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Multipurpose prevention technologies for sexual and reproductive health: mapping global needs for introduction of new preventive products☆,☆☆,★,★★

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Abstract

Objectives: Worldwide, women face sexual and reproductive health (SRH) risks including unintended pregnancy and sexually transmitted infections (STIs) including HIV. Multipurpose prevention technologies (MPTs) combine protection against two or more SRH risks into one product. Male and female condoms are the only currently available MPT products, but several other forms of MPTs are in development. We examined the global distribution of selected SRH issues to determine where various risks have the greatest geographical overlap.

Study design: We examined four indicators relevant to MPTs in development: HIV prevalence, herpes simplex virus type 2 prevalence (HSV-2), human papillomavirus prevalence (HPV) and the proportion of women with unmet need for modern contraception. Using ArcGIS Desktop, we mapped these indicators individually and in combination on choropleth and graduated symbol maps. We conducted a principal components analysis to reduce data and enable visual mapping of all four indicators on one graphic to identify overlap.

Results: Our findings document the greatest overlapping risks in Sub-Saharan Africa, and we specify countries in greatest need by specific MPT indication.

Conclusions: These results can inform strategic planning for MPT introduction, market segmentation and demand generation; data limitations also highlight the need for improved (non-HIV) STI surveillance globally.

Implications: MPTs are products in development with the potential to empower women to prevent two or more SRH risks. Geographic analysis of overlapping SRH risks demonstrates particularly high need in Sub-Saharan Africa. This study can help to inform strategic planning for MPT introduction, market segmentation and demand generation.

Keywords: Multipurpose prevention technologies; Unintended pregnancy; HIV; HSV-2; HPV

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★ Details of ethics approval: Our study used publically available secondary data and thus did not require institutional review board approval.

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1. Introduction

For women, the primary sexual and reproductive health risks of unprotected sex are unintended pregnancy and a variety of sexually transmitted infections (STIs), including HIV. Male and female condoms are the only currently available products that provide simultaneous protection against these risks, but acceptability (and cost issues, for female condoms) has constrained their widespread use [1–2]. A single, safe, effective, acceptable and accessible product for women that combines protection from multiple risks could have significant benefits for individual and public health.

The emerging field of multipurpose prevention technologies (MPTs) builds upon previous prevention strategy development efforts (such as development of HIV-preventive microbicides) by combining contraception with STI (including HIV) prevention. According to the World Health Organization (WHO), eight STIs contribute the greatest burden of disease attributable to STIs [3]. Four of these STIs are curable (chlamydia, gonorrhea, syphilis and trichomoniasis); the others are incurable viral infections, including the following:

(1) HIV in 2013, an estimated 35 million people were living with HIV, and 2.1 million people were newly infected. Sub-Saharan Africa remains the most affected region [4].

(2) Herpes simplex virus type 2 (HSV-2) causes the majority of cases of genital herpes. In 2012, 417 million people were living with HSV-2 worldwide, with women comprising 64% of those infected and prevalence highest in Africa. Although generally asymptomatic, HSV-2 is associated with considerable morbidity and increased risks of HIV acquisition [5].

(3) Hepatitis B virus kills approximately 700,000 people a year, with prevalence highest in sub-Saharan Africa and East Asia. Routine inclusion of a vaccine in infant immunization programs worldwide has already prevented an estimated 1.3 million deaths from chronic liver disease and cancer [6].

(4) Human papillomavirus (HPV) infection causes more than 500,000 cases of cervical cancer and 250,000 cervical cancer deaths every year, 85–90% of which are in low- and middle-income countries. Routine immunization programs in 45 primarily high-income countries include the highly effective HPV vaccine. Thus, a comprehensive approach to HPV prevention should include vaccination and other measures [7].

In many regions of the world, the impact of HSV-2 and HPV on population health is of greater concern than that of HIV due to greater HSV-2 and HPV prevalence relative to HIV. MPTs that protect against these three viral STIs and

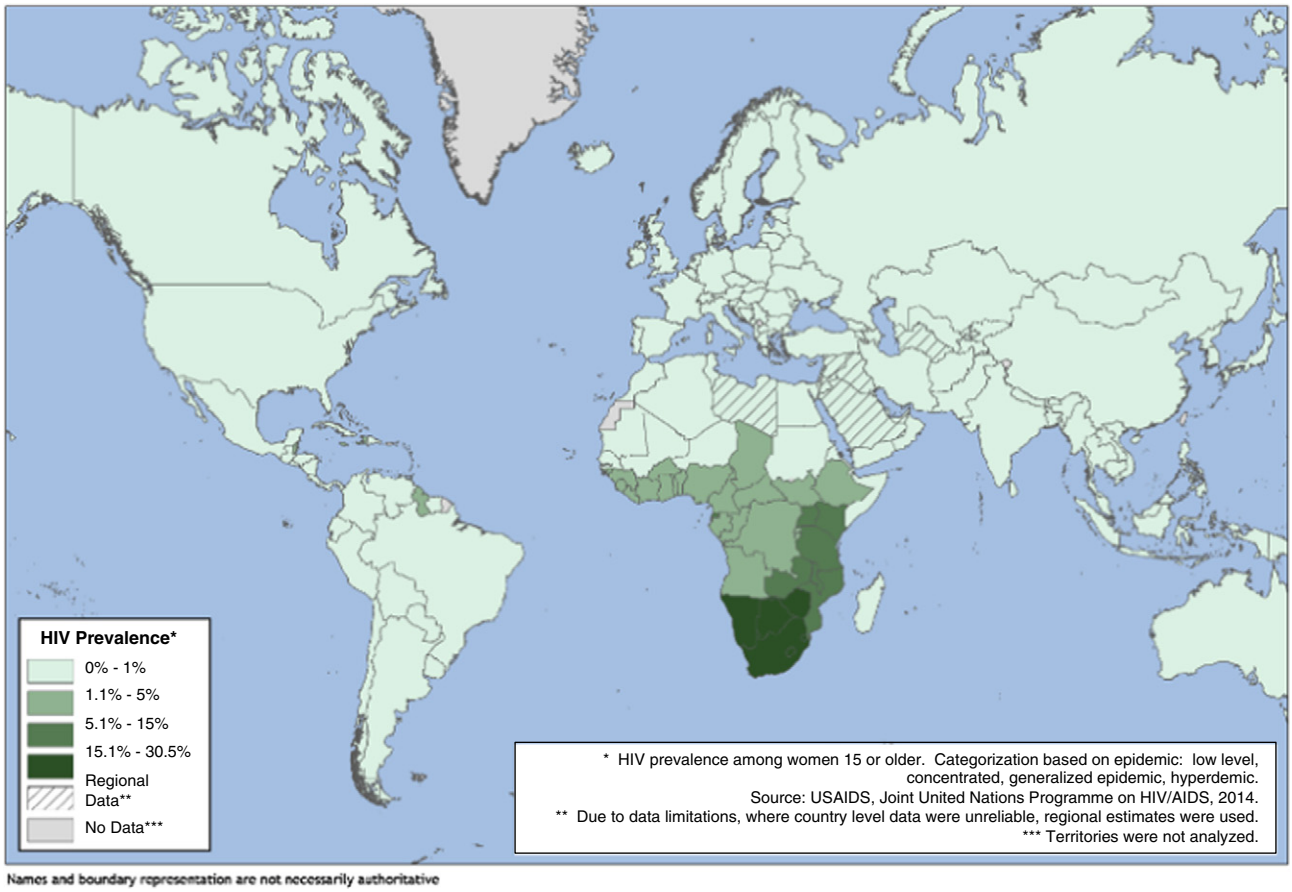

Fig. 1. HIV prevalence among women aged 15 years and older by country or region.

