iScience

CellPress
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Review

Social determinants of sex disparities in cancer in Southeast Asia

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SUMMARY

Sex disparities in cancer exist along the cancer spectrum, ranging from genomic predisposition and behavioral risk factors to access to screening, diagnostics, treatment, and survivorship care. A growing body of research is studying the biological underpinnings of these differences, from cancer risk to tumor biology to treatment response. It is well known, however, that the social determinants of health play a large role across the cancer disease continuum, which encompasses risk, prevention, diagnosis, treatment, survivorship, rehabilitation, and palliative care. Less literature focuses on the gendered disparities that are epidemiologic in nature, especially in Southeast Asia (SEA), a diverse region that is home to nearly 670 million people, where most are lower middle income countries, and where socioeconomic and cultural factors increase cancer risk for women. In this review, we highlight the social drivers of gendered disparities, namely the geographic, environmental, sociocultural, economic, and political forces that contribute to the increased mortality and poorer health outcomes in the region.

INTRODUCTION

Differences and disparities along the lines of sex exist across the cancer spectrum, ranging from genomic predisposition and behavioral risk factors to access to screening, diagnostics, treatment, and survivorship care. It is important to note that sex (and its relation to gender, a social construct) can be understood as a biologic and genetically determined variable around which social constructs are formed.[1,2] We use "sex differences," therefore, to describe the prevalence of gene variants and polymorphisms; the interaction between sex hormones and organs with cancer predisposition, treatment response, and outcome; and biologic differences in immune response, metabolism, and tumor microenvironment.[3–5]

In contrast, "sex disparities" are group differences that would not occur in a just and equitable society.[6,7] Sex disparities include differences that relate to the marginalization and oppression of women[8–10]; opportunities (and barriers) to access health-affirming resources such as employment, legal equity, and unbiased care[11]; and discrimination experienced by women and sexual minorities such as *trans* individuals and people who identify as non-binary.[12]

Although a growing body of research is studying the biological underpinnings of sex differences, less is known about social determinants of health that play critical and complex roles across the cancer disease continuum, encompassing risk, prevention, diagnosis, treatment, survivorship, rehabilitation, and palliative care. Little is known about drivers of sex disparities that are epidemiologic in nature, especially in Southeast Asia (SEA), a diverse region that is home to nearly 670 million people, where most reside in lower-middle income countries, and where socioeconomic and cultural factors increase cancer risk for women.[13–15] We therefore explore unique epidemiologic patterns affecting the Southeast Asian region and their mediators, such as environmental exposure, lifestyle, genetic predispositions, access to and utilization of preventive cancer services, and social determinants of health.

It is critical to note that sex differences and sex disparities are intersectional in nature, owing to the interacting biologic and sociocultural forces that influence sex and health. For instance, cervical cancer vaccination, screening, and treatment have traditionally been directed toward cisgender women.[16,17] However, barriers to accessing these services have also been found to negatively impact persons with cervixes of various gender identities, such as non-binary and transgender individuals.[17,18] Although group differences

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https://doi.org/10.1016/j.isci.2023.107110

between men and women in the incidence of breast cancer represent sex differences, disparities exist in access to timely treatment and diagnosis.[15,19–21]

In this review, we shed light on the social drivers of sex disparities, including the geographic, environmental, sociocultural, economic, and political forces that contribute to the increased mortality and poorer health outcomes in the region. We highlight sociocultural forces that impact access to cancer care in Southeast Asia, cognizant that these factors interact intimately with biologically determined sex.

PROFILE OF ASEAN COUNTRIES

The Association of Southeast Asian Nations (ASEAN) is composed of ten countries comprising continental Southeast Asia and the surrounding maritime states: Brunei Darussalam, Cambodia, Indonesia, Lao PDR, Malaysia, Myanmar (Burma), the Philippines, Singapore, Thailand, and Vietnam.[22] These Southeast Asian nations are a diverse conglomerate of cultures, religions, ancestry, ethnolinguistic identities, political structures, and economic development, demarcated by geographic boundaries and self-declared autonomy[14] (see Table 1).

Although behavioral preferences and healthcare decisions ultimately occur at the individual level, there are important considerations that affect care across the cancer spectrum in the ASEAN region. Religious diversity plays a role, as well as the traditional Asian values of conservatism and collectivism. Topography and urbanization weigh on ease of access to cancer care, and historically marginalized groups, like indigenous and gender-fluid peoples, face additional barriers to health-seeking and social or state support.

Cancer is now the leading cause of disability-adjusted life years (DALYs) in higher income ASEAN groups, namely, Singapore, Brunei, and Thailand.[23] Cancer has steadily risen in rank in the region since the 1990s, and currently persists in the top five causes of DALYs and the top three causes of mortality for both sexes.[23] There is a higher incidence of cancer cases in women but more mortalities in ASEAN men.[24]

It is interesting to note that breast cancer has now surpassed lung cancer as the leading contributor to global cancer incidence,[24] and two-thirds of cancer diagnoses in patients below 50 years old—the majority of the economically productive age group—occur in women.[25] This is echoed by ASEAN cancer statistics. Of 1.1 million new cancer cases in 2020, breast and cervical cancer comprised over 20% of total cancer incidence in Southeast Asia, and they were the third and fourth leading causes of regional cancer deaths, respectively.[23] Weighting these statistics is the variable of inequity; low- and middle-income countries (LMICs) shoulder the bulk of the cancer mortality burden, with seven out of ten cancer deaths occurring in LMICs.[26] LMICs also carry a disproportionate burden of infection-related cancers, like gastric, hepatocellular, and cervical malignancies.Table 2 details sex-specific incidence and mortality rates of the most prevalent cancers and leading causes of cancer mortality in ASEAN countries.[27]

GEOGRAPHIC AND ENVIRONMENTAL DRIVERS

Geographic disparities in health service delivery

Sung et al. (2011) discuss how the enormity of SEA's socioeconomic, political, and cultural diversity, found even within countries, has produced vastly differing natures of health systems at varying stages of evolution, all coexisting in a single region.[24] SEA is home to approximately 9% of the world population, with 43% living in urban areas; this is less than the world average, but there is much variation (i.e., 15% in Cambodia to 100% in Singapore).[24]

Found in the region are not only some of the fastest rates of demographic transition in the world in terms of population aging, fertility reductions, and rural-to-urban migration, but also of rapid epidemiological transition, with disease burden shifting largely from infectious to non-communicable diseases.[28] Culture and religion color demographic transitions, such as how Catholicism influences the relatively slower uptake of family planning programs in the Philippines. Increasing longevity, on the other hand, is a result of the diminishing burden from communicable, maternal, and perinatal diseases.

