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DEBATE

Give PrEP a chance: moving on from the “risk compensation” concept

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Abstract

Introduction: While bio-behavioural interventions (BIs) for sexually transmitted infections (STIs) and HIV prevention have shown their effectiveness (e.g. treatment for syphilis, HPV vaccination or pre-exposure prophylaxis [PrEP]), they have also aroused major concerns regarding behavioural changes that could counteract their benefit. Risk compensation (RC) fears concerning BIs in the HIV/STIs prevention field are intimately linked to representations, judgements and social control on sexual behaviour. With an increasing number of PrEP studies describing a rise in STIs due to RC, this paper argues for a shift away from the focus on RC and proposes a more constructive approach to respond to the needs of people living with HIV and populations most at risk.

Discussion: The concept of RC, stemming from road safety and derived from economic theory, relies on rational theoretical models of human behaviour. Although widely applied in several contexts its use has been reasonably questioned. Major methodological issues regarding RC have been raised within HIV/AIDS literature. Although behavioural changes (e.g. condomless sex and number of sexual partners) are often erroneously assimilated with RC, there is no evidence that behavioural changes have undermined the effectiveness of previous and current BIs. Still, PrEP has not escaped RC concerns. Increases in condomless sex within the context of growing uptake of PrEP signals a continued need for integrated and innovative HIV and STI prevention strategies and a comprehensive sexual health approach. Routine HIV/STI testing, peer-led counselling, and identification of sexual health needs within the PrEP model of care could become a gold standard in the sexual health field for all populations.

Conclusions: RC remains a frequent argument against the availability and provision of prevention methods for vulnerable populations. Individuals should be able to benefit from the full panel of BIs options available, to find and adapt methods according to their needs. Current, past and future PrEP users, with other stakeholders, may provide valuable insight into innovative solutions and programmes to control HIV and other STIs.

Keywords: bio-behavioural prevention; PrEP; risk compensation; sexual behaviour; sexually transmitted infections; HIV

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1 | INTRODUCTION

In 2015, in spite of strong evidence of the efficacy of pre-exposure prophylaxis (PrEP) to prevent HIV infection [1-4] and WHO recommendations [5], a rebuttal to the Lancet HIV editorial “PrEP: why are we waiting?” stated that decision-makers lacked information regarding the “normative aspects” of PrEP use [6]. More precisely, they explained that the main reason for not implementing this bio-behavioural intervention (BI) was lack of information regarding “people’s own responsibility to use a condom, the relevance of being free of fear of HIV infection when having sex, and the relative importance of preventing HIV versus a possible rise in other sexually transmitted diseases because of reduced condom use” [6]. This quote makes explicit important points that have overshadowed PrEP and other BI: moral judgements on sex and HIV prevention as a means of controlling sex [7-9].

What the PrEP example shows is nothing new. In the last decades, other prevention tools were all met with caution as they could possibly induce behavioural changes leading to an increased risk and consequently counteract the benefit of the prevention tool in question: the oral contraceptive pill in the 1950s [10,11], treatment for syphilis in the 1960s [12] and 1970s [13,14], needle exchange programmes for injecting drug users [15-17], the morning-after pill [18], and more recently HPV vaccination [19-21]. Although different BI for HIV prevention have shown their effectiveness (e.g. condoms, male circumcision, highly-active antiretroviral treatment (HAART), post-exposure prophylaxis (PEP), treatment as prevention (TasP) and pre-exposure prophylaxis (PrEP)), each and every one has aroused concerns regarding “risk compensation” (RC) [22-25]. The HIV/AIDS field has scarcely challenged the use of the RC concept [26] at the expense of focusing on other positive aspects of BI such as increased quality of

(sexual) life, empowerment to discuss safer sex and to disclose HIV status, reduced fear of transmitting or getting HIV, or the possibility to re-engage in sexual activity after an HIV diagnosis, to name a few [27-29].

At the start of the epidemic, sexually transmitted infections (STIs) were already present and a health concern [30]. Most likely due to its fatal nature and lack of treatment, demanding specific medical interventions and innovations, HIV/AIDS was treated separately from other STIs. Evidence that STIs facilitate HIV transmission led to recognition of an "epidemiological synergy" between HIV and other STIs, thus leading to calls for prevention programmes and strategies that addressed both HIV and other STIs [31,32]. Whereas some prevention methods such as condoms provide protection against HIV and other STIs, other "no barrier" HIV prevention strategies such as TasP and PrEP have changed the scene.