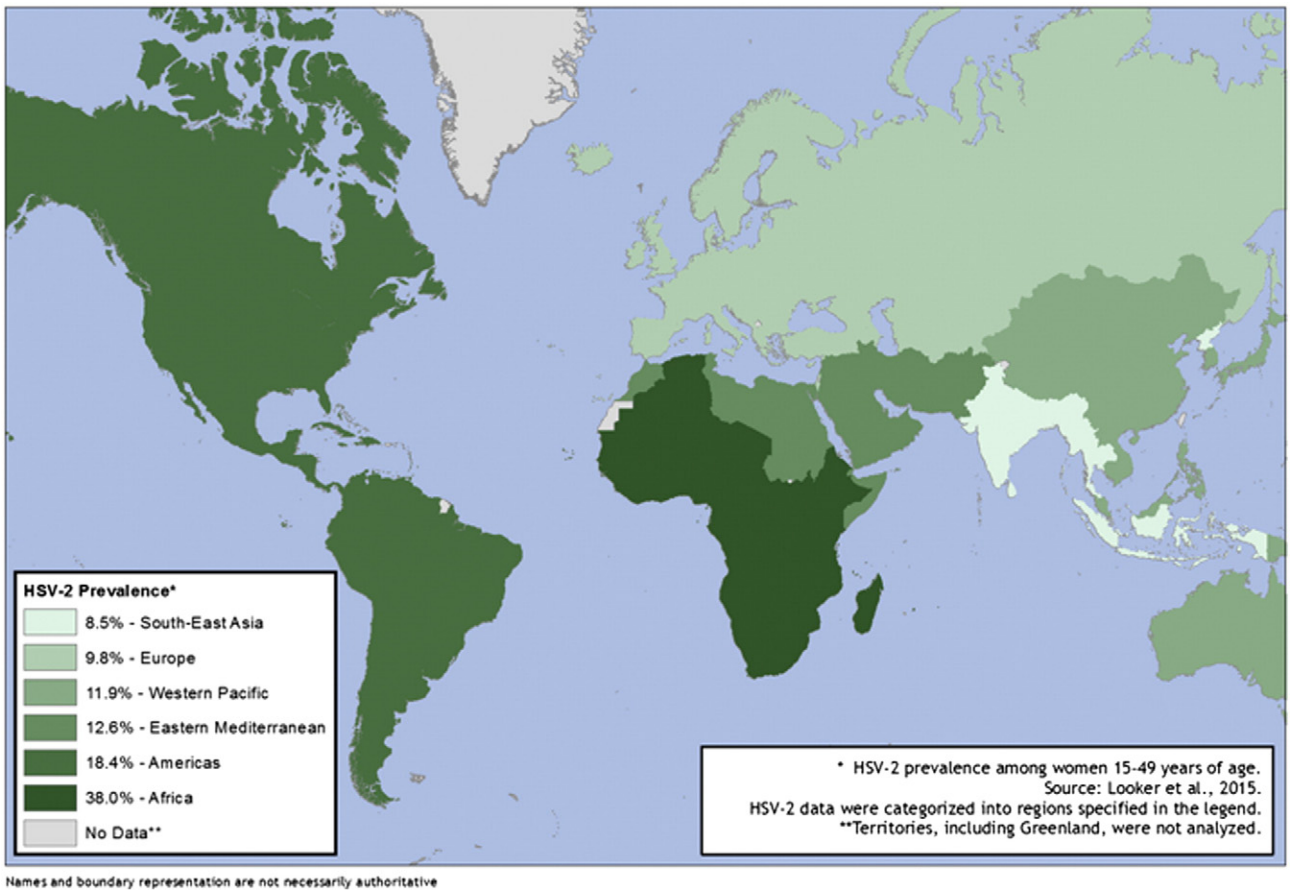

Fig. 2. HSV-2 prevalence among women aged 15–49 years by region.

unintended pregnancy could substantially improve public health. Thus, we aimed to examine the global distribution of four MPT targets [HIV, HSV-2, HPV and unmet need for modern contraception (UNMC)] to document and visualize where intersecting risks indicate the greatest need for MPTs. We present a broad, population-level overview of overlapping burdens that could be ameliorated by access to effective MPTs.

2. Methods

2.1. Indicator selection and categorization

We conducted expert interviews and a literature review to inform indicator selection, and we obtained prevalence estimates for each indicator. Since prevalence reflects the proportion of individuals living with a particular condition, it does not explicitly capture individuals in need of an MPT for prevention (i.e., people at risk of acquiring the infection) or with an interest in using an MPT. However, prevalence is a widely understood indicator that indicates the degree of health burden.

Availability of data varied by country and indicator and was limited for HSV-2 and HPV. We used regional data where country-level data were unavailable. We included only independent states and excluded Vatican City, Andorra, Nauru and Tuvalu due to lack of data.

We used 2013 Joint United Nations Programme on HIV and AIDS (UNAIDS) country-level HIV prevalence estimates for women aged 15 years and older [8], calculated using a standardized estimation methodology across countries [9]. We derived estimates for certain countries from unpublished country-level figures provided by UNAIDS[1].

[1] UNAIDS does not provide country-level estimates for countries where concern exists about data accuracy, where the total population is less than 250,000 or where estimates from country teams were not provided [10] (M. Mahy, "personal email correspondence," ed, 2014). These countries include Argentina, Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Canada, China, Croatia, Equatorial Guinea, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Japan, Kazakhstan, Latvia, Lithuania, Luxembourg, Malta, Mauritania, Montenegro, the Netherlands, New Zealand, North Korea, Norway, Oman, the Philippines, Poland, Portugal, Russia, Singapore, Slovakia, Slovenia, South Korea, Sweden, Turkey and the United States. Values are reported as a range in online Appendix A. Where no UNAIDS country-level estimate was available, regional averages were substituted for the following: Antigua and Barbuda, Bahrain, Brunei, Comoros, Dominica, Federated States of Micronesia, Grenada, Iraq, Jordan, Kuwait, Lebanon, Libya, Palau, Qatar, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Samoa, Saudi Arabia, Seychelles, Solomon Islands, Syria, Timor-Leste, Tonga, Turkmenistan, United Arab Emirates and Vanuatu. Liechtenstein, Monaco and San Marino were not assigned a regional value or a country-level estimate as they are not UNAIDS countries included in any estimates.