Naturally, and most especially when compounded with regional socioeconomic and political factors, the conglomeration creates the palpable disparity in health service delivery even across neighboring countries. Rapid but non-inclusive socioeconomic development contributes to public health challenges: urbanization

Table 1. Economic and cancer profiles of ASEAN countries (International Agency for Research on Cancer, 2020)

	World Bank Income Group[a]	Most prevalent[b] cancers (overall), 2020	Most prevalent[b] cancers in males, 2020	Most prevalent[b] cancers in females, 2020	Leading causes of cancer deaths[c] (overall), 2020	Leading causes of cancer deaths[c] in males, 2020	Leading causes of cancer deaths[c] in females, 2020
Brunei Darussalam	HIC	Breast (18.8%), Colorectal (16.3%), Cervix uteri (6.1%)	Colorectal (23.2%), Prostate (14.5%), Nasopharynx (9.3%)	Breast (32.0%), Colorectal (11.4%), Cervix uteri (10.4%)	Lung (21.7%), Colorectal (13.1%), Liver (8.1%)	Lung (22.9%), Colorectal (14.8%), Liver (12.3%)	Lung (20.2%), Breast (14.6%), Colorectal (11.1%)
Cambodia	LMIC	Breast (13.0%), Liver (10.3%), Colorectal (9.5%)	Liver (16.6%), Colorectal (10.9%), Lung (9.4%)	Breast (21.9%), Cervix uteri (12.0%), Colorectal (8.5%)	Liver (23.3%), Lung (13.1%), Colorectal (7.3%)	Liver (30.1%), Lung (16.2%), Colorectal (6.8%)	Liver (16.1%), Breast (12.9%), Cervix uteri (10.4%)
Indonesia	LMIC	Breast (21.3%), Cervix uteri (9.8%), Colorectal (8.5%)	Colorectal (12.9%), Prostate (11.0%), Nasopharynx (10.7%)	Breast (36.1%), Cervix uteri (16.7%), Ovary (6.7%)	Lung (13.2%), Breast (9.6%), Cervix uteri (9.0%)	Lung (18.5%), Liver (12.9%), Colorectal (9.3%)	Breast (20.4%), Cervix uteri (19.1%), Ovary (8.7%)
Lao PDR	LMIC	Breast (15.5%), Colorectal (9.4%), Liver (8.3%)	Liver (13.2%), Lung (10.9%), Colorectal (10.8%)	Breast (27.3%), Colorectal (8.4%), Cervix uteri (8.3%)	Liver (19.2%), Lung (14.4%), Stomach (9.1%)	Liver (23.7%), Lung (18.3%), Stomach (10.2%)	Breast (16.3%), Liver (13.4%), Lung (9.3%)
Malaysia	UMIC	Breast (23.0%), Colorectal (13.9%), Prostate (6.2%)	Colorectal (17.3%), Prostate (14.6%), Nasopharynx (9.8%)	Breast (39.8%), Colorectal (11.4%), Ovary (6.7%)	Lung (15.3%), Breast (11.9%), Colorectal (11.7%)	Lung (22.3%), Colorectal (11.8%), Liver (9.4%)	Breast (25.1%), Colorectal 11.6%), Ovary (8.4%)
Myanmar	LMIC	Breast (12.2%), Cervix uteri (11.3%), Colorectal (7.8%)	Stomach (10.0%), Colorectal (9.5%), Lung (8.3%)	Breast (20.8%), Cervix uteri (19.3%), Colorectal (6.5%)	Lung (14.3%), Stomach (11.9%), Liver (10.0%)	Lung (15.4%), Stomach (13.4%), Liver (12.9%)	Cervix uteri (16.9%), Lung (13.2%), Breast (11.2%)
Philippines	LMIC	Breast (24.0%), Colorectal (11.6%), Prostate (7.6%)	Prostate (20%), Colorectal (16.5%), Lung (10.1%)	Breast (38.8%), Cervix uteri (9.1%), Colorectal (8.5%)	Lung (18.4%), Liver (10.7%), Breast (10.7%)	Lung (25.4%), Liver (14.9%), Colorectal (10.8%)	Breast (21.8%), Lung (11.2%), Colorectal (9.0%)
Singapore	HIC	Breast (22.1%), Colorectal (16.0%), Prostate (11.1%)	Prostate (23.8%), Colorectal (19.7%), Lung (7.4%)	Breast (41.3%), Colorectal (12.9%), Corpus uteri (7.8%)	Lung (21.6%), Colorectal (14.9), Liver (10.5%)	Lung (25.9%), Colorectal (15.0%), Liver (13.3%)	Breast (18.0%), Lung (15.9%), Colorectal (14.8%)
Thailand	UMIC	Breast (17.9%), Colorectal (12.9%), Prostate (7.2%)	Prostate (16.7%), Colorectal (14.8%), Liver (9.8%)	Breast (31.3%), Colorectal (11.4%), Cervix uteri (10.1%)	Liver (21.4%), Lung (16.3%), Colorectal (9.2%)	Liver (26.3%), Lung (19.5%), Colorectal (8.4%)	Liver (15.5%), Breast (14.6%), Lung (12.6%)
Vietnam	LMIC	Breast (17.2%), Colorectal (10.9%), Liver (8.1%), Lung (8.1%)	Liver (13.4%), Colorectal (12.4%), Lung (12%)	Breast (31.8%), Colorectal (9.6%), Corpus uteri (7.3%)	Liver (20.6%), Lung (19.4%), Stomach (11.9%)	Liver (26.1%), Lung (22.9%), Stomach (12.1%)	Breast (19.4%), Lung (14.0%), Liver (12.1%)
ASEAN Region (Overall)		Breast (20%), Colorectal (10.5%), Cervix uteri (7%), Lung (5.5%), Prostate (5.2%)	Colorectal (13.8%), Prostate (12.5%), Lung (8.6%), Nasopharynx (7.2%), Liver (7.2%)	Breast (34.4%), Cervix uteri (12.0%), Colorectal (8.1%), Ovary (5.5%), Thyroid (5.2%)	Lung (15.9%), Liver (13.9%), Breast (8.5%), Colorectal (8.3%), Cervix uteri (5.6%)	Lung (20.5%), Liver (18.5%), Colorectal (8.6%), Stomach (5.4%), Nasopharynx (5.0%)	Breast (18.6%), Cervix uteri (12.2%), Lung (10.5%), Liver (8.4%), Colorectal (7.9%)

[a]World Bank income groups are based on gross national income per capita in USD as of July 1, 2021. *High-income countries (HIC)*: 12,696 USD or more. *Upper-middle income countries (UMIC)*: 4,096 to 12,695 USD; *Lower middle-income countries (LMIC)*: 1,046 to 4,095 USD; *Low-income countries (LIC)*: 1,045 USD or less.

[b]Estimated number of prevalent cases (5-year) in 2020 by GLOBOCAN.

[c]Estimated number of deaths in 2020 by GLOBOCAN.