In the context of an increasing number of PrEP studies describing a rise in STIs due to "RC," this paper provides a critical view of the origin, use and consequences of this concept in the HIV prevention field and argues for a shift away from the focus on RC. In a time when more effort is needed to reduce the number of new infections among key populations (KP) and their sexual partners [33], and STIs are a health concern, we propose a more constructive approach that responds to the needs of people living with HIV (PLHIV) and most-at-risk populations.

2 | DISCUSSION

2.1 | Is RC a pertinent and valid framework?

Although RC has been used interchangeably with "disinhibition" in scientific literature, these are in fact two different concepts [14]. *Disinhibition* refers to the lowering or absence of self-restraint to avoid risk [14,34]; for example when an inebriated person is aggressive or engages in sexual risk behaviour (SRB) because he/she no longer cares about the risk [35]. *Risk compensation* is related to the "risk equilibrium" which is defined as "a system in which individuals accept a certain level of subjectively estimated (or perceived) risk to their health in exchange for benefits they expect to receive from (an) activity" [36].

Since most of the literature regarding BI refers to RC, it is worth focusing on the origins of this widely used concept. The National Highway Traffic Safety Administration (USA), with the goal of preventing road injuries, issued in 1968 29 Federal Motor Vehicle Safety Standards (FMVSS) regarding features such as seat belts. In 1975, economist Sam Peltzman, evaluated FMVSS with the perspective that since safety is an exchangeable "good," individuals would exchange safety for "driving intensity" if the car is safer than expected [37]. His results, since proven to be erroneous [38], led to the conclusion that security standards had no effect on overall traffic fatalities and increased pedestrian deaths. Decades of debates on these results, but also on others such as those showing seat belt laws were not effective [39-41], introduced RC as a plausible framework to understand road safety despite experiments unable to provide useful evidence and evaluation contaminated by poor data and uncontrolled factors [42].

There exist well-established psychosocial theories and models to approach the behavioural change in relation to health,

such as, amongst others, the theory of reasoned action/planned behaviour [43-46], the transtheoretical model of behaviour change [47] or the information-motivation-skills model [48-50]. However, the road safety field has focused on so-called "risk models," such as the "Threat-avoidance model" [51], the "Model of drivers' decision making and behaviour" [52] or the "Risk Homeostasis Model" [53], in which the risk concept plays a major role. The concept of risk homeostasis or RC described in 1982 claims that human behaviour falls under the same mechanism as a thermostat [54]. Thus, interventions to prevent car accidents, or the use of helmets by bicycle riders [55], would not be useful since individuals would change their behaviour so that their level of risk stays constant [56,57]. The RC concept relies on rational theoretical models of human behaviour, derived from economic theory, that have been widely criticised [58-60], nevertheless it has attracted great attention [61]. Otherwise, literature has shown that seat belts and helmets do not lead to behavioural changes leading to a risk increase and are, undoubtedly, effective [60,62,63].

Methodological issues regarding RC have been also raised within HIV/AIDS literature [64]. To accurately claim that a BI leads to an increased risk for HIV, a randomized control trial would have to compare a group believing that the intervention would reduce risk with another group believing that the intervention would not reduce risk [22]. Because of ethical issues, this design is not a viable option [64]. Other methodological considerations have been drawn [23]: (1) studies are mostly focused on behavioural measures, failing to account for the possibility that changes in attitudes or risk perceptions (essential to the RC theory) may occur before behaviour change; (2) timing in the change of attitudes and behaviour is important but not always clear; condomless sex (CLS) can precede "optimistic attitudes" regarding HIV exposure; (3) some studies did not find that change in behaviour led to risk increase [2,65-69]; (4) even if changes in behaviour or risk perception are observed they will likely not undermine the high effectiveness of the prevention strategy [23]; (5) interventions are not considered from a community level, therefore are limited to an individual approach [23].

2.2 | Evidence of changes in sexual behaviour or evidence of "risk compensation"?