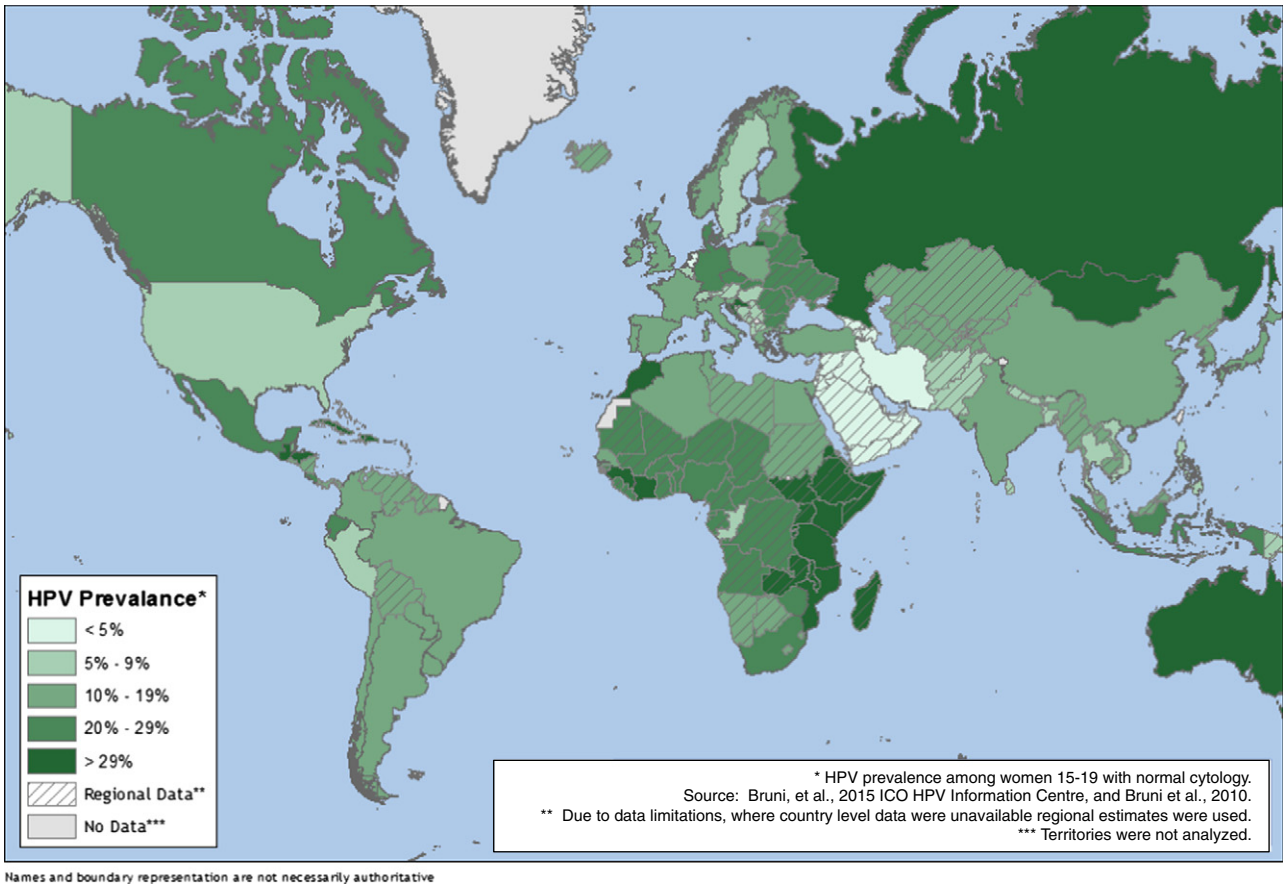

Fig. 3. HPV prevalence among women aged 15–49 years by country or region.

Country-level HSV-2 surveillance varies and is often incomplete. We obtained prevalence data among women aged 15–49 years from a review of HSV-2 seroprevalence studies that calculated pooled prevalence values by age and sex for each of the six WHO regions[2] [5].

Similarly, country-level HPV surveillance varies and is often incomplete. HPV is a transient infection, unlike HIV and HSV-2, and prevalence peaks at younger ages, just after sexual onset, then decreases [11]. For the purpose of this population-level overview and because subgroup data are not routinely available, we restricted to women aged 15–49 years. We obtained country-level estimates from the Institut Català d'Oncologia (ICO) Information Centre on HPV and Cancer [12], as well as adjusted regional estimates from a 2010 meta-analysis[3] [13]. We limited estimates to women with normal cervical cytology to best approximate prevalence in the general population but inclusive of all HPV genotypes. HPV prevalence estimates between countries may not be comparable due to the use of different HPV detection techniques, study design and methods and age distributions within the 15- to 49-year age group; adjusted regional prevalences can be compared.

UNMC captures the proportion of women aged 15–49 years who are married or in union, sexually active and fecund, and who report wanting to stop or delay childbearing for at least 2 years, but are not using a modern contraceptive method[4] [14]. This indicator intends to measure the gap between women's reproductive intentions and their use of highly effective contraceptive options [15]. We chose this indicator instead of unintended pregnancy, given greater country-level data availability and a larger denominator of sexually active women in union (compared with women with a recent pregnancy). We also considered using the indicator "demand for modern contraception," which would offer insight into women looking to use contraceptive methods (as some women with UNMC may still not use a modern method, even if available). However, demand would not highlight areas of particular epidemiological burdens akin to the HIV/STI

[2] Africa, Americas, Eastern Mediterranean, Europe, South-East Asia and Western Pacific.

[3] Middle Africa, Central Asia and Oceania were not available in the 2010 meta-analysis because no data met the quality standards. The Sub-Saharan Africa regional estimate was used for Middle Africa, and the Asia regional estimate was used for Central Asia. An Oceania regional estimate was available from the 2012 update in the ICO HPV Information Centre database. Only one study was available for the Caribbean regional estimate.

[4] Modern contraceptive methods include female and male sterilization, oral contraceptive pills, an intrauterine device, male or female condoms, injectable contraceptives, the contraceptive implant, barrier methods and emergency contraception, according to the United Nations Department of Social and Economic Affairs.