Table 2. Sex-specific incidence and mortality rates of the eleven most prevalent cancers and leading causes of cancer deaths in the ASEAN countries (International Agency for Research on Cancer, 2020)

Cancer site	Country Code	[a]Incidence		[a]Mortality		Cancer site	Country Code	[a]Incidence		[a]Mortality	
		M	F	M	F			M	F	M	F
Breast	BN		55.9		12.5	Naso-pharyngeal	BN	13.4	6.4	8.0	3.4
	KH		23.5		10.3		KH	3.4	1.1	2.8	0.71
	ID		44.0		15.3		ID	10.7	3.0	7.7	1.9
	LA		36.7		15.8		LA	5.9	3.1	4.7	2.2
	MY		49.3		20.7		MY	9.5	3.1	6.5	1.9
	MM		22.0		9.6		MM	5.5	2.2	4.0	1.5
	PH		52.7		19.3		PH	4.4	1.8	3.4	0.95
	SG		77.9		17.8		SG	6.8	2.3	4.7	0.88
	TH		37.8		12.7		TH	3.3	1.2	2.0	0.70
	VN		34.2		13.8		VN	8.1	2.8	5.1	1.7
Cervix	BN		20.8		5.7	Ovary	BN		17.4		7.4
	KH		14.0		8.3		KH		5.5		3.9
	ID		24.4		14.4		ID		10.0		6.6
	LA		12.0		6.7		LA		6.3		4.4
	MY		10.2		5.8		MY		10.8		6.9
	MM		22.6		14.4		MM		6.3		4.2
	PH		15.2		7.9		PH		10.4		6.6
	SG		6.9		3.3		SG		11.2		5.2
	TH		16.4		7.4		TH		7.9		4.7
	VN		6.6		3.4		VN		2.4		1.5
Colorectal	BN	42.2	27.7	18.1	11.2	Prostate	BN	23.0		5.0	
	KH	13.7	11.2	8.4	6.7		KH	5.3		2.7	
	ID	16.5	8.6	9.2	4.6		ID	11.6		4.5	
	LA	16.1	14.2	10.1	7.9		LA	4.3		2.1	
	MY	21.2	18.0	11.0	9.4		MY	13.1		5.4	
	MM	11.8	8.2	7.3	4.8		MM	4.0		2.0	
	PH	23.7	15.1	13.4	7.8		PH	23.4		10.8	
	SG	38.6	27.4	19.8	12.8		SG	34.3		7.3	
	TH	19.0	15.2	9.7	7.5		TH	14.6		5.9	
	VN	17.6	11.6	9.1	5.5		VN	12.2		5.1	
Corpus uteri	BN		9.4		1.1	Stomach	BN	17.5	9.6	11.8	5.6
	KH		3.3		1.1		KH	5.2	3.1	4.6	2.6
	ID		5.3		1.8		ID	2.2	0.51	1.9	0.41
	LA		3.3		1.0		LA	17.3	8.9	15.0	7.5
	MY		8.3		2.5		MY	5.9	2.8	4.8	2.2
	MM		2.7		0.83		MM	17.7	10.6	15.7	9.2
	PH		8.7		2.6		PH	4.8	2.9	4.4	2.3
	SG		16.4		3.1		SG	9.0	5.6	7.5	4.7
	TH		7.6		2.1		TH	4.0	3.1	3.1	2.1
	VN		8.9		2.1		VN	21.7	10.6	17.8	8.5
Liver	BN	17.4	3.5	14.3	3.2	Thyroid	BN	3.1	9.4	–	1.2
	KH	37.6	14.5	35.6	13.6		KH	1.6	7.0	0.53	1.0
	ID	12.7	3.5	12.5	3.4		ID	3.0	6.2	0.70	1.0
	LA	35.7	14.2	33.6	13.3		LA	1.9	8.6	0.45	1.2
	MY	9.3	3.6	8.8	3.4		MY	1.4	3.1	0.35	0.51
	MM	14.7	6.3	14.2	6.2		MM	1.5	3.8	0.30	0.50
	PH	17.8	6.1	16.8	5.7		PH	3.0	9.2	0.60	0.98
	SG	18.6	5.9	17.4	5.6		SG	3.6	9.7	0.40	0.62
	TH	33.8	12.9	33.0	12.3		TH	1.4	6.4	0.18	0.45
	VN	38.0	9.8	36.3	9.3		VN	1.9	7.6	0.32	0.80

(*Continued on next page*)

Table 2. *Continued*

Cancer site	Country Code	[a]Incidence M	[a]Incidence F	[a]Mortality M	[a]Mortality F	Cancer site	Country Code	[a]Incidence M	[a]Incidence F	[a]Mortality M	[a]Mortality F
Lung	BN	36.2	28.0	29.4	20.6						
	KH	23.0	9.4	20.3	8.2						
	ID	20.1	6.2	18.1	5.5						
	LA	30.3	10.8	26.9	9.3						
	MY	23.6	7.3	20.9	6.2						
	MM	19.9	12.7	18.5	11.7						
	PH	33.6	11.3	30.3	10.0						
	SG	37.3	16.8	34.4	13.9						
	TH	27.4	11.9	23.3	9.9						
	VN	36.8	11.8	33.7	10.4						

BN = Brunei Darussalam, KH = Cambodia, ID = Indonesia, LA = Lao PDR, MY = Malaysia, MM = Myanmar, PH = Philippines, SG = Singapore, TH = Thailand, VN = Vietnam.

[a]Incidence and mortality statistics are age-standardized rates per 100,000 population in 2020, based on the GLOBOCAN 2020 data published by the IARC.

coupled with high-density living amplifies the burden of infectious disease outbreaks in many parts of the region.

The ASEAN is also known to be the most disaster-prone region in the world, plagued frequently by typhoons, earthquakes, forest fires, floods, and pollution. The machination of climate change hums in the background, and ASEAN countries are some of the hardest hit but also ill-equipped to respond[29]—a gruesome combination. The environment accounts for a quarter of deaths in the developing world. Notwithstanding direct infrastructure damage, it also potentially exacerbates vector-borne diseases.

Healthcare systems range from tax-based financing to socialized. Modern medical technology is globally available but financially inaccessible to the majority of the region's population. As such, recent years have borne witness to the rise of novel health systems such as corporatized public hospitals, and medical tourism as a form of health service delivery—reflecting a trend of private overtaking public health spending in growth. For many, however, healthcare financing boils down to rampant out-of-pocket spending for health in the region despite a greater push for universal coverage in recent years.

The growing pressure for socialized universal healthcare favoring the underserved may be attributed to an increasingly educated and democratized constituency, now more than ever conscious of human rights, in light of the described demographic and epidemiologic transitions. Meanwhile, the expansion of middle-class urban populations demanding higher quality care drives up involvement of private health providers who remain out of the scope of social health protection policies, while also driving up out-of-pocket expenses. This further causes downstream effects of disproportionate health worker and specialist density skewed heavily toward urban centers, causing disparities in health service delivery even within countries themselves.