Despite the emergence of various forms of BI, strategies such as male circumcision [25] and condom promotion were suspected of engendering RC [70]. However, these strategies did not induce enough behavioural changes to have an impact on their effectiveness [71,72]. The advent of HAART in 1996 led to obvious beneficial clinical effects. HIV was no longer perceived as a life-threatening disease [73-75], generating fears of unintended effects on sexual behaviour [76,77] and on the incidence of STIs [78]. Increasing public information on how an undetectable viral load reduces the level of infectiousness of HIV-positive individuals [65], which was then confirmed in the "Swiss Statement" [79], also followed the same path. Whereas evidence of RC should be shown in the decreased effectiveness of a given BI to prevent HIV transmission, most of the literature aiming to find and evaluate evidence of RC, primarily concern behavioural changes. A meta-analysis [80] was undertaken aiming to determine if ART use was associated with changes in "unprotected" sex and STI diagnoses.

Among 56 studies, condomless sex was found to be lower in participants receiving ART compared to those who were not (OR: 0.73 (95% CI: 0.64 to 0.83); $p < 0.001$). Among 11 studies, STI diagnoses were found to be lower among participants receiving ART compared to those who were not (OR: 0.58 (95% CI: 0.33 to 1.01); $p = 0.053$).

As a BI, PrEP has shown to be a viable method for those that do not systematically use condoms, ineffectively use other risk reduction strategies (RRS), or wish to have an extra layer of protection [81,82]. The demonstrated efficacy and effectiveness of PrEP among other KP, which led to expanding WHO PrEP recommendations, has been followed by numerous studies aiming to evaluate "RC" among PrEP users, some of which have been analysed in systematic reviews and meta-analyses. STIs have been a major focus of these studies. While STIs are an obvious health concern and prevention strategies must be fully implemented in order to reduce their incidence, opportunities can be missed for those most at risk for HIV and other STIs if reflection on STI is restricted to the BI framework. First, because BI do not aim to reduce STI but HIV incidence. Second, because even if a same behaviour, CLS, leads to HIV and other STIs, the underlying psycho-social mechanisms to prevent the former and the latter are different [27]. STIs do not represent for individuals the same health concern as HIV, and the information, motivation and skills required to mobilise to prevent STIs are therefore different.

In a systematic review and meta-analysis of the effectiveness of oral PrEP among at-risk populations, sexual behaviour (defined as condom use and number of sexual partners, and used to identify the presence of RC) was studied as an outcome in addition to HIV infection, adverse events, and antiretroviral drug resistance [83]. This analysis found that PrEP effectively protected against HIV infection across all populations. Although the authors found no evidence of RC with PrEP, and no evidence of RC in open-label extension (OLE) studies which are more likely to show "real-world use," they caution that study participants benefited from behaviour counselling and were previously trial participants [83].

A systematic analysis of OLE and demonstration studies investigated the effect of PrEP use on SRB [84]. While the authors rightly excluded studies that measured beliefs about PrEP use and/or predicted future behaviour, increase in "risky sexual behaviours" and "risk compensation" are used synonymously. "RC" was measured by using several outcomes, however, due to inconsistency across the studies in the measures of CLS and number of condomless partners, meta-analysis was limited to STI diagnosis. Although there is evidence to suggest that an increase in number of CLS partners and general decline in condom use, this may be restricted to the proportion of MSM who already reported these behaviours [84].

The impact of PrEP use on SRB and RRS has also been examined in qualitative studies. Among 41 participants of the PROUD PrEP study [81], only half of them declared an increase in "risk taking behaviour." The participants reported using various RRS before using PrEP (e.g. strategic positioning, sero-sorting, PEP use), however, all reported (some) CLS. Overall, given inconsistent condom use and situations and contexts that may lead to increased risk taking, participants declared that PrEP filled a prevention gap or added another layer of protection for participants already at high risk [81].

A qualitative sub-study conducted with iPrEx OLE participants [27] found that, in opposition to feelings of worry and concern regarding HIV infection that pervaded respondents' lives, PrEP enabled to replace them with feelings of safety. For participants not using condoms prior to PrEP, thinking of a "PrEP-as-condom-replacement theory" had no sense. For those using condoms and willing to use PrEP to engage in CLS, did not actually engage in CLS. More interestingly, respondents reporting sexual behavioural changes (going "crazy") declared that the possible emergence of a STI was a reminder of PrEP's limits [27]. Changes were therefore more emotional than behavioural.

