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Review

Designing a multipurpose technology for acceptability and adherence

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ABSTRACT

Multipurpose Prevention Technologies (MPTs) are new tools aimed at reducing or preventing multiple and overlapping sexual and reproductive health risks faced by women and couples around the globe. While MPTs could prove more acceptable and easier to adhere to than single-purpose prevention products, continuing high rates of HIV and unintended pregnancy remind us that these new products will need to be efficacious, acceptable and effectively used to achieve a public health impact. In this paper, we describe how a range of research methods can be applied during the pre-clinical phase of product development to inform decisions related to formulation and vehicle or product delivery mechanisms, and consider how choices in product-related characteristics may influence future demand for, delivery and use of future products. We draw on examples from the development of new single-purpose HIV and contraceptive products and then extend our discussion to the development of MPTs, including vaginal rings and injections. This article is based on a presentation at the "Product Development Workshop 2013: HIV and Multipurpose Prevention Technologies," held in Arlington, Virginia on February 21–22, 2013. It forms part of a special supplement to *Antiviral Research*.

Contents

1. Introduction

Globally, women and couples face multiple and overlapping sexual and reproductive health risks (SRH). For example, an estimated 500 million cases of treatable sexually transmitted infections (STIs) occur annually, disproportionately affecting sub-Saharan African and South Asian men and women. When untreated, STIs are a leading cause of infertility and may triple the risk of HIV acquisition (World Health Organization Media Centre, 2013). Despite downward trends in new HIV infections, 34 million people are currently living with HIV, the vast majority in sub-Saharan Africa where almost 60% of prevalent HIV infections are in women (Joint United Nations Programme on HIV/AIDS (UNAIDS), 2011). Young women aged 15–24 account for about one-quarter of all new infections, but almost one-third of new infections in sub-Saharan Africa (Joint United Nations Programme on HIV/AIDS (UNAIDS), 2012). More than two million adolescent women in this region experience unintended pregnancies each year (Guttmacher Institute and IPPF, 2010).

Multipurpose Prevention Technologies (MPTs) are new prevention tools aimed at two or more SRH risks, including treatable STIs,

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HIV and unintended pregnancy (Holt, 2010). At present, male and female condoms are the most common and widespread MPT. A number of other MPT approaches are currently being considered, including injectables that might be co-formulated or co-administered, vaginal and/or rectally-inserted gels, oral pills or devices including vaginal rings. One MPT currently in development is a one-month vaginal ring able to release a contraceptive progestin and an antiviral agent to reduce the risk of HIV (Holt, 2010).

MPTs, by virtue of having dual indications, could prove more acceptable and easier to adhere to than single purpose prevention products. However, the continuing high rates of HIV and unplanned pregnancy, despite widespread availability of effective and low cost prevention methods, reminds us that the relationship between development of effective technologies and public health impact is not often linear. Consequently, social and behavioral scientists have an important role to play in identifying the range of factors likely to influence individuals' willingness and ability to initiate and effectively use MPT products, thus informing the choice of product candidates for development and/or testing that best fit the needs and preferences of populations who might benefit from them (Tolley and Severy, 2006; Morrow and Ruiz, 2008).

1.1. Acceptability and adherence (A^2) conceptualized

Acceptability has been conceptualized largely as a favorable "attitude" towards a product, predisposing a person to be willing to use it (see Table 1 for glossary of terms). Acceptability is influenced by a number of underlying factors – a person's perceived risk; expectations related to product effectiveness, as well as to social-behavioral challenges of using the product, including perceived ease of use, concerns about side effects, and/or impact on daily life (Tolley and Severy, 2006; Severy et al., 2005). In the context of choice, acceptability may be measured as the selection of one product or behavior over another or the continued use of the product over time. However, in the absence of an approved product, acceptability has been assessed hypothetically or as it relates to proxy products (Severy et al., 2005).

