO 2018). Excluding HIV, nearly 60% of sexually transmitted infection (STI) deaths are in females, and 9 out of 10 of these are due to

syphilis. Owing in large part to gains during the Millennium Development Goal period, maternal deaths are responsible for less than two percent of mortality among females in this category (WHO 2017).

The sex disaggregation of mortality attributable to noncommunicable diseases is similar to that of communicable and nutritional conditions, with just over half of total deaths recorded in males in 2016. Males outnumber females in deaths due to cancers, substance use, and respiratory diseases, while there are more deaths in females due to diabetes, musculoskeletal diseases, and neurological conditions. For example, two-thirds of deaths from Alzheimer's and dementia are in women. Disparities in rates of substance use in LMICs, primarily alcohol and tobacco, lead to male deaths dominating mortality from associated neoplasms, including oral cancer (72%), liver cancer (67%), and lung cancer (73%) (WHO 2017). Sex-specific cancers such as prostate and testicular cancer in males and cervical, uterine, and ovarian cancer in females account for only 4-6% of all neoplasm deaths.

Over two-thirds of injury deaths occur in males, making this the category with the greatest sex discrepancy. The largest differences between males and females are due to road traffic fatalities, drowning, and exposure to mechanical forces, with males comprising 77%, 66%, and 67% of deaths from those injuries, respectively (WHO 2017). Some of this disparity may be attributed to the fact that men tend to partake in riskier behavior and often work in more dangerous environments. By contrast, most deaths due to fire and hot substances are in females, likely influenced by differences in social responsibilities, such as cooking (Mock and others 2017). Deaths from intentional injuries, such as self-harm, interpersonal violence, and collective

violence, are also male-dominated. However, the share of injury deaths that occur in women have increased by 5% over the past five years (WHO 2017).

2. Methods

This paper builds upon the methodology developed by Watkins and others (2017) for the *Disease Control Priorities, 3rd edition* series to model the health consequences of a proposed priority list of interventions for EUHC (Jamison, Alwan, and others 2018).

2.1 Sex-disaggregation of projected mortality impact

To extend Watkin et al.'s (2017) analysis, we calculated the projected cause-specific mortality in 2030 by sex, using sex disaggregated 2015 mortality rates from the WHO Global Health Estimates and male and female population projections for 2030 from the United Nations Population Division (UNPD). We used equal measures of intervention effect size for males and females. We assumed equal baseline coverage levels for males and females and calculated the amount of scale up needed to move from current coverage in 2015 to full coverage (defined as 80%) for each EUHC interventions for which death is an outcome of interest. We multiplied the intervention-specific coverage gap to an estimation of the number of deaths expected in 2030

assuming no change in coverage to obtain the expected reduction in overall and cause-specific mortality from full implementation of the *DCP3*'s EUHC.

2.2 Comparison of sex-disaggregated YLLs and life expectancy measures

Using the results of the sex-disaggregated analysis for deaths averted described above, we converted the projected impact of EUHC to years of life lost (YLLs). Two analyses were done. First, projections were modeled assuming equal age-specific frontier life expectancies for both males and females using current WHO standard life-expectancy tables. However, these current approaches to measuring gender-specific years of life lost by both the World Health Organization and the GBD Study use life tables that arguably underestimate the relative disease burden in females. We undertook one possible approach to correct for this potential bias by examining the relative impact of the gender balance in EUHC using different frontier life expectancies. To do this we reduced the life expectancy of males for each WHO age category by the median male-female difference used in the 1990 GBD study, an average of approximately 2.5 years per age category. This is the last year for which different frontier life expectancies were consistently used for males and females.[1]

2.3 Intervention Baseline Coverage

A clear limitation of *DCP3*'s modelling approach is that it uses identical baseline coverage assumptions for males and females. This is likely a reasonable assumption for certain types of

[1] Personal communication with Mathers, C, April 2018.

interventions that are routine and broadly available, such as childhood immunizations or postnatal care. But for many of the health services included in EUHC, an assumption of equal coverage levels among males and females is implausible. To examine the importance of this assumption to the overall findings from our impact modelling, we searched for sex-specific coverage data for a number of interventions in *DCP3*'s packages. Perhaps unsurprisingly, reliable information on coverage by sex for LICs and lower-middle-income countries is limited outside of certain well-funded conditions.