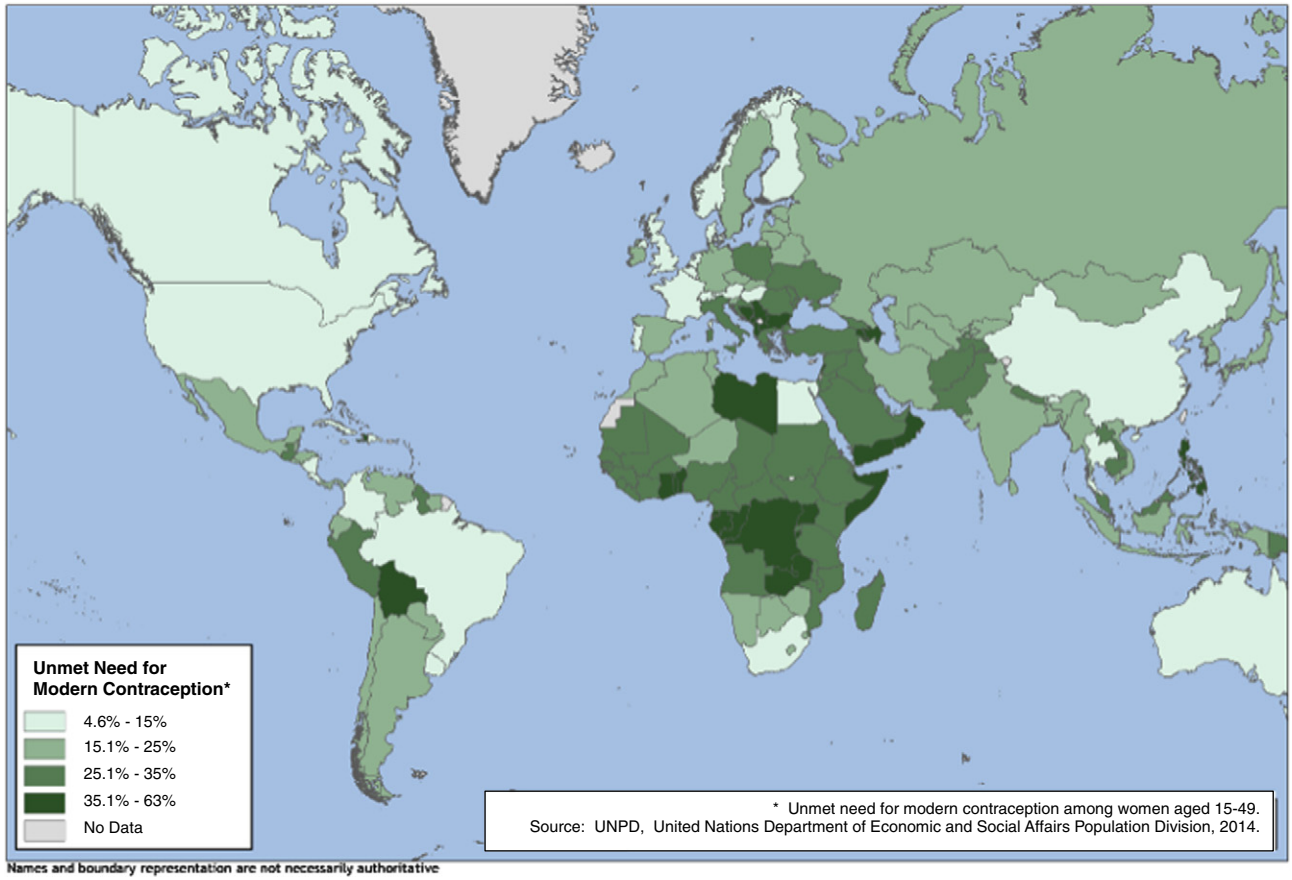

Fig. 4. UNMC among women aged 15–49 years by country.

indicators. We used median estimates from the United Nations' 2012 Population Division annual estimates[5] [14,16].

For HIV and HPV, we utilized field standards for data categorization [17]. WHO and UNAIDS categorize four epidemiological scenarios for HIV prevalence: low level (≤1%), concentrated (>1% and ≤5%), generalized (>5% and ≤15%) and hyperendemic (>15%) [18]. The ICO HPV Information Centre uses the following categories: <5%, 5–9%, 10–19%, 20–29% and ≥30%. Since UNMC has no standard categorization scheme, we used Jenks optimization (with rounded cutpoints), which places cutpoints at natural gaps in the data distribution [17,19]. We included a separate category for each of the six WHO regions used for HSV-2 data.

2.2. Principal components analysis

To analyze variation among STI/HIV prevalence and UNMC, we used principal components analysis (PCA), a data reduction technique commonly used to construct indices for concepts difficult to quantify with a single metric. This analysis also enables information on all four indicators to be displayed on a single map. We conducted PCA calculations using Stata 13.1/SE with all four indicators included as the variables in the analysis, and we replaced missing data points using the sample average. We interpret our results as exploratory due to the limited range of indicators used, the limited range of variation within the indicators and the sample size constraints capped by the number of countries for which data are available. Caveats aside, the application of PCA on these data can be illustrative for identifying geographic areas to target MPTs.

2.3. Graphical analysis

We present full numeric data for each indicator by country in online Appendix A. To facilitate understanding of the global overlapping risks, we visually represent these data in global choropleth maps. We used ArcGIS Desktop 10.2.2 [20] with ColorBrewer [21] to create single-layer choropleth maps for each indicator, a map showing UNMC as graduated symbols overlaid on the HIV choropleth map, and all other possible combinations of two indicators (available upon request). We mapped results of the PCA, which provided the best possible representation of all four indicators on a single map. We generated stacked bar graphs to examine the additive burden of each indicator by country (presented only for sub-Saharan Africa; others available upon request).

[5] Several smaller countries do not have data available (see online Appendix A).

Table 1
Example MPT products in development and corresponding high-burden geographic areas

	Intended indications for various multipurpose prevention technology products (existing [*] or in development)	Top 5 countries with greatest additive burden of indicators	Countries simultaneously in top 2 highest categories of indicator burden
Quadruple indication MPTS	**Unmet need for modern contraception and HIV and HSV–2 and HPV** • *MZCL combination topical gel* • *MZCL combination IVR* • Poly–[1,4–phenylene–(1–carboxy) methylene] (PPCM) SAMMA gel Results presented in Map 6, Figure 1, and Appendix A.	Comoros, Guinea, Tanzania, Uganda, Zambia Based upon ranking the total summed prevalence of all 4 individual indicators	Angola, Benin, Bolivia, Burundi, Cameroon, Central African Republic, Comoros, Congo (Brazzaville), Congo (Kinshasa), Equatorial Guinea, Eritrea, Gabon, Ghana, Haiti,Liberia, Mali, Mauritania, Samoa, Senegal,Sao Tome and Principe, Sierra Leone, Somalia, South Sudan,The Gambia, Togo, Uganda, Zambia Principal component 1 (HIV, HSV–2, HPV) medium–high or high. Principal component 2 (unmet need for modern contraception) medium–high or high.
Triple indication MPTs	**Unmet need for modern contraception and HIV and HSV–2** • Male condoms* • Female condoms* • *90 day tenofovir plus levonorgestrel IVR* • Tenofovir disoproxil fumarate (TDF) plus levonorgestrel IVR • *SILCS diaphragm plus tenofovir gel* Results presented on map by request.	Congo (Brazzaville), Lesotho, Swaziland, Uganda, Zambia Based upon ranking the total summed prevalence of 3 individual indicators	Comoros, Equatorial Guinea, Kenya, Malawi, Mozambique, Tanzania, Uganda, Zambia Unmet need for modern contraception >25%. HIV prevalence > 5%. HSV–2 prevalence >18.3%.
	HIV and HSV–2 and HPV • *Griffithsin gel* • *Griffithsin plus Zinc acetate in Carraguard gel* • *MIV–150 plus Zinc acetate in Carraguard gel* Results presented in Map 6.	Guinea, Mozambique, Swaziland, Tanzania, Zambia Based upon ranking the total summed prevalence of 3 individual indicators	Comoros, Equatorial Guinea, Kenya, Malawi, Mozambique, Seychelles, South Africa, Tanzania, Zimbabwe HIV prevalence > 5%. HSV–2 prevalence >18.3%. HPV prevalence >19%.
Dual indication MPTs	**Unmet need for modern contraception and HIV** • *Dapivirine plus levonorgestrel IVR* • Biorings TM IVR • Viciviroc (MK4176) + MK2048 + Progestin IVR Results presented in Map 5.	Albania, Azerbaijan, Bosnia & Herzegovina, Macedonia, Swaziland (the next 5 are all Sub–Saharan African Countries) Based upon ranking the total summed prevalence of 2 individual indicators	Comoros, Equatorial Guinea, Kenya, Malawi, Mozambique, Tanzania, Uganda, Zambia Unmet need for modern contraception >25%. HIV prevalence > 5%.