In contrast, adherence is a behavioral construct related to the extent to which a product is used as intended. Dimensions of adherence include timing of product use, dosage taken, consistency and duration of use. Adherence requirements can vary greatly by product. For example, daily use of an oral pill or vaginal gel requires the user to routinize product use and to remember to carry products when traveling or when daily routines are disrupted. Furthermore, product use would be needed even during periods when protection might not be. Unlike daily gel use, pericoital gel use would be on an "as-needed" basis, but would involve anticipating when a sexual encounter might happen or incorporating gel insertion into the sex act. Although vaginal rings may be inserted and removed by the user, adherence to vaginal ring use requires one to "do nothing" – or just leave the ring in for the intended duration. Additionally, monthly or bi-monthly vaginal rings or injections would require the user to return to a clinic within the correct timeframe for resupply.

Acceptability does not always lead to high adherence and adherence may be achieved in the absence of acceptability. Although, when users are free to choose among a range of viable options, acceptability is assumed to be a key factor driving adherence (Severy et al., 2005).

The possibility of conflating these two constructs is particularly high within the context of clinical trial research, in which participants are requested to adhere to a product of unknown efficacy, may enroll in trials for reasons unrelated to product use, or may achieve high adherence within trials without the intention for future product use, should it be found efficacious. As Morrow and Hendrix point out, the absence of an approved product with which to study "acceptability" as a phenomenon in its own right' has led the HIV prevention field to focus more on 'adherence', using it as a surrogate for 'acceptability' (Morrow and Hendrix, 2010). Indeed, much attention in recent HIV prevention research has focused on how to measure microbicide and PrEP adherence within clinical trial testing (Woodsong et al., 2013). However, it is increasingly clear that the context of product use within a clinical trial and adherence to products once approved and introduced through a country's health system may differ in important ways (Morrow and Hendrix, 2010; Woodsong et al., 2013; Tolley et al., 2013).

1.2. Continuum of A^2 factors

Ultimately, efficacious, new products will not have an impact if they are not initiated and effectively used by those at risk. As shown in Fig. 1, these factors fit along a continuum, from product-related attributes to the profiles of potential/intended users as well as the service delivery and wider sociocultural contexts within which the product will be used. Therefore, research is required during early product development and clinical testing to identify and intervene upon the factors that will influence the product's eventual acceptability and use adherence.

In this paper, we describe how a range of research methods can be applied during pre-clinical phases of product development to inform decisions related to formulation and vehicle or product delivery mechanisms, and consider how choices in product-related characteristics may influence future demand for, delivery and use of future products. We draw on examples from the development of new single-purpose HIV and contraceptive products and then extend our discussion to the development of MPTs, including vaginal rings and injections.

2. Methods for assessing "acceptability"

Research into product acceptability (or those factors underlying it) may employ multiple approaches – from qualitative, in-depth exploration of hypothetical or proxy product decision-making and use experiences to more structured assessments of individual preferences for sets of product attributes through conjoint analysis or discrete choice experiments. The examples presented in this paper make use of different social-behavioral science research approaches, including psychometric scales, qualitative research and structured elicitation of preferences, to integrate user perspectives into the product development process (see Table 1 glossary).

2.1. Users' sensory perceptions of physicochemical properties

Morrow and colleagues borrow from sensory evaluation science, a field with strong ties to the food and cosmetics industries, to better understand and measure users' sensory perceptions and experiences of products in order to inform product design and formulation. Her approach is based on the premise that a product's physicochemical properties and rheological performance characteristics, which affect how well a product formulation dissolves, spreads, or is absorbed and available within the tissues, are the same ones that impact the user's sensations, perceptions and experiences. Furthermore, users' sensory perceptions and experiences of these properties can be objectively evaluated, provided that the assessment tools and language are carefully crafted. By understanding how potential users' sensations and experiences relate to a diverse set of formulations, perceptibility data can be linked with data on the physicochemical properties of various formulations in order to optimize product development decisions (Morrow and Hendrix, 2010).