Recently, Holt and Murphy [23] have introduced the concept of community-level RC in the context of PrEP in which "changes in risk perceptions and behaviour (could occur) as a result of increased optimism about avoiding HIV among people not directly protected by PrEP." However, due to increased PrEP uptake and consistent PrEP use among PrEP users, protection at the community-level actually increased (reduction of HIV incidence). They propose monitoring changes in sexual behaviour in addition to attitudes to PrEP and perceived HIV risk. This could measure HIV "prevention optimism" defined as "the belief that it is easier to avoid HIV infection or transmission because of PrEP and that it is more acceptable and safer to engage in condomless sex because the risk of HIV is perceived to be reduced" [23]. Further research is needed to explore the impact of "optimism," particularly among non-PrEP users.

2.3 | PrEP: a concern or an opportunity for STI control?

PrEP is a significant step forward in the fight against HIV, not only for its impact on HIV transmission, but also its opportunity to increase the frequency of HIV and other STIs testing, to promote early diagnosis and treatment of HIV and other STIs. According to one modelling study, high PrEP coverage among MSM could lead to an important decline in STI incidence, largely attributed to routine testing which allows early detection and treatment of asymptomatic STIs [85]. PrEP also has the potential to alleviate fears of HIV, to allow for a more fulfilling sex life [26,27], and to empower individuals to protect themselves and others [86]. Adapted and quality counselling around PrEP, sometimes community-based, may be a favourable environment to have a discussion on sexual behaviour, drug use and other sexual health needs [28,87,88].

Several studies, however, have shown barriers on the part of medical providers to have such discussions [87,89], and on the part of patients [90,91] to share information regarding their sexual behaviour. Behavioural changes associated with BI need to be studied, however, there is still a major health issue: reaching, informing, testing, treating and empowering individuals, in order to integrate them into a preventive health path, not only for HIV but also for other STI.

Peer-led counselling, offered in the ANRS-Ipergay [4] and currently offered in the ANRS-Prevenir study [92] by the French community-based organisation AIDES, moves away from a "curative health system" perspective in which health consultations are driven by symptoms, towards a health path for HIV-negative individuals that addresses overall sexual health based on the individual needs at a given point in life

[88]. From the perspective of PrEP users, peer counsellors use both their personal and community experience to inform and discuss the spectrum of prevention methods and how they may fit with individual needs. Building individual capacity to evaluate personal risk, and thus, empower PrEP users to find prevention strategies that meet their needs for a satisfying sexual life, can potentially have lasting effects, regardless of the duration of PrEP use. Although limited, longitudinal data on PrEP use has shown important decreases in retention over time [93,94]. Changes in sexual behaviours, perceived HIV risk, financial cost, adverse effects and problems related to adherence have been identified as reasons for PrEP discontinuation [93,95]. It is therefore increasingly important to address the fact that PrEP users may not be lifetime users and to put individuals on a preventive health path that is sustainable after PrEP discontinuation. Current PrEP studies should explore this issue to find potential solutions to minimize HIV and STI risk when individuals choose to no longer use PrEP.

Global rates of STI, which were rising before PrEP [30], remain a concern. While rising STI rates among PrEP users may be partially explained by increased testing in multiple anatomic sites within the context of PrEP follow-up, other bio-behavioural interventions, in addition to information, counselling and notification, must be explored. Over time, it is possible that repeat STI testing may result in a change of behaviour, particularly among those with high-risk behaviours who may come to realise the limits of PrEP (e.g. repeat STIs) [27] and therefore may implement or return to other prevention methods.

New interventions should systematically be accompanied by measures to better inform on STIs, to reinforce individual perception of STI risk and to promote behavioural changes adapted to individual needs. These behavioural changes could result in condom use for some individuals, however, there are other interesting alternatives such as partner notification or BI for STIs. Recent studies on the prophylactic use of doxycycline for bacterial STIs have shown promising results post-exposure [96] and used daily [97], but remain to be confirmed in studies with longer follow-up [98]. Use of doxycycline may be particularly pertinent among PrEP users who experience recurrent STIs; a recent analysis has shown that among MSM PrEP users, 25% participants accounted for a little more than three-quarters of all STIs [99].

Such an integrated sexual health approach has a lot to learn from the PrEP model, which could become a gold standard in handling prevention. The PrEP model needs to be developed and expanded not only for those at risk for HIV, and among them, mostly for MSM, but also for all the populations, which could also prevent STIs. Women, migrants, transgender individuals, drug users could take benefit of a comprehensive health offer (as with PrEP).