(continued on next page)

Table 1 *(continued)*

Dual indication MPTs	**HSV–2 and HPV** • Carraguard gel Results presented on map by request.	Cote D' Ivoire, Guinea, Kenya, Mozambique, Tanzania, Based upon ranking the total summed prevalence of 2 individual indicators	Angola, Antigua & Barbuda, Barbados, Burundi, Cameroon, Canada, Central African Republic, Chad, Comoros, Congo (Kinshasa), Costa Rica, Cote D' Ivoire, Cuba, Dominica, Dominican Republic, Ecuador, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Grenada, Guatemala, Guinea, Haiti, Honduras, Jamaica, Kenya, Madagascar, Malawi, Mauritius, Mexico, Mozambique, Nigeria, Rwanda, Saint Kitts & Nevis, Saint Lucia, Saint Vincent & the Grenadines, Sao Tome & Principe, South Africa, South Sudan, Tanzania, The Bahamas, Trinidad & Tobago, Uganda, Zambia, Zimbabwe HSV–2 prevalence >18.3%. HPV prevalence >19%.
	HIV and HSV–2 • *1.0% Tenofovir gel* • *Griffithsin Nanofiber Delivery System* • Tenofovir and Acyclovir IVR • Tenofovir and IQP–0528 • Tenofovir Disoproxil Fumarate (TDF) IVR • *Tenofovir IVR* • SR–2P Gel • VivaGel • Mapp66 (mAb) film • Tenofovir Alafenamide (TAF) oral • *Tenofovir film* • Tenofovir vaginal tablet • TFV/FTC vaginal tablet Results presented on map by request.	Botswana, Lesotho, South Africa, Swaziland, Zimbabwe Based upon ranking the total summed prevalence of 2 individual indicators	Angola, Botswana, Comoros, Equatorial Guinea, Kenya, Lesotho, Malawi, Mozambique, Namibia, Seychelles, South Africa, Swaziland, Tanzania, Uganda, Zimbabwe HIV prevalence > 5%. HSV–2 prevalence >18.3%.

This is not a comprehensive list of all MPTs in development. IVR=intravaginal ring. Italicized products have recently been invested in by United States Agency for International Development. List includes only products intended to prevent against two or more of the following indications: unintended pregnancy, HIV, HSV-2 or HPV. Some products listed may have additional expected indications not reflected in this table (e.g., bacterial vaginosis, chlamydia, gonorrhea, etc.). Source for product information: the Initiative for Multipurpose Prevention Technologies for Reproductive Health MPT database (http://mpts101.org/mpt-database/mpts-topical-gel, accessed 10/18/2014).
[a]Existing MPT, all other products listed are not yet proven and still in development.

3. Results

3.1. Individual indicators

Southern Africa had the greatest HIV prevalence (among women aged 15 years and older), followed by Eastern and Western Africa (Fig. 1). Swaziland had the highest prevalence (30.1%), followed by Lesotho (24.9%) and Botswana (24.9%).

Africa had the highest HSV-2 prevalence at 38% (Fig. 2). The other five regions had the following HSV-2 prevalence estimates: 18.4% in the Americas, 12.6% in the Eastern Mediterranean, 11.9% in the Western Pacific, 9.8% in Europe and 8.5% in South-East Asia.

Cervical HPV infection is highly prevalent in adult women in most of countries. Sub-Saharan Africa, Eastern Europe, Latin America and Pacific countries had the highest levels of HPV (Fig. 3). Western Asia and Southern and Western Europe had HPV estimates below 10%. Notably, countries in Southern Africa with particularly high prevalence of HIV and HSV-2 had moderate HPV prevalence, although this could be due to the lack of country-specific HSV-2 and HPV data; Eastern Africa generally had the highest HPV prevalence.

Compared to STI prevalence, UNMC varies more within regions, possibly reflecting the availability of country-level data and potentially because of diverse drivers for this indicator (e.g., contraceptive access, attitudes toward contraceptive use) (Fig. 4). Eastern Europe, Central Asia and Middle Africa, as well as the Philippines and Bolivia, had the highest levels of