One informative example is coverage of antiretroviral therapy for adults living with HIV, for which male- and female-specific estimates are available for nearly all countries from UNAIDS (UNAIDS 2018). In 2015 for low-income countries, the largest discrepancies in ART coverage levels were seen in Burkina Faso (+29% women), Tanzania and Niger (both +23% women) and Eritrea (+21% men). The smallest male-female coverage differences were seen in Ethiopia, Bangladesh, and the Democratic Republic of the Congo, all of which had sex-specific coverage rates within 3% points of each other. In lower-middle-income countries the largest differences were seen in Morocco, Georgia, and Honduras, which had coverage rates favoring women by 29%, 26%, and 25% respectively. Taking a weighted average of the individual country rates gave an estimated coverage of 44% for males and 60% for females in low-income countries and 29% for males and 43% for females in lower-middle-income countries. A sensitivity analysis

was conducted by recalculating the projected mortality impact of *DCP3's* HIV treatment interventions with these sex-specific baseline coverage assumptions.

3. Results

3.1 Mortality

The results from the modeled mortality reduction analysis are seen in Tables 1a and 1b. In both low- and lower-middle-income countries *DCP3*'s EUHC package and highest priority subset of interventions are projected to avert more male deaths than female deaths. Overall, in low-income countries we would expect full scale up (80% coverage) of the 218 EUHC interventions to avert 1.1 billion premature deaths among males in 2030, with 41% of those coming from male children under 5. For females EUHC is projected to avert 970 thousand premature deaths, with 37% of those in children under 5. The largest discrepancies in favor of males come from projected reductions in tuberculosis, cardiovascular disease, and road traffic fatalities. In lower-middle-income countries, a projected 2.3 million deaths would be averted in males compared to 1.9 million deaths in females from scaling up EUHC. The cause-specific contributors to this pro-

male discrepancy are similar in lower-middle-income countries to that of LICs, with the addition of stronger gains for males seen in deaths averted due to HIV/AIDS.

[See **Table 1**: Projected Deaths Averted by Sex in 2030 using the *DCP3* model a) LIC and b) LMICs]

While averting more male deaths overall, *DCP3*'s EUHC package averts a greater proportion of female mortality than male mortality, in both LICs and lower-middle-income countries. This is primarily driven by highly effective interventions for maternal conditions and the near exclusive focus within neoplasms on interventions to address breast and cervical cancer.

3.2 Years of Life Lost

The projected impact of EUHC on premature years of life lost among males and females can be seen in Table 2 and Tables 3a and 3b. Using the standard approach of equal frontier life expectancies for both sexes, in low-income countries approximately 68.4 million YLLs in males and 62.4 million YLLs in females could be averted in 2030. The projected gains for males are approximately 16% greater than projected gains for females in the youngest ages (0-4). This sex discrepancy in LICs disappears for ages 5-69. This stands in contrast to lower-middle-income countries where a male bias in YLLs averted persists after 5 years of age. In lower-middle-income countries EUHC could avert approximately 130 million YLLs among males in 2030 compared to 109 million YLLs among females. Males are projected to experience greater gains

in all age categories except 15-29 years, with the advantage peaking among the 30-49 age group (not shown in the table).

[See **Table 2**: Projected YLLs Averted by Sex in 2030 from EUHC using the *DCP3* model]

Repeating the analysis using lower life expectancy assumptions for males leads to a predictable, but substantial, reduction of 4% in the disparity of YLLs averted by EUHC in both low- and lower-middle-income countries. This is in line with the percentage reduction seen in overall YLLs projected in 2030 when moving from the equal life expectancy to lower male life expectancy assumption. In both LICs and lower-middle income countries the effect of reducing male life expectancy is seen most substantially in the impact of interventions addressing cardiovascular disease and other NCDs.

[See **Table 3**: Projected YLLs Averted by EUHC in 2030 using the *DCP3* model, by sex a) LICs and b) LMICs]

3.3 Intervention Baseline Coverage

Table 4 shows the results of the mortality impact model when using sex-specific baseline coverage rates as compared to *DCP3's* original assumption of equal baseline coverage rates. The results of this analysis reveal the sensitivity of the model to decisions about sex differences coverage. When equal baseline coverage assumptions are used, scaling up ART services is expected to avert approximately 15% more deaths due to HIV/AIDS in males than in females. In

contrast, when the sex-specific baseline coverage rates are used, this estimate nearly triples. This is due to the comparatively higher current coverage of ART among women. The results in lower-middle-income countries are less dramatic, but still reinforce the finding that not using sex-specific coverage data underestimates the relative impact that EUHC is likely to have on men and women.

