Simultaneous risks, simultaneous protection:
A critical path to "multipurpose" prevention products for women

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Background

Unprotected sex puts women worldwide at simultaneous risk of HIV, other STIs, and unintended pregnancy, all of which can impose heavy burdens on morbidity and mortality. "Multipurpose Prevention Technologies" (MPTs) integrating contraception and prevention of HIV/other STIs would address these combined risks and, with potentially improved uptake, enhance public health impact.

Risks Worldwide. . .

- 86 million unintended pregnancies worldwide annually
- 222 million women in low-resource settings with unmet need for contraception
- 358,000 deaths due to complications from pregnancy & childbirth
- 4 million newborn deaths
- 2.7 million new HIV infections, more in SSA, young women
- 1.8 million AIDS deaths
- 275,000 deaths from cervical cancer
- 20 million new genital herpes infections
- 340 million "curable" STI infections (trichomonas, chlamydia, gonorrhea, syphilis)

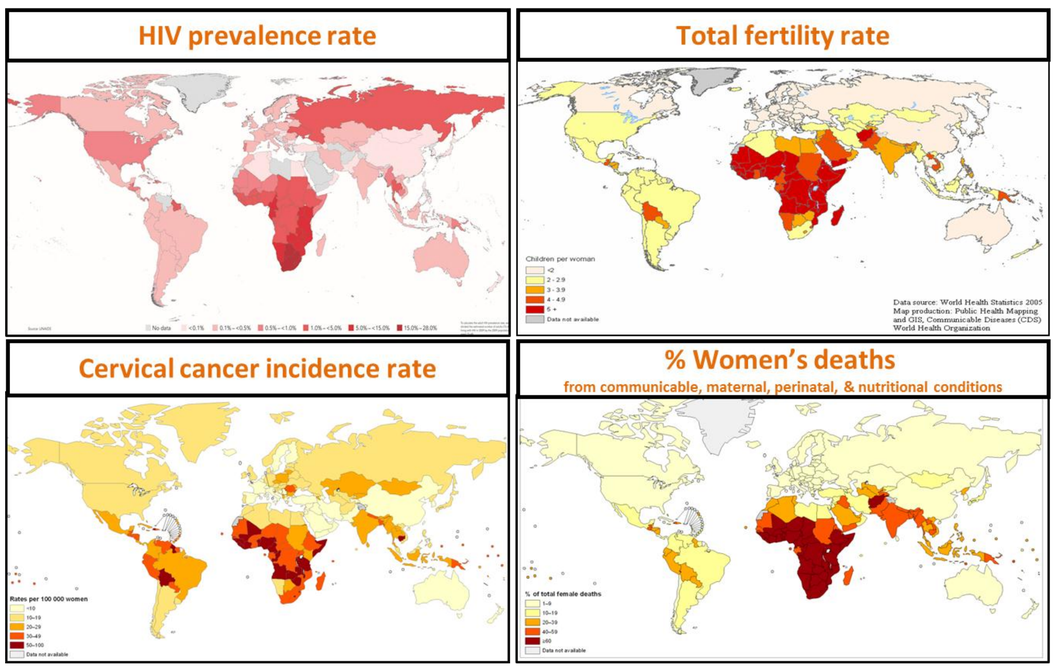


Figure 1. Priority regions for family planning and HIV/STI prevention options for women and girls. Sub-Saharan Africa and South Asia are the two regions hit hardest by high rates of fertility, HIV and HPV, all of which contribute to an unacceptably high percentage of women's deaths in these regions.

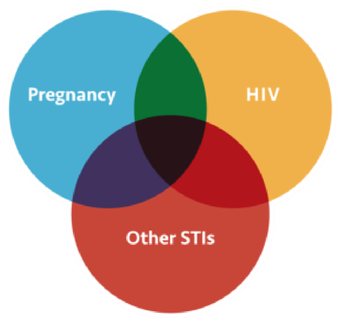
Protection?

- Prevention methods for any major risk are limited, non-existent, or partner-dependent
- Many constraints on access to/use of available methods
- Most available methods address single indications . . .
- Each with different regimens, provider types and preferences, and agendas

Solution?