Geographic disparities in infection-related cancers

The International Agency for Research on Cancer (IARC) has data on major cancers from a large number of countries and geographical regions including SEA, which shows that 13 of the 35 studied cancer sites were deemed to have an enigmatic sex difference. Excess male risk was found in 32 of 35 sites, whereas only three out of 35 stood out as having female excess risk: thyroid, gallbladder and biliary tract, and anus. Underpinning etiologies that have been hypothesized but ultimately fell short include: larger body size and higher basal metabolic rate in men; sex steroid hormones; purely genetic and chromosomal reasons; lower iron levels in women; and of particular note: increased propensity of women to mount stronger immune responses to infection.[30]

Notwithstanding sex-specific cancers, we find significant variation even within SEA in the expression of certain cancers when juxtaposed with prior oncogenic infections. Human Papilloma Virus (HPV), particularly HPV-16, is identified as an independent risk factor in the pathogenesis of squamous cell cancers other than at the cervix, with the highest prevalence in cancers of the tonsil and the base of the tongue. HPV in oral

cancers was found to be more prevalent in Asia (33%) than in Europe (16%) and North America (16.1%), as well as more common in males than females.[31] However, in Thailand it was found that there was a trend of increasing percentage of HPV-associated oral squamous cell carcinoma from 2005 to 2010, which disproportionately affected more females than males.[32]

It must still not be discounted that geographic heterogeneity of HPV involvement in head and neck squamous cell carcinoma (HNSCC) has been observed over the last few years. A study in the Philippines found that only 2.4% (2 out of 82 valid samples) were HPV DNA-positive, suggesting a probably very low prevalence of HPV-associated HNSCC among Filipino adults living in a rural region of the Philippines.[33] A follow-up study examining serologic profiles showing low HPV titers corroborated the molecular analyses done earlier on the same population.[34] Differences between Thailand and the Philippines would suggest that regional differences in exposure modify the primary effect of HPV infection on the predisposition to developing specific HNSCCs.

A global study on Epstein-Barr virus (EBV)-associated cancers found that nasopharyngeal carcinoma (NPC) comprised a large proportion of all EBV-cancers, and that Western and Southeastern Asia (China, Malaysia, Singapore) are the highest rate regions, with excess male risk. Even when they immigrated, patients originating from North Africa, Southeast Asia and Asian Arab countries had higher NPC rates.[35]

Geography, ethnicity, and lung cancer in non-smokers

Let us now consider the case of lung cancer in non-smokers (LCINS) preferentially involving Asian women. In 2006, the National Cancer Centre Singapore (NCCS) found that almost a third (32%) of cases of non-small cell lung cancer (NSCLC), which comprised the vast majority of lung cancers, occurred among never-smokers.[36] This proportion has since increased to 48% within roughly a decade, as indicated by a follow-up NCCS study in 2018.[37] The vast majority of these never-smokers (68.5%) were women.

The 2018 NCCS follow-up study found that the proportion of LCINS with positive *EGFR* mutations was significantly higher ($p < 0.001$) than in former- and current-smokers (67% versus 38% and 17%, respectively). The rate of lung adenocarcinoma *EGFR* mutation in Singapore appears to signal a trend for the rest of Asia, because two independent studies done on Chinese never-smoker females converge on a rate of 70–76% *EGFR* mutation rate for the East Asian country.[38,39] A third study corroborating this estimate analyzed lung adenocarcinomas from never-smokers resected at a single center in China, and included samples from never-smoker men (21%), but these were far outnumbered by samples from never-smoker women (79%).[40]

To this effect, the proportion of LCINS has been found by epidemiologic studies to be higher in the neighboring region of East Asia—exceeding one-third of all lung cancers in China (39.7%), South Korea (38%), and Japan (32.8%)—a trend which has been increasing over time. The notably high relative abundance of LCINS was considered to be a consequence of low smoking prevalence in East Asian females with lung cancer, ranging from 5.2% (China) to 28.3% (Hong Kong)—both significantly lower than that in their Caucasian counterparts (53%–91%). Smoking rates among male patients, in contrast, were found to be comparable across East Asian and Western Countries.[41]

This trend shared by Asian regions, however, appears to be exclusive to patients of Asian ethnicity, because the rates of *EGFR* mutations in lung cancer among Caucasians were found to be lower (7–17%).[42]

The phenomenon of LCINS among Asian women may be attributed to a distinct epidemiologic entity because when taken in contrast with their female Caucasian counterparts, Asian women appear to still be at greater risk of lung cancer. Ever-smokers account for only five percent of Chinese women in Singapore,[43] whereas regular smokers comprised roughly thrice that among women in Italy (15.2%).[44] And yet, despite the demonstrably large gap in tobacco exposure, GLOBOCAN 2020 data shows almost equivalent age-standardized incidence rates (world) between countries such as Singapore (16.8%) and Italy (16.4%).[23]

Environmental exposures exert an independent yet compounding force alongside genomic predisposition on the manifestation of cancers among the sexes and the resultant variation therein. Known risk factors have been named, such as second-hand smoke exposure at home or at the workplace, suspected carcinogens such as radon, or biomass burning for cooking and heating particularly in poorly ventilated areas.

Table 3. National prevalence (%) of smoked tobacco and smokeless tobacco in the ASEAN region (World Health Organization, 2021[a]; Tan and Dorotheo, 2018[b])

	Tobacco smoking prevalence (%)[a]			Smokeless tobacco prevalence (%)[b]			
	M	F	B	M	F	B	
Brunei Darrusalam	30.4	2.5	16.5	1.7	2.1	1.9	STEPS Survey 2015-16
Cambodia	32.6	1.8	17.2	0.8	8.6	4.9	National Adult Tobacco Survey of 2014
Indonesia	72.6	2.6	37.6	3.9	4.8	4.3	Basic Health Research 2013
Lao PDR	48.4	5.9	27.2	0.5	8.6	4.3	National Adult Tobacco Survey 2015
Malaysia	42.4	0.6	21.5	20.4	0.8	10.9	National Health and Morbidity Survey 2015
Myanmar	38.6	4.0	21.3	62.2	24.1	43.2	National Survey of Diabetes and Risk 2014
Philippines	40.6	6.8	23.7	2.7	0.7	1.7	Global Adult Tobacco Survey 2015
Singapore	28.3	5.1	16.7	–	–	–	–
Thailand	38.1	1.6	19.9	1.5	2.7	2.1	National Statistics Office 2018
Vietnam	45.9	1.2	23.5	0.8	2.0	1.4	Global Adult Tobacco Survey 2015

[a]Age-standardized prevalence estimates for current tobacco smoking among persons aged 15 and above, 2019, World Health Organization.
[b]Smokeless tobacco (ST) refers to tobacco-containing products that are consumed by chewing, sniffing, or placing in the mouth, rather than smoking.