[See **Table 4**. Projected Deaths Averted due to HIV/AIDS in *DCP3*'s EUHC using Equal and Sex-Specific Baseline Coverage Assumptions]

4. Discussion

This work reveals the importance of examining the gender-specific implications of universal health coverage. Sex-disaggregated analyses of the impact of *DCP3*'s package for essential UHC shows a higher projected benefit for males relative to females. This projected male advantage persists across multiple ways of measuring mortality by gender (deaths, YLLs using equal life expectancies, and YLLs using a lower life expectancy for males than females). While perhaps not immediately intuitive, the higher relative reduction in male mortality is not surprising, given the higher number of male deaths that are projected overall in 2030 if no improvements in UHC coverage are made (Table 1).

This paper represents only a first step in incorporating sex-specific data and considerations into Universal Health Coverage in *DCP3*. To be most useful to policymakers and program planners, these types of analyses must be done at the national and sub-national level, using local data. But those analyses will never be feasible if sex-disaggregated data on intervention effectiveness, health services utilization rates, and costs aren't available. Integrating sex and gender into global

health policy analysis can transform the interpretation of results as significantly as when this type of data is included in biomedical trials. We must continue to call on researchers and implementers to collect, analyze, and report on results in a sex-disaggregated way, not as an analytical afterthought, but as an essential component of study, program, and policy design.

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7. Tables and Figures

Table 1. Projected Deaths Averted by Sex in 2030 using the *DCP3* model

a) Low-income countries

	Baseline # of Projected deaths, 2030		Expected reduction HPP		Expected reduction EUHC	
	Males	**Females**	**Males**	**Females**	**Males**	**Females**
By age group						
0-4	1,200	1,000	350	290	430	360
5-69	2,900	2,300	510	480	630	610
0-69	4,100	3,400	860	770	1,100	970
	% of Projected Deaths Averted		*21%*	*23%*	*26%*	*29%*
By cause group (5-69)						
Group I	990	940	290	300	320	330
Tuberculosis	230	100	*75*	*34*	*91*	*41*
HIV/AIDS	240	200	*96*	*81*	110	94
Malaria	44	43	26	26	26	26
Maternal conditions	-	170	-	*75*	-	*86*
Other diseases	480	420	94	86	94	86
Group II	1,300	1,200	*190*	*170*	270	260
Neoplasms	300	360	*1*	*9*	*1*	*38*
Cardiovascular diseases	500	430	*130*	*110*	*200*	*160*
Other diseases	540	390	*61*	*50*	*72*	*60*
Group III	550	230	*30*	*12*	*43*	*17*
Road injuries	190	67	*24*	*9*	*34*	*12*
Other injuries	360	160	*6*	*4*	*9*	*5*

Notes:

Based on models developed for Watkins et al (2018)

[a]All numbers are in thousands

[b]Country income classification is based on World Bank Income Categories as of July 2014

Numbers in *italics* indicate a male-female difference >10%

b) Lower middle-income countries

	Baseline # of Projected deaths, 2030		Expected reduction HPP		Expected reduction EUHC	
	Males	**Females**	**Males**	**Females**	**Males**	**Females**
By age group						
0-4	1,800	1,600	580	510	700	610
5-69	8,300	5,800	1,200	960	1,600	1,300
0-69	10,100	7,400	1,800	1,500	2,300	1,900
	% of Projected Deaths Averted		*18%*	*20%*	*23%*	*26%*
By cause group (5-69)						
Group I	1,800	1,400	*470*	*370*	*530*	*420*
Tuberculosis	620	280	*200*	*91*	*240*	*110*
HIV/AIDS	290	190	*140*	*90*	*160*	*100*
Malaria	31	24	*15*	*11*	*15*	*11*
Maternal conditions	-	200	-	*79*	-	*92*
Other diseases	810	750	*120*	*100*	*120*	*100*
Group II	5,100	3,800	*700*	*570*	*1,030*	*840*
Neoplasms	910	900	*17*	*86*	*23*	*130*
Cardiovascular diseases	2,400	1,500	*540*	*350*	*830*	*540*
Other diseases	1,800	1,300	140	140	180	170
Group III	1,400	590	*50*	*20*	*73*	*28*
Road injuries	450	110	*38*	*9*	*55*	*13*
Other injuries	920	480	*12*	*10*	17	15

Notes:

Based on models developed for Watkins et al (2018)

[a]All numbers are in thousands

[b]Country income classification is based on World Bank Income Categories as of July 2014