Multipurpose Prevention Technologies (MPTs)

Single products integrating contraception & prevention of HIV & other sexually transmitted infections



Methods and Research Strategy

Hypothesis: Different global regions have different epidemiological dynamics, reproductive health needs and public health priorities, so priorities for MPT research and development will also differ.

Objectives

- Identify MPT products with highest potential for public health impact
- Provide guidance for donors, product developers & regulators re strategies for MPT R&D & investment needs

Materials and Methods

- Established Target Product Profile (TPP) Working Groups
- Constructed TPPs defining ideal & minimally acceptable product attributes; critical technical parameters; considerations of costs, time, regulatory complexity, manufacturing & distribution
- Strategic sequence of quantitative surveys & qualitative interviews among sexual & reproductive health researchers & providers in Africa, Asia, Europe, USA
- Expert review, consolidation of consensus views, capture of outlier positions
- Established Scientific Agenda Working Group (SAWG) to compile & describe integrated "pipeline" of candidates with contraceptive, anti-HIV, & anti-STI activity, & relevant "platform" components
- Review of existing guidance on combination products, ongoing interaction with regulatory authorities, to clarify clinical path

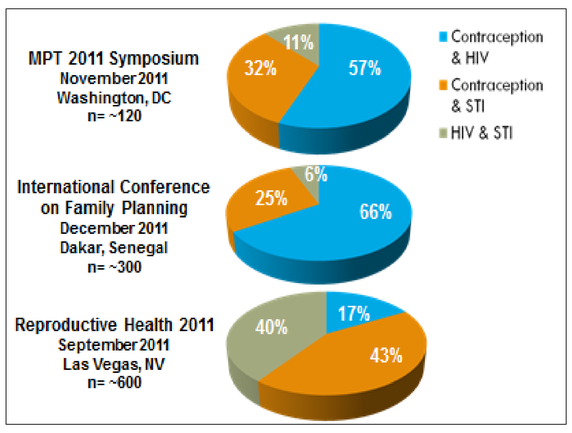


Figure 2. Priority Indications: According to *ad hoc* ePolls conducted among reproductive health experts at key convenings in 2011.

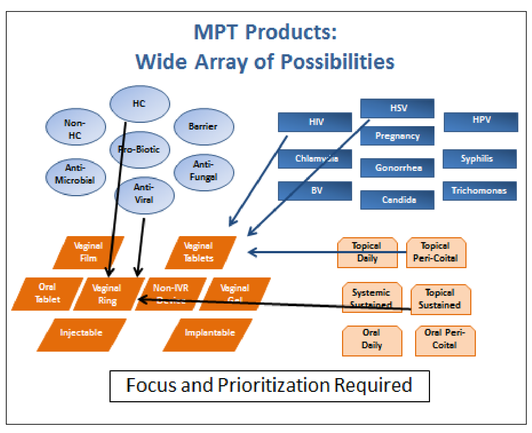


Figure 3. Multiple possible components for a Drug-Drug or Drug-Device for a multipurpose reproductive health technology.

Results: Key Findings & Actions

Priority Indications

1. HIV & pregnancy
2. HIV & STI (HSV, HPV, BV)
3. STI & pregnancy
4. Other STIs, with contraception not a priority

Dosage Forms

- Sustained release
- Topical preferred over oral
- Pericoital preferred over daily
- Major determining factor: adherence
- Highest development priority: vaginal rings

Efficacy Targets

- HIV: 40-80%; STI: at least 40%
- Contraception: current levels

Side Effects

- No worse than single-indication products

Regulatory Points

- MPTs by definition are "multi-indication combination products"
- Regulatory approach will vary for each MPT:
  - MPTs comprising only investigational components pose unique regulatory challenges
  - MPTs including approved components may rely on available information for those components.
- Depending on components, FDA guidance for combination drug products may apply
- Early consultation with regulatory authorities preferable since MPTs entail unique, product-specific regulatory considerations
- MPT review should involve experts from different fields, collaboration among international RAs, national health authorities

Figure 4. Emerging ***Multipurpose Prevention Technologies (MPTs)*** include drug combinations, drug & device combinations, bacterial therapeutics, multivalent vaccines and nanoparticles.