However, these appear to fail to account for findings as a large fraction of LCINS cannot be definitively associated with established environmental risk factors.[45]

A fitting example of what would be the intersection between geographic and sociocultural drivers of sex disparities in SEA cancer: fumes and smoke from wok cooking—a practice largely designated to Chinese women—have recently been shown to be related with lung cancer in non-smoker Han Chinese women in a dose–response fashion. This risk could even be mitigated by a large margin of up to half with long-term use of a fume extractor while cooking.[46]

SOCIOCULTURAL NORMS AND PRACTICES CONTRIBUTING TO SEX DISPARITIES

Tobacco and betel quid chewing

On average, one in five adults in the ASEAN region use tobacco, with population prevalence ranging from 16.5% in Brunei to as high as 37.6% in Indonesia.[47,48] Stratification by sex, however, reveals a stark difference in male and female smoking prevalence (%), with national male estimates (28.3 [95% CI 20.5, 36.1] in Singapore to 72.6 [95% CI 56.0, 89.3] in Indonesia) much higher than national female estimates (0.6 [95% CI 0.4, 0.8] in Malaysia to 6.8 [95% CI 5.4, 8.2] in the Philippines) (see Table 3).[48]

Significant in the ASEAN region is the high prevalence of smokeless tobacco, which comes in numerous forms in South and Southeast Asia,[49] alongside other carcinogenic substances like betel quid. Popular forms of smokeless tobacco in Myanmar are betel leaf and areca nut, lahpet (fermented tea leaves), cheroot (thin, filterless, rolled cigars), and snuff.[50–52] In Thailand, there are hand-rolled cigarettes, betel quid, oral and nasal snuff, and chewed tobacco.[52] Chewed tobacco, betel quid, snuff, and hand-rolled tobacco are common forms in the Philippines, Cambodia, and Indonesia.[49,52]

Smokeless tobacco use is most prevalent in Myanmar (43.2%), Malaysia (10.9%), and Cambodia (4.9%).[53,54] These substances are more popular than tobacco smoking among women, given their cultural acceptability and perceived safety, especially among older adults in rural communities and persons from lower wealth quintiles and lower educational attainment.[51,52,55] In fact, smokeless tobacco rates in countries like Cambodia and Thailand are higher in women compared to their male counterparts,[53] and in Myanmar, a high percentage of women are dual or mixed tobacco users, which is associated with greater difficulty with smoking cessation.[52] Lung cancer risk is higher in Northern Thailand women who chew Miang (fermented wild tea leaves) and smoke tobacco using cigarettes and Khiyoh (long, hand-rolled cigars).[56] Smokeless tobacco also increases the risk for oral, pharyngeal, and esophageal cancers and premalignant lesions,[53,57] and this risk is significantly higher with chewed forms of smokeless tobacco and female users.[57]

In some communities in the Philippines, the practice of reverse smoking, wherein the lit end of the cigarette is placed in the mouth, is predominantly female-associated and increases the incidence of palatal changes, which may increase the risk for palatal carcinoma.[58] There are few published studies on the subject, although some cited reasons for reverse smoking include preventing cigarette ashes from falling on laundered clothes, counteracting the odor of soiled diapers when washing, keeping the body warm while planting rice, and driving away mosquitos while gathering sweet potatoes.[58] Reverse smoking is also seen in older women from rural India[59] and other countries in South and Central America, South Asia, and the Caribbean.[58]

Many anti-tobacco programs and policies have historically been gender-blind,[60] despite the evidence that men and women have different motivations, perceptions, and attitudes regarding tobacco use, as well as varying biological responses. Although tobacco use in males is influenced by their social environment and structural factors like economic conditions, research on female usage associates tobacco consumption with the desire to control weight, manage negative emotions, alleviate stress, and address pregnancy-related symptoms.[60–63] Although individual reasons exist for initiating and continuing consumption of these substances, the common themes and similarities in some Asian traditions, norms, and gender roles across ASEAN societies necessitate a discussion on their implications for policing tobacco use and other carcinogenic substances like betel quid.

In Cambodian, Burmese, Lao, and Vietnamese societies, tobacco use is culturally accepted and central to traditions, ceremonies, and social niceties; cigarettes are offered to monks and used to pray for ancestors, chewing betel nut with tobacco is symbolic of loyalty in engagements and weddings, and tobacco is offered to welcome guests and make social connections.[64–66] In communities like the Kratie Province in northeast Cambodia, however, stigma exists against young women who smoke tobacco, who are branded "fire women".[64] Although social disapproval can be protective against smoking, it may instead push young female users to other forms of tobacco. The decisions behind initiating tobacco smoking are multifactorial; many women in the Khmer Rouge regime started using tobacco for solace and to prevent insect bites on the rice fields during rainy seasons. Some are influenced by male family members, and notably, tobacco—both smoked and smokeless—is used by pregnant women to alleviate morning sickness.[63,64] In a study by Singh et al., one out of five women in a rural Cambodian community started chewing tobacco to relieve morning sickness.[63]

This gendered acceptance of tobacco smoking in Cambodia is reflected in other countries like Malaysia and Vietnam. Smoking is more prevalent in men given its acceptability and association with masculinity and machismo; smoking among women, however, is considered inappropriate and ill-mannered.[61,67] Although males are more likely to initiate smoking, studies suggest that on average, females have more difficulty quitting, and some theorize that a significant barrier to smoking cessation is the potential weight gain.[61,62]

We also take, for example, the attribution of betel quid chewing to masculinity in Myanmar culture—where smokeless tobacco use is most prevalent—and its utility as a psychoactive energizer for work and as a lubricant in the social and business arenas. Betel quid is a preparation made from the betel leaf and areca nut with slaked slime, which is often mixed with tobacco by seasoned users.[50,65] The practice is deeply rooted in traditional Burmese culture and offered ceremonially to guests, and it is likewise found in neighboring countries like Indonesia, Philippines, Malaysia, Thailand, Cambodia, Laos, and Vietnam.[50,68] Betel quid in itself is carcinogenic and linked to precancerous and cancerous lesions of the oral cavity.[68,69] Despite knowledge of its health-associated risks, many Burmese men continue to chew betel quid as a show of independence and daring, two qualities commonly valued in society.[65] Betel quid also acts as a stimulant by increasing energy and reducing fatigue for working-class men and laborers who work in physically demanding and exploitative working conditions.[65] Betel quid chewing may start young, with male students experimenting because of peer influence, curiosity, and the desire to feel manly and confident.[65] Although analyses of betel quid chewing behavior usually focus on men because of the high prevalence, betel quid chewing is likewise popular among Burmese women. Betel quid is perceived as safer than tobacco smoking, and the added tobacco leaves serve as breath-fresheners and mouth-cleansers.[51]

Mitigating the risks for head, neck, and lung cancers requires a gendered approach to tobacco control and carcinogenic substance use. Gender-sensitive anti-tobacco campaigns and policies necessitate recognition of the ever-evolving sociocultural landscapes that influence user attitudes and behaviors, and the consequent need to augment existing public health research to reflect the gender norms and values of

the times. The tobacco industry continues to expand, targeting even the youth with novel products like the electronic nicotine delivery systems and flavor capsule cigarettes; tobacco is difficult to regulate given its numerous forms, targeted point-of-sale advertisements, and the lucrative informal economy. To prevent a tobacco pandemic among ASEAN women and youth, advocacy, healthcare, and public education must keep pace with industry.

Complementary and alternative medicine

Complementary and alternative medicine (CAM) use has been linked to financial toxicity[70] and poorer prognosis when it delays the delivery of conventional cancer therapies.[71] Studies suggest gender implications in cancer outcomes because there is a significant association between sex and the use of CAM,[70,72] although the association in ASEAN is less clear, given limited population-based prevalence studies on CAM usage.