Numbers in *italics* indicate a male-female difference >10%

Table 2. Projected YLLs Averted by Sex in 2030 from EUHC using the *DCP3* model

Assumption	**Equal Life Expectancy**			**Lower Male Life Expectancy[b]**			
Low-income Countries	YLLs Averted*		% Difference (F:M)	YLLs Averted*		% Difference (F:M)	
	Males	Females		Males	Females		Difference in Males
0-69	68,400	62,400	(0.09)	65,400	62,400	(0.05)	3,000
0-4	38,600	32,400	(0.16)	37,500	32,400	(0.14)	1,100
5-69	29,900	30,000	0.01	28,000	30,000	0.07	1,900
Lower-middle-income Countries							
	Males	Females		Males	Females		Difference in Males
0-69	129,800	108,700	(0.16)	123,200	108,700	(0.12)	6,600
0-4	62,600	54,700	(0.13)	60,800	54,700	(0.10)	1,800
5-69	67,200	54,000	(0.20)	62,400	54,000	(0.13)	4,800

Notes:

Based on models developed for Watkins et al (2018)

*All numbers are in thousands. Numbers in (parentheses) are negative

[a] Life expectancy for males reduced by the difference used in GBD 1990

Table 3. Projected YLLs Averted by EUHC in 2030 using the *DCP3* model, by sex

	a) Low-income countries[b]			
	Absolute # of YLLs Averted, 2030		Sex Difference in YLLs Averted	
			Same FLE	*Lower Male FLE*
	Males	**Females**	**M-F**	**M-F**
By age group				
0-4	39	32	6.2	5.1
5-69	30	30	(0.16)	(2.1)
0-69	69	62	6.0	3.0
By cause group (5-69)				
Group I	17	19	(2.2)	(3.2)
Tuberculosis	3.7	1.8	1.9	1.6
HIV/AIDS	5.8	5.1	0.8	0.4
Malaria	1.6	1.6	(0.0)	(0.1)
Maternal conditions	-	5.3	(5.3)	(5.3)
Other diseases	5.3	10	(4.9)	(5.2)
Group II	11	10	0.6	(0.2)
Neoplasms	0.08	1.6	(1.5)	(1.5)
Cardiovascular diseases	7.4	6.1	1.4	0.8
Other diseases	3.3	2.7	0.7	0.4
Group III	2.5	1.0	1.5	1.4
Road injuries	2.0	0.66	1.3	1.2
Other injuries	0.52	0.30	0.2	0.2

Notes:

Based on models developed for Watkins et al (2018)

[a]All numbers are in millions. Numbers in (parentheses) are negative.

[b]Country income classification is based on World Bank Income Categories as of July 2014

b) Lower middle-income countries[b]

	Absolute number of YLLs Averted, 2030		Sex Difference in YLLs Averted	
			Same FLE	*Lower Male FLE*
	Males	**Females**	**M-F**	**M-F**
By age group				
0-4	63	55	7.9	6.1
5-69	67	54	13	8.3
0-69	130	109	21	14
By cause group (5-69)				
Group I	25	22	3.3	1.8
Tuberculosis	10	4.8	5.2	4.5
HIV/AIDS	8.1	5.4	2.7	2.2
Malaria	0.8	0.66	0.14	0.10
Maternal conditions	-	5.6	5.6	(5.6)
Other diseases	6.0	5	0.88	0.53
Group II	38	31	7.4	4.3
Neoplasms	0.9	5.4	4.5	(4.6)
Cardiovascular diseases	31	19	11.5	9.1
Other diseases	7.0	6.6	0.34	(0.19)
Group III	3.9	1.4	2.5	2.2
Road injuries	3.0	0.69	2.3	2.2
Other injuries	0.83	0.70	0.12	0.07

Notes:

Based on models developed for Watkins et al (2018)

[a]All numbers are in millions. Numbers in (parentheses) are negative.

[b]Country income classification is based on World Bank Income Categories as of July 2014

Table 4. Projected Deaths Averted due to HIV/AIDS in *DCP3*'s EUHC using Equal and Sex-Specific Baseline Coverage Assumptions

	Low-income			**Lower-middle-income**		
	Projected deaths averted		% More male deaths averted	Projected deaths averted		% More male deaths averted
	Male	Female		Male	Female	
Equal Baseline Coverage	110,000	94,000	**15%**	160,000	100,000	**38%**
Sex-Specific Coverage	110,000	64,000	**42%**	150,000	85,000	**43%**