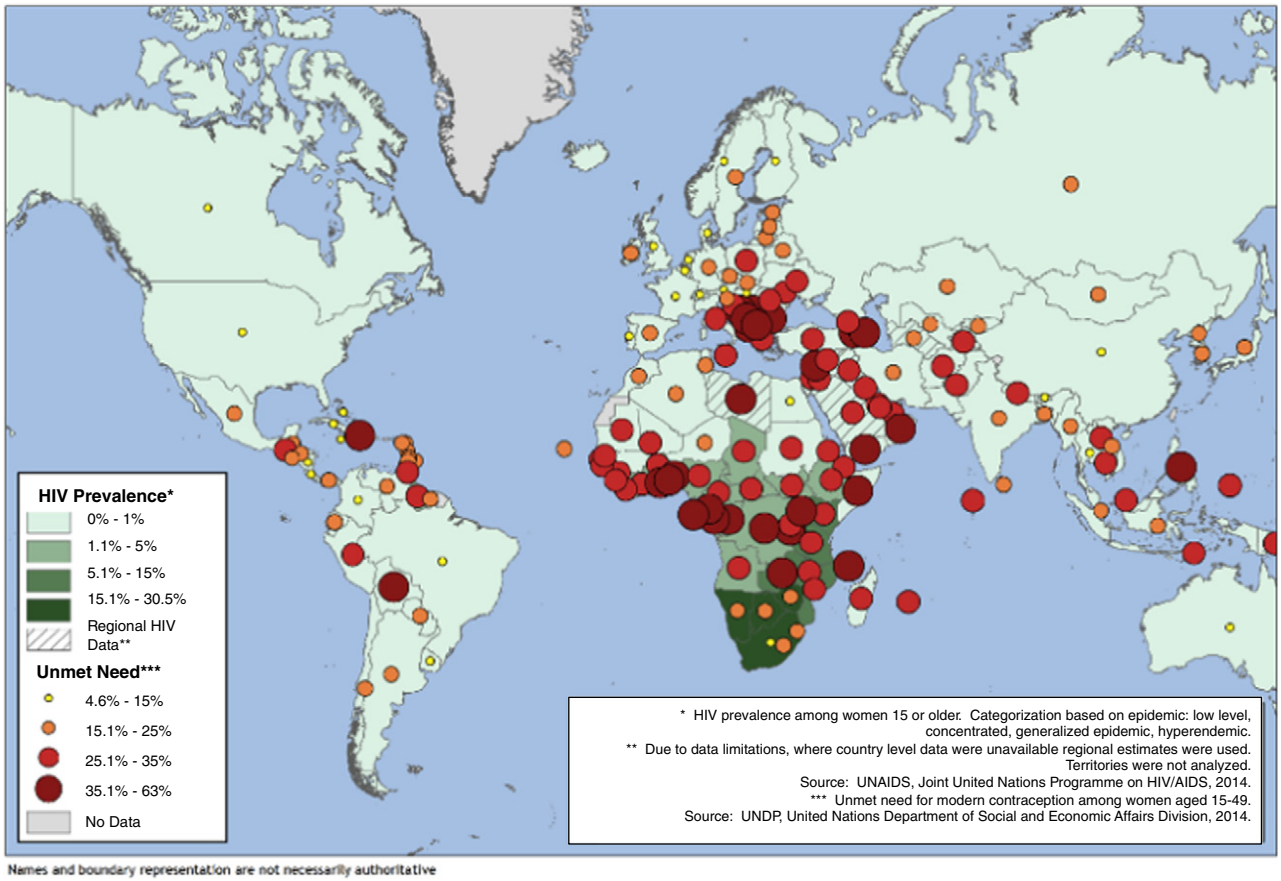

Fig. 5. HIV prevalence and UNMC among women.

UNMC, while North America, Western Europe, parts of South America, China and Australia had the lowest.

3.2. HIV and UNMC

Table 1 matches MPT indications to the countries with the greatest simultaneous burden of these indicators. No country with the highest prevalence of HIV also ranked in the highest two levels of UNMC (Fig. 5). Four countries with UNMC >35% overlapped with the second highest HIV prevalence category (5–15%): Zambia, Uganda, Equatorial Guinea and Comoros. Tanzania, Kenya, Mozambique and Malawi ranked in the second highest category for both HIV and UNMC.

An alternative way of assessing overlap is to examine additive prevalence. Among all countries, Albania had the greatest additive HIV prevalence (0.02%) and UNMC (63%), driven almost exclusively by high UNMC. Other countries highlighted by this method include Azerbaijan, Bosnia and Herzegovina, Macedonia and Swaziland (see Table 1).

3.3. Geographical overlap of all four indicators

UNMC correlates weakly with HSV-2 ($r=0.2027$, $p<.01$) and does not correlate with HIV ($r=-0.0125$) or HPV prevalence ($r=-0.0571$). HPV is moderately correlated with HIV ($r=0.2068$, $p<.01$) and strongly correlated with HSV-2 ($r=0.4716$, $p<.001$). HSV-2 and HIV are most strongly correlated ($r=0.5317$, $p<.001$).

The PCA accounted for the intercorrelation between STIs, identified two components with key information and estimated the proportion of total variance explained by each. Nearly 50% of the variance in these data is explained by Component 1 (which generally captures STI variation, including HPV, HSV-2 and HIV) and over 25% by Component 2 (which generally captures variation in UNMC). Component 1 has similar positive factor loadings across the three STIs and a low loading on UNMC, while Component 2 loads heavily on UNMC and lightly on the STIs (Appendix B). Some countries were higher on one component or the other; some were moderately high on both (see Fig. 6 and Table 1).

Sub-Saharan Africa had the highest values for Component 1, while Eastern Europe and Central Asia and Middle Africa had the highest values for Component 2 (Fig. 6). Countries simultaneously in the top two levels for both Components include Angola, Benin, Bolivia, Burundi, Cameroon, Central African Republic, Comoros, Congo (Brazzaville and Kinshasa), Equatorial Guinea, Eritrea, Gabon, the Gambia, Ghana, Haiti,

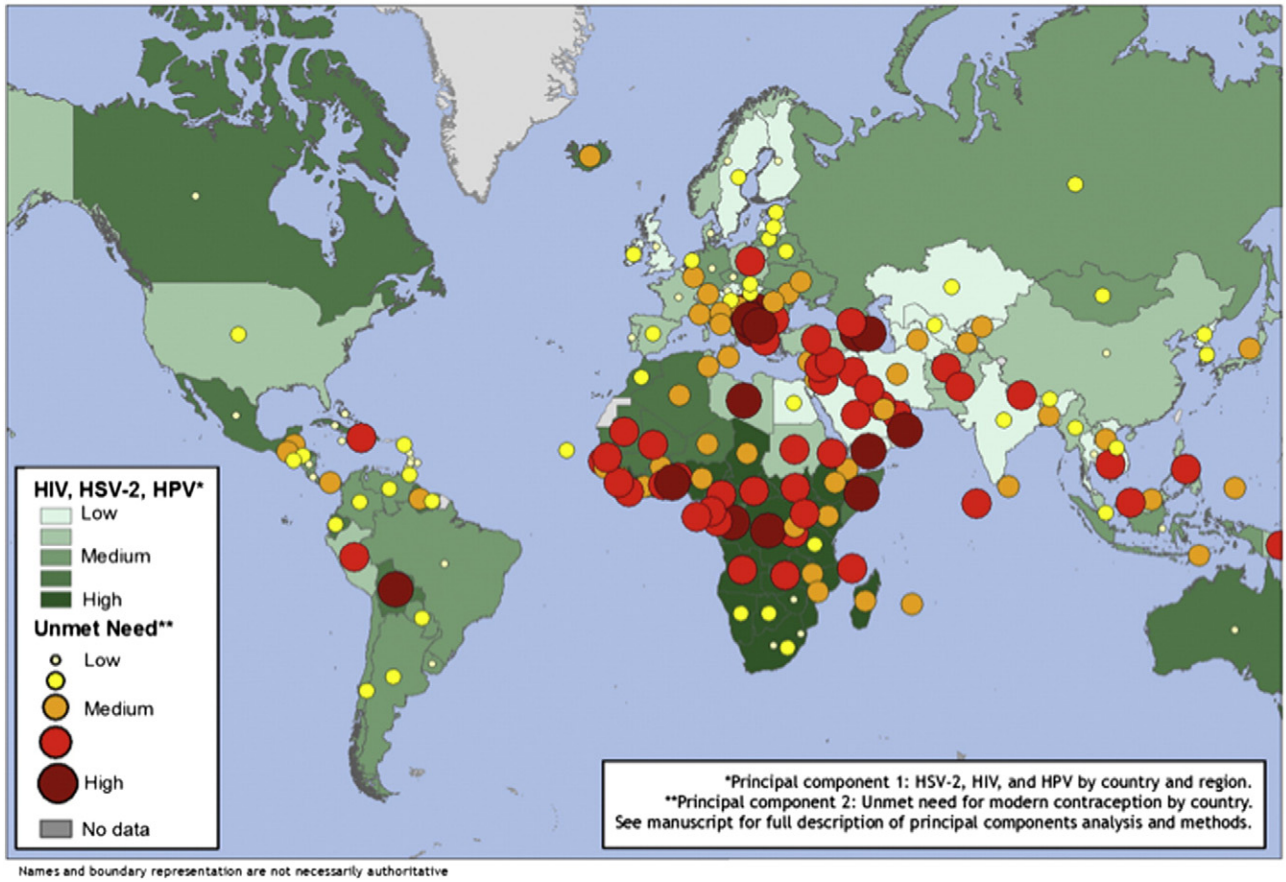

Fig. 6. HIV, HSV-2, HPV and UNMC among women.