Sociodemographic factors and patient profiles also factor in on usage. In a cross-sectional study of patients with gynecologic cancer in a Thai hospital, CAM use was significantly associated with rural residency and women having received multiple cancer treatment modalities.[73] A study in a rural Malaysian population showed that those over 50 years of age tend to be the highest frequency users of most CAM modalities, and there are differences between age groups in terms of their preferred modalities. Similarly, specific CAM modalities may disproportionately influence behaviors among women; for example, in a study by Teow et al., yoga and vitamin use were more prevalent among female study participants.[74] Teow et al. also show that women averse to conventional therapies are more likely to use CAM and that CAM users believe CAM is safer and healthier than conventional treatment.[72] These beliefs and attitudes toward CAM are echoed by subpopulations in Indonesia and the Philippines, where CAM is valued, more accessible, and oftentimes more affordable than conventional cancer therapies.[75,76]

Financial toxicity from CAM usage is significant in upper-middle-income ASEAN countries like Malaysia and Thailand.[70] Households spend 42.9% of their out-of-pocket (OOP) expenditures on CAM in the year following cancer diagnosis, compared to 8.6% of annual total out-of-pocket health costs in lower-middle-income country households.[70] The high OOP costs on CAM increase the risk of financial catastrophe and medical impoverishment for upper-middle-income countries, and the risk is significantly higher for economically disadvantaged households.[70]

For lower-middle-income countries like the Philippines and Myanmar, however, CAM is not associated with adverse financial outcomes.[70] CAM is in fact a viable primary treatment alternative because of the unaffordability of conventional cancer therapies (CCTs) alongside structural barriers to healthcare access, i.e., low socioeconomic status, geographic limitations.[70,76,77] These health and structural inequities cause delays in treatment and decrease the 5-year overall survival of patients with cancer.[71] Although there are other factors that influence the delay or even refusal of CCTs (e.g., patient philosophy, poor health literacy, stigma and disempowerment), these are beyond the scope of this article and warrant local formal academic investigations by the ASEAN countries to inform policy making and implementation strategies in their national cancer programs.

Gender norms and sexual minority groups

Most Southeast Asian societies subscribe to a patriarchal ideology, with the strongest forms of gender discrimination related to family and civil liberties. In many ASEAN cultural contexts, the systematic disempowerment of women in social institutions has led both women and men to believe that a woman is subordinate with a utility limited to unpaid care and domestic work.[78] The duty to put family before one's self has become an ingrained social expectation for many women, which, compounded with healthcare-associated costs and difficulties in finding childcare services, all contribute to a woman's late presentation in the course of her illness.[78,79] These barriers are further magnified by poverty.[78,79]

Moreover, many men act as the primary decision maker over their partner's health care, as reported by 31% of women in Timor-Leste to as much as 47% of women in the Philippines.[80] This dynamic places women at a disadvantage, especially when it comes to gynecologic and reproductive health concerns. Gender inequality also figures in sexual relations, where power imbalances can hamper a woman's ability to ask her partner to wear a condom or comfortably bring up testing for sexually transmitted infections (STI).

This also holds true for historically vulnerable groups including non-binary women and minors, especially when intersected with systemic issues like poverty and homelessness. From these situations arise occupations like commercial sex work, which increases the risk for STIs, sexually transmitted oncogenic viruses, and human immunodeficiency virus (HIV).[81,82] Commercial sex work is an occupation often misunderstood, criminalized, and invisible to state support. The discrimination faced by sex workers, magnified by the stigma of an HIV diagnosis, creates nearly insurmountable barriers to accessing health, legal, and social services.[81]

Cervical and breast cancer are two other highly stigmatized conditions in Southeast Asia, especially cervical cancer in strongly devout communities that consider sexual activity before marriage immoral. Religion plays a role in linking morality and purity to the woman's identity, hence the idea of cervical cancer arising from a sexually transmitted virus or promiscuity generates shame; even accessing sexual and reproductive health services such as contraceptives can be considered an interference with divine will.[80] In the Bangsamoro Autonomous Region of Muslim Mindanao and Caraga regions in the Philippines, young women risk discrimination, mistreatment, and even refusal of services from healthcare providers for requesting sexual and reproductive health services since this is viewed as encouraging promiscuity; it is common for healthcare providers to ask for the husband's consent before providing family planning information or contraceptives.[80,83]

In addition, Asian women are more private about their bodies and feel embarrassment in cervical and breast examinations by health personnel, commonly leading to deferral of these exams.[75,84] Another barrier to early screening is health literacy, with many Southeast Asian women having negative perceptions of cancer screening because of fatalism and poor understanding of the disease.[15,84] Shame and stigma allow women to keep their cancer diagnoses secret for years without seeking medical treatment, contributing to upstaging and elevated mortality incidence.[75]

An underrepresented group in cancer research and national cancer registries is the lesbian, gay, bisexual, transgender, and queer/questioning (LGBTQ+) community; gender and sexual minorities have higher risk for cancer because of lower screening rates and late-stage presentation underlaid by stigma, socioeconomic challenges, and barriers to healthcare access (e.g., gender-discriminatory insurance policies).[83,85,86] One study found that people who identify as lesbians are at higher risk for female-specific cancers because of factors like fewer pregnancies and less months breastfeeding, and breast cancer risk is increased in transgender women because of the feminizing hormone therapy prescribed in gender transitioning.[85] Gay men have increased risk for anal cancer from human papillomavirus exposure and HIV-associated cancers.[85] Transgender men with female reproductive organs would still need gynecologic checkups before sex affirmation surgery, but gender dysphoria stemming from the recommendation to undergo a traditionally female exam despite identifying as a male can induce psychological and emotional distress and hinder cervical cancer screening uptake.[86] Moreover, the lack of gender inclusivity in legal frameworks, medical society screening guidelines, and health practitioner training can hinder access to appropriate, sensitive care.[85,86] For example, the *kathoey* in Thailand and gender-fluid counterparts in ASEAN countries face stigma from healthcare workers during health consults, cancer screening, and the provision of reproductive health services.[83]

Ethnicity, culture, and religion

Cancer outcomes are also affected by ethnicity, a social construct impacted by an individual's social milieu, and one with correlates with genetic ancestry.[87] Although ethnicity has no direct link to tumor biology and treatment response, ethnic groups in Southeast Asia may nonetheless differ in cancer epidemiology and outcomes because of group differences in exposures, resources, cultural contexts, and access to care that impact women's health. These factors are subsequently linked to treatment response; work in other race/ethnicity groups suggests that social forces can exert effects on tumor biology through downstream differences in inflammation, oxidative stress, and immune function.[88] In Singapore and Malaysia, the three major ethnic groups are Chinese, Indian, and Malay. Among the three, Chinese patients with cancer have better response to chemotherapy like doxorubicin, whereas Indians and Malays are more likely to have aggressive tumors.[89] It is possible that certain polymorphisms are more common in certain groups that may be associated with tumor factors and treatment response.[89] However, it is also likely that these differences are driven by disparities in terms of access to care, as has been demonstrated in other settings that seek to examine racial and ethnic cancer disparities.[87,90]

Table 4. Unemployment as a % of the Female/Male labor force, respectively, in the ASEAN region (2020, modeled estimate)