Key Attributes & Parameters

- 40° C storage, 36-month shelf life
- Concealable presentation
- No lifestyle effects
- Ease of provision in low-resource settings

Variability in Priorities/Needs

- Sub-Saharan Africa: HIV & pregnancy; STI emphasis on HSV2, BV, TV, HPV
- India: pregnancy & HIV
- China: STI/HIV
- USA (health-care providers): pregnancy/ non-HIV STIs (65%), pregnancy/HIV (25%)

MPT Vaccines

- Request for Concepts for RH Combination Vaccines elicited 11 submissions & wide array of biological & technological options

Pipeline

- Wide array of MPT product possibilities in preclinical stages:
  - 90-day TNF/LNG IVR (pregnancy, HIV, & HSV)
  - MIV-150, Zn-acetate carrageenan gel (HIV, HSV, HPV?)
  - MZL pericoital gel & 30-day MZL vaginal ring (HIV, STI, pregnancy)
  - 60-day dapivirine+HC vaginal ring (HIV, pregnancy)
  - SILCS diaphragm & 1.0% tenofovir gel (barrier contraception via SILCS, HIV/HSV prevention via gel)
- New technology: TMC-278 (rilpivirine) long-acting injectable

Conclusions

Promising innovations include multipurpose vaccines and gels, easier to use vaginal rings and single-sized diaphragms that may provide simultaneous protection against unintended pregnancy and infection, and have a major impact on the health of women and their families worldwide.

Progress

- Linked, interdisciplinary approach has built framework for:
  - Identifying priorities needs & preferences
  - Analyzing MPT pipeline
  - Identifying gaps
  - Mapping a plausible "critical path"
  - Guiding investment
- General development priorities & fundamental design targets for MPT products exist
- MPT product development consistent with priorities & TPPs under way

Challenges

- Regional differences
- Unique, product-specific regulatory considerations
- Pipeline sufficiency? Gaps?
- Hormonal contraception & HIV relationships relevance ?
- Trial designs (to test efficacy without placebo control)
- Resources (money, trial capacity, participants, development partnerships)

Bottom Line… the path to an "ideal" MPT is not linear

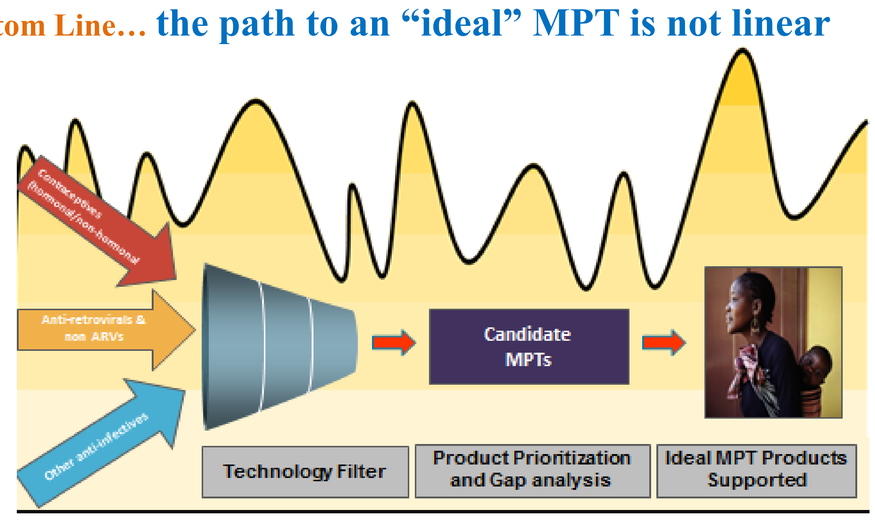


Figure 5. Typical of product development in general, the path to an 'IDEAL' MPT will not be a linear one.

References

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Presented at AIDS 2012 – Washington, D.C., USA