Liberia, Mali, Mauritania, Samoa, Senegal, Sao Tome and Principe, Somalia, South Sudan, Togo, Uganda and Zambia.

Sub-Saharan Africa was consistently highlighted as a region of particular need using both PCA and the additive technique (Table 1; Fig. 7 shows additive prevalence for Sub-Saharan Africa). Comoros, Guinea, Tanzania, Uganda and Zambia represent the top five countries with the largest additive prevalence of all four indicators. However, specific MPT indications may give rise to different ideal focus countries (Table 1). For example, while HIV prevalence alone is greatest in Swaziland, Lesotho and Botswana, an MPT intravaginal ring (IVR) that combines an antiretroviral medication (e.g., dapivirine), with a contraceptive hormone (such as levonorgestrel), could provide significant impact in Zambia, Uganda and Tanzania where UNMC is also high.

4. Discussion

Mapping the burden of viral STIs including HIV and UNMC is an important step in identifying where MPTs could offer the greatest impact. This analysis provides the first examination of regional variation in the overlap of indications for MPTs globally, documents that the potential impact of MPTs is likely greatest in Sub-Saharan Africa and identifies individual countries where targeted efforts may be most useful for specific MPT indications.

While a useful step, this analysis occurs within a context of scarce and imperfect data and with no singular ideal approach to examining overlapping burdens. Limitations of PCA include the need to assume normally distributed data; UNMC met this criterion, but HIV, HSV-2 and HPV prevalence data skewed toward zero. We conducted a sensitivity analysis for the PCA, using both the full dataset and an outlier-adjusted set of data, where outliers falling more than three standard deviations from the mean value for each variable were removed; overall, the general pattern remains the same across both models[6]. The two ranking approaches examined generally point to similar focus

[6] Appendix C presents a graphical comparison of the country results for Component 1 when including the outliers, Albania, Botswana, Lesotho, Namibia, South Africa, Swaziland, Tanzania and Zimbabwe versus excluding the outliers to account for the assumption of normal distributions. The overall pattern of need remains similar. The KMO measure of sampling adequacy (0.4770) for the full dataset is less robust compared with the KMO for the outlier-excluded dataset (0.6343).

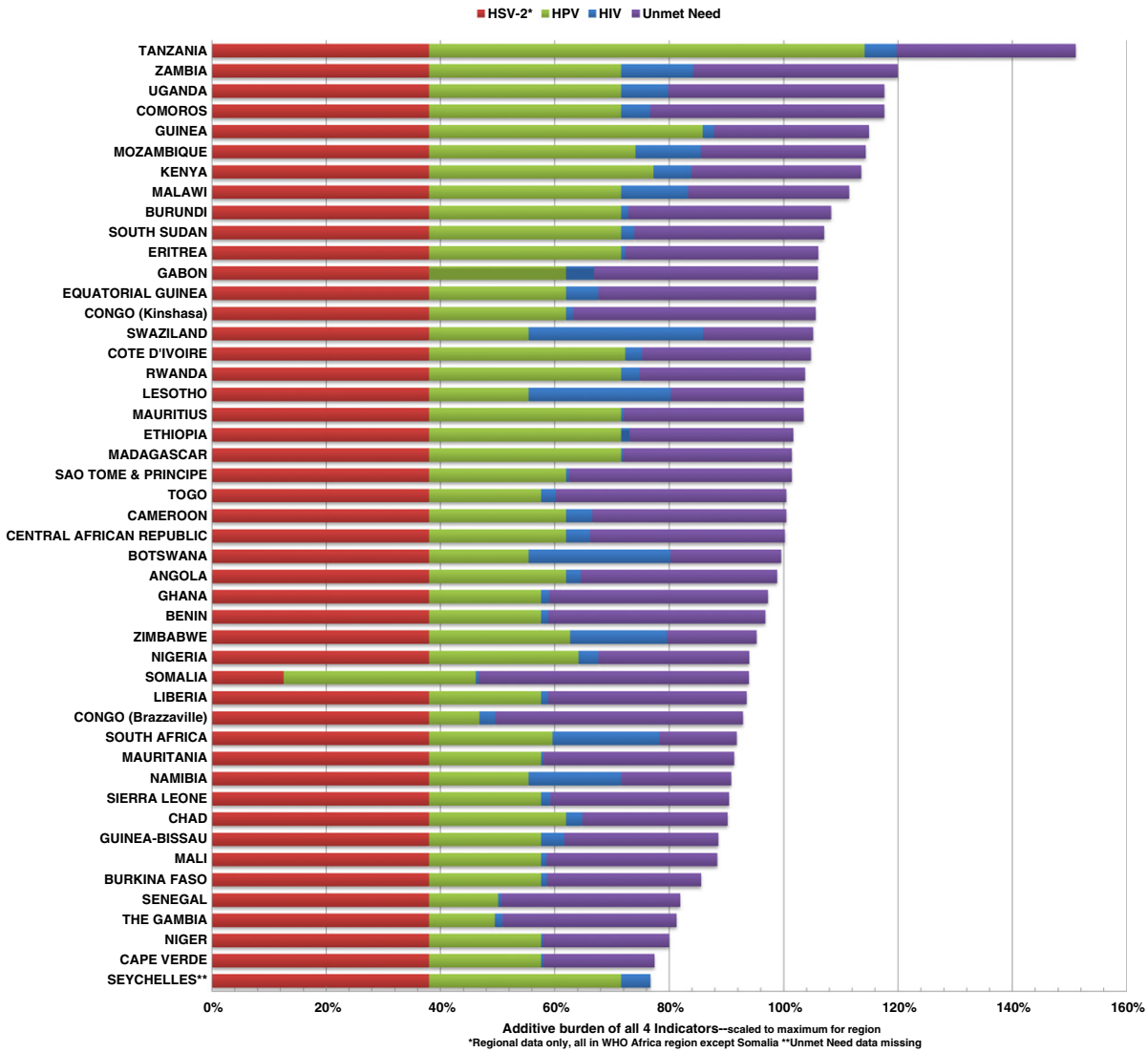

Fig. 7. Additive indicator prevalence by country, Sub-Saharan Africa.

regions, but the additive prevalence approach highlights more countries in Eastern Europe and Central Asia, driven primarily by UNMC. Since HSV-2 and HPV estimates are largely regional, reduced variation between countries could impact additive prevalence ranking results, especially since the majority of countries in Africa share the same regional HSV-2 estimate for the entirety of WHO Africa region. The break points for data categorization impact our examination of countries simultaneously in the highest categories. For example, HIV prevalence included only 15 countries in the top two categories, whereas HSV-2 prevalence included 83 countries in the top two categories.