	Irrespective of education			With basic education			With intermediate education			With advanced education		
	F	M	F:M ratio	F With basic educ	M With basic educ	F:M ratio	F With int educ	M With int educ	F:M ratio	F With adv educ	M F With adv educ	F:M ratio
Brunei	9.12	6.68	1.37									
Myanmar	1.19	0.97	1.23									
Cambodia	0.38	0.29	1.31									
Timor-Leste	6.42	3.63	1.77									
Indonesia	3.79	4.61	0.82	2.16	3.3	0.65	7.44	7.18	1.04	4.6	4.6	1.00
Lao PDR	0.98	1.08	0.91									
Malaysia	4.67	4.4	1.06	3.89	4.12	0.94	4.89	4.45	1.10	4.6	4.63	0.99
Philippines	2.71	2.40	1.13									
Singapore	4.39	3.89	1.13	5.35	5.5	0.97	6.64	5.48	1.21	5.23	4.5	1.16
Thailand	1.09	1.11	0.98	0.69	1.02	0.68	1.41	1.37	1.03	2.22	2.12	1.05
Vietnam	2.82	2.00	1.41	1.77	1.65	1.07	3.25	2.27	1.43	5.91	2.99	1.98

Blank fields = unavailable.

With regard to cancer epidemiology, ethnicity is also connected to socioeconomic status, religion, cultural values, diet, and lifestyles. Chinese patients more likely have higher income and education status, consume more soy, and consume the least dietary fat, all of which are associated with breast cancer.[89] In relation to cultural practices, the predominant religions of these ethnic groups—Buddhism, Christianity, Hinduism, and Islam—have different doctrines which may influence health beliefs, relationships with partners, disease awareness, and health literacy, all of which can affect the timing of consult and stage of presentation for patients with cancer.[89] For example, in Singapore, Chinese-ethnicity women were found to have greater incidence of HPV-associated cancers than women of Malay or Indian descent, which may not only reflect sociocultural practices and variations in sexual norms, but also differential barriers to vaccination and screening.[91]

SOCIOECONOMIC DETERMINANTS OF SEX DISPARITIES IN CANCER

Sex disparities in employment and education also feed into sex disparities in cancer care. Women are thrust into lower wages and more likely to engage in unregulated forms of employment, translating to fewer work protections. Ultimately, it means women have fewer resources relative to men for coping with the financial toxicities of cancer, especially when living in countries without robust social security systems.[92]

Unemployment

Consider World Bank data on unemployment as a function of both gender and education (World Bank, 2022) made freely available, tabulated in Table 4.

Irrespective of educational attainment, a larger proportion of the female labor force in the ASEAN is unemployed. If women attain an intermediate level of education, a larger proportion of women in that educational level remain unemployed still, compared to men of similar attainment.

Of interest, among the labor force with basic education, the trend reverses and instead of women, a larger proportion of men do not gain employment. On the other hand, the effect of advanced education on unemployment appears to be equivocal between men and women—except for Vietnam where the proportion of women with advanced education remaining unemployed is almost double that of men.

Vulnerable employment

Vulnerable employment is defined as the sum of the employment status groups of own-account workers (self-employed without hired employees) and contributing family workers, who contribute to a family business but are generally unpaid. By definition, this group is the least likely to have formal work arrangements

Table 5. Rates (%) of salaried employment and vulnerable employment in the ASEAN region, disaggregated by sex (2019, modeled ILO estimate)

	Wage and salaried workers			Vulnerably employed		
	Females	Males	F:M ratio	Females	Males	F:M ratio
Brunei	89.35	92.24	0.97	8.62	4.56	1.89
Myanmar	35.13	35.05	1.00	63.74	61.53	1.04
Cambodia	46.76	58.74	0.80	53.17	41.13	1.29
Timor-Leste	19.89	39.88	0.50	79.15	58.88	1.34
Indonesia	41.04	52.95	0.78	57.08	42.52	1.34
Lao PDR	18.5	31.82	0.58	81.28	67.54	1.20
Malaysia	71.24	73.45	0.97	27.1	21.74	1.25
Philippines	60.43	66.01	0.92	37.41	30.55	1.22
Singapore	91.32	83.12	1.10	6.15	11.39	0.54
Thailand	49.74	46.69	1.07	48.84	46.82	1.04
Vietnam	41.1	49.92	0.82	57.76	47.29	1.22

and the least likely to have social protection and safety nets to guard against economic shocks, which often leaves them incapable of generating sufficient savings to offset these shocks.[93]

A definite trend using global data has demonstrated that the lower a country's economic indicators, informal employment increases; this burden is disproportionately taken on by more women than men, as shown in Table 5.

Save for some exemptions, the overwhelming trend in ASEAN countries is that women, by proportion, are employed less in the formal economy and are instead thrust into non-standard—and consequently more vulnerable—forms of employment. Ultimately, this translates to decreased income stability and increased susceptibility to financial catastrophe in the face of expenses relating to cancer care. It is estimated that women held only 38 percent of all salaried jobs in the region in 2015.[94]

Women tend to be overrepresented in unpaid care work as well, particularly in SEA, South Asia, and Pacific Island countries. As women take up the bulk of unpaid childcare and eldercare, opportunities for formal employment and career advancement further diminishes. And so, in countries where women increasingly fill in the gaps where universal healthcare service must satisfy, access to decent work likewise deteriorates.[94]

Career advancement and gender pay gap

Even when women beat the odds, they hit a glass ceiling. When ILO conducted a survey in 2013 across 418 Asia-Pacific enterprises, they found that women comprised less than ten percent of senior managers and less than 5% of CEOs. In all the ASEAN Member States, except for the Philippines, women earn less than men, ranging from a modest gap in Malaysia and Thailand to about one-quarter in Cambodia and Singapore.[94]

Health-seeking behavior and preventive services

A combination of paltry financial resources from informal sector work, deficient social security benefits, and gendered sociocultural expectations shouldered asymmetrically by women are all contributory to the poor health-seeking behavior in ASEAN women.[92]

The Philippines is a frontrunner in Asia for breast cancer mortality, where more than half of patients are diagnosed with late-stage disease.[95] The case is worse for cervical cancer, the second most common malignancy of Filipino women, because three-quarters of cervical cancer is diagnosed at advanced stages.[96] However, fewer than one in ten Filipinas receive screening, and at one tertiary outpatient clinic of 383 Filipinas, only a little over half had ever even heard of cervical cancer.[15]

Many Filipino women still tend to neglect preventive healthcare measures in favor of their responsibilities as wage earners, wives, and mothers, motivated greatly by a fear of imposing financial burdens on the family. This is understandable, especially when taken with the fact that the average cost of mammography and Pap smear in the Philippines is roughly 4x and 2x, respectively, the minimum daily wage.[15,97] On top of financial hurdles, the technologic and human resources required are peripherally scarce as well, because the majority of cytologic screening facilities and trained cytopathologists are concentrated at the national capital.