The clear need for higher-quality, country-level data, particularly on HSV-2 and HPV, persists. Some estimates were based on few or older surveys, some pooled estimates were derived from heterogeneous studies, and except for general inclusion criteria (e.g., use of a type-specific assay for HSV-2 and adjustment of the HSV-2 prevalence data for test sensitivity and specificity), studies were not assessed for quality [5,13,22]. For instance, a single study provided the high estimate for Tanzania's HPV prevalence and Southern African countries have high HPV prevalence but fewer studies contribute to the 15- to 49-year-old analysis than for other age groups. A minority of studies used representative surveys [5,13,22]. We cannot present confidence intervals, given limitations in data availability.

Furthermore, because prevalence may vary substantially by subpopulation, the field needs routinely available, relevant, disaggregated data to help identify the subpopulations within countries at greatest need for MPTs. Averages may mask underlying subgroup variation [9]. Age may be particularly important, since prevalence of these four indicators

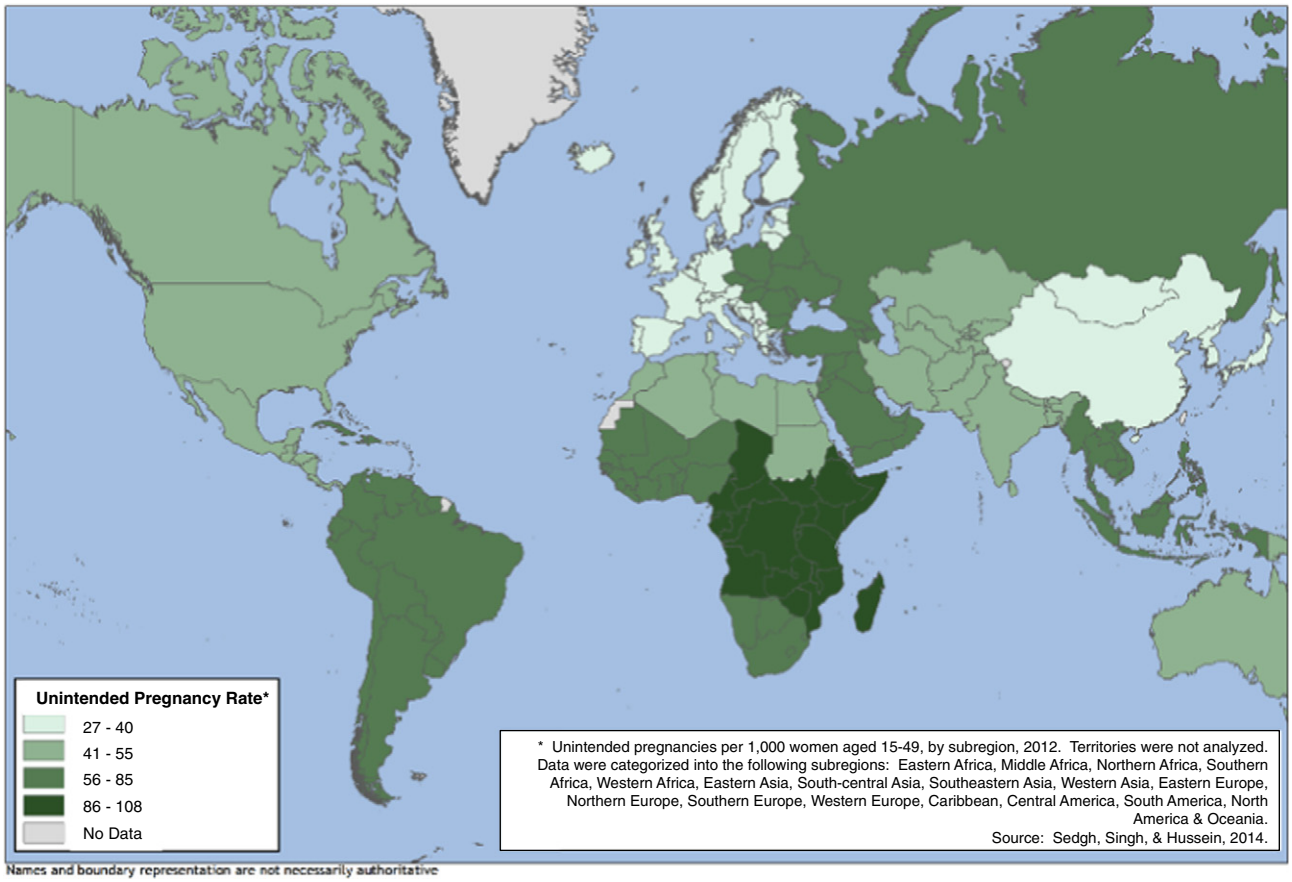

Fig. 8. Unintended pregnancy rate per 1000 women aged 15–49 years by subregion.

(particularly HPV, which is transient) varies by age, and age composition varies between countries. Other sources of uncertainty include the variability of HPV detection methods and variation in HPV types among different populations [23].

We used expert input and data availability to guide indicator selection, and we considered alternate indicators. For example, UNMC includes a large denominator of women (e.g., not restricted to currently pregnant women) and country-level estimates are available, but we also considered subregional data for unintended pregnancy rates [24]. Comparing Fig. 4 (UNMC) and Fig. 8 suggests a similar regional trend across Middle Africa, but it highlights some differences: for example, compared with UNMC, unintended pregnancy rates are generally higher in Southern Africa, South America and North America and are lower in Eastern Europe and Central Asia. As another alternative, contraceptive prevalence rate could identify locations where specific contraceptive methods incorporated into MPTs may already be acceptable to women but may highlight areas where contraceptive use is already high and the need for additional pregnancy prevention tools is less urgent. While we have highlighted countries with a high burden of UNMC or unintended pregnancy rates, countries with a lower burden may have strong family planning platforms for programs and policies to build upon and incorporate the HIV and STI prevention aspects of MPTs, especially as HIV prevention becomes more widely available.

Including bacterial STIs in future work would help highlight their potential importance for MPT development, especially as antibiotic resistance grows [25]. Bacterial STIs including gonorrhea and chlamydia are highly prevalent and have long-term negative health effects, such as infertility [26]. Some bacterial STIs, such as syphilis, have established surveillance systems and recent data available [27].

While this paper aims to compare worldwide, country-level overlap of three viral STIs and UNMC, it is important to note that MPTs may be greatly beneficial and further enhance the contraceptive mix and STI prevention toolkit even in countries not highlighted in this analysis. For example, assessing UNMC would not represent potential MPT users who already use a modern contraceptive method but would prefer an MPT.

Furthermore, in many of the countries identified as having a high need for MPTs, gender inequality and sociocultural norms that limit women's ability to control their own fertility and health persist. In addition to promoting women's health, MPTs have the potential to empower women and girls and yield progress in other development goals, such as poverty and gender inequality.

In sum, understanding which countries bear the greatest combined burdens of various risks can help to inform strategic planning for MPT introduction, market segmentation and demand generation. Our analysis highlights regions with the greatest epidemiological need according to designated parameters of selected indicators, while qualitative data can guide development of MPTs that women will actually use [28]. Both kinds of information will be necessary for MPTs to reach their greatest potential to improve women's lives and global public health.

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