Combined with poor health literacy, stigma, and disadvantageous misconceptions about pain, consultation is typically only sought when symptoms become difficult to ignore, typically already at advanced stages of cancer. A school-based HPV vaccination program was introduced in 2016, but has been underwhelming in its subnational reach.[15] In contrast, through multisectoral collaboration overcoming resource limitations, a similar HPV vaccination program in Malaysia has seen excellent parental consent rates (95%), dose completion rates (98%), and population coverage (80%), with vaccine wastage remaining low.[98]

Cancer and COVID-19

SEA has seen prolonged and stringent forms of movement restrictions, particularly in Malaysia, Singapore, Thailand, and the Philippines, even causing unemployment to skyrocket to all-time highs in the Philippines and Malaysia. This prolonged loss of income understandably hit harder for those in the informal sector, who often live from one paycheck to another.[99]

We reiterate that in SEA the unemployed and vulnerably employed are both disadvantaged demographics among whom women are overrepresented. And so we add to the growing list of ways the pandemic has magnified pre-existing inequities that have long since existed in life and health: as a direct result, many patients with cancer resort to maladaptive remedies such as skipping clinic appointments and underdosing on medication. These are social pressures more insidiously imposed on and felt by women, driven by the gender and cultural norms that weave the fabric of their social reality. Often, patients are forced to choose between paying for treatment or feeding their family.[92,99]

Not only did the pandemic impact baseline coping capacity of the already disadvantaged, even for patients with cancer intent on pursuing treatment, many treatment delays were experienced because hospitals in Malaysia and Philippines scaled back many urgent and non-urgent treatments, elective surgeries, and admissions to streamline resources allocated to COVID-19 response.

Impact of cancer on employment

Patients with cancer are more likely to be unemployed, or file for bankruptcy.[92,100,101] Not only that, it was recently found that Malaysian breast cancer survivors had even experienced work discrimination because of their cancer. Some culminated in forced resignation after management anticipated a decline in their productivity.[99] It is likely that similar themes of discrimination favoring organizational interest over individual welfare have also been exacerbated by the pandemic.

Conversely, breast cancer survivors having accommodating employers was associated with 2.5 times the odds of post-treatment job retention, even after controlling for age, income, and health insurance.[102] These are social safeguards that cannot exist in conditions of vulnerable employment, which have been silently assigned to women in SEA.

CONCLUSIONS

In Figure 1, we depict the interdependence of the drivers of cancer-sex disparities acting at different stages across the continuum of cancer. Generally, the impact of biologic and direct care-related drivers (in blue) across the cancer spectrum is directly manifest and may span multiple stages. Socioeconomic drivers (in yellow) provide the context within which the former may be modified and expressed. Note that biologic determinants of cancer risk (in deep blue) are considered sex differences rather than sex disparities, and so are beyond the domain of influence of socioeconomic drivers (in yellow), but contribute nonetheless to the lived experiences of people with cancer.

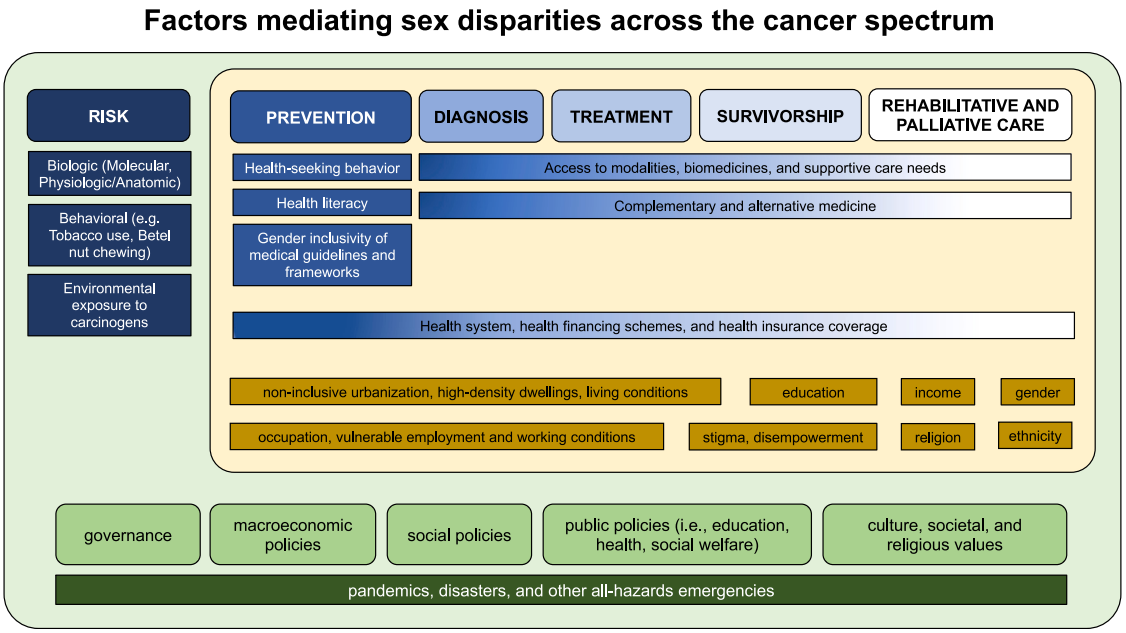

Figure 1. Factors mediating sex disparities across the cancer spectrum

All of the aforementioned exist within a much broader stage that is composed mostly of top-to-bottom structural determinants (in green), only lightly touched on in this article but is greatly discussed in the WHO CSDH (Commission on Social Determinants of Health) conceptual framework on social determinants of health.[103]

This review is but a glimpse of the social factors that drive sex and gender disparities in cancer care in Southeast Asia and is by no means panoptic. There is a need to strengthen national research arms to generate more evidence on such determinants and to create evidence-based policies for culture-specific interventions. Cancer research in the ASEAN is disproportionately influenced by data from the high-income and upper middle-income countries, which can skew—or generalize—the perspective of Southeast Asia in global discourse. Although there are national models of good practices (for example, Thailand's breast cancer care network and Singapore's smokeless tobacco ban), the degree to which these systems and policies can be adopted in other countries will depend on their sociocultural, geopolitical, and socioeconomic environments and resources.

We underscore that these issues, although unique in their presentation in ASEAN, mirror disparities faced by women across the world. Although many of these issues may be universal, the unique historical, sociocultural, and sociopolitical context of ASEAN can impact the ability of women in the region to access cancer care equitably. Further work looking at the intersection of different determinants of health ranging from social to political, as well as how these forces interact with individuals' identities, should assess parallels between women in ASEAN and other regions.

Ultimately, the ways in which social determinants of health mediate sex differences in cancer do not exist in siloes. People exist at the intersection of their identities, underscoring the need to use the lens of intersectionality in the study of cancer disparities in the ASEAN region and globally. For example, a woman who experiences both poverty and geographic barriers in access to care may not be able to access care if only socioeconomic factors are improved. Similarly, a *trans* man who has been linguistically and culturally minoritized may not be aware of the need for cervical cancer screening if efforts to improve health literacy are only available in majority languages. Much work remains in ASEAN countries to design interventions that tackle sex differences and sex disparities in cancer with a holistic and intersectional approach to care.

DECLARATION OF INTERESTS

Author disclosures. ECD is funded in part through the Cancer Center Support Grant from the National Cancer Institute (P30 CA008748). All other authors declare no competing interests.

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