If we want this to become a reality several conditions are needed. First, work with health-care providers is needed. In order not to limit prevention options of patients, non-judgmental discussion on sexual behaviour, and drug use, has to be ensured. Improving the patient-provider relationship can be key to moving away from RC focus to a positive and integrated sexual health approach.

Second, medical practice and HIV prevention research will benefit from knowledge from other disciplines and methods.

For example, qualitative studies can provide new and complementary information to already existing data. Additionally, a more critical approach to the theories or concepts exported from other fields would allow for a more efficient response to eliminate the epidemic and respond to the health needs of KP.

Finally, effective STI control will not be possible without political will, corresponding funding and implication of all stakeholders to test interventions such as partner notification, integration of sex education programmes in schools, or legislative changes regarding antibiotic treatment among others [30].

3 | CONCLUSIONS

Effective BI for HIV and STIs have been plagued by debates of RC for centuries. The concept of RC, stemming from the field of road safety, has been the subject of theoretical controversy and its use has been reasonably questioned. And yet, RC remains a frequent argument to justify moral judgements against the availability and provision of prevention methods for vulnerable populations who already experience stigma and discrimination [100]. Unsurprisingly, PrEP and its possible large-scale implementation has also been discussed within the framework of RC potentially undermining its efficacy. Would the availability of an effective HIV vaccination prompt the same debates?

Gaps to improve and guarantee access to testing, treatment and to reach an undetectable viral load for KP are a harsh reality, which means that the end of the HIV epidemic will not happen anytime soon. Lack of access to HIV/STI treatment and prevention is deeply linked to the shame associated with them and to the stigma and discrimination that those with the disease have to face from some health providers. For these reasons, the full range of existing prevention options has to be made available. With the information and support provided by healthcare providers, and by community stakeholders, individuals must have the opportunity to choose the prevention method(s) that best respond to their health needs at a given point of their (sexual) life and thus protect themselves. From a human rights perspective, BI access should not be barred based on the presence (absence) of STIs or changes in sexual behaviour [28]. Finally, the role of community-based stakeholders cannot be overlooked in increasing knowledge regarding sexual health and the empowerment of populations deemed “at risk” to identify and adapt prevention strategies that best fit their needs.

HIV and STIs cannot be thought and addressed in a social vacuum [26,101]. Interdisciplinarity, community perspectives and long-term evidence from PrEP cohorts are needed to disentangle the effects of the combination of different BI that coexist with societal changes that have an impact on individual and community behaviours and social representations of sex, sexual orientation and experience of STIs, including HIV. Despite proven efficacy and effectiveness of PrEP, scientific literature seems to have been more concerned on how PrEP could “increase risk” instead of on how it reduces it or on how PrEP could lead to the empowerment of individuals regarding sexual health [27,28]. Science, working hand-in-hand with communities, can dramatically improve the response not only to HIV but also to other STIs by implementing and

assessing adapted interventions that are based on individual health needs.

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COMPETING INTERESTS

DRC and RMD declare no conflicts of interest. JMM is on the advisory boards for Gilead Sciences, Merck and ViiV.

AUTHORS' CONTRIBUTIONS

DRC, RMD and JMM, discussed key ideas and concepts forming the basis of this debate article. RMD and DRC wrote the manuscript. All authors reviewed and approved the final version.

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REFERENCES

1. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. **2011**;365(6):493–505.
2. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Pre-exposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. **2010**;363(27):2587–99.
3. McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet*. **2016**;387(10013):53–60.
4. Molina J-M, Capitant C, Spire B, Pialoux G, Cotte L, Charreau I, et al. On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection. *N Engl J Med*. **2015**;373(23):2237–46.
5. World Health Organization. Policy Brief: WHO expands recommendation on oral pre-exposure prophylaxis of HIV infection (PrEP) [Internet]. **2015** [cited 2019 Jan 12]. Available from: <https://www-who-int.gate2.inist.fr/hiv/pub/prep/policy-brief-prep-2015/en/>
6. Jansen MPM, Tromp N, Baltussen R. PrEP: why we are waiting. *Lancet HIV*. **2016**;3(1):e11–2.
7. Golub SA, Gamarel KE, Surace A. Demographic differences in PrEP-related stereotypes: implications for implementation. *AIDS Behav*. **2017**;21(5):1229–35.
8. Golub SA. PrEP messaging: taking "Risk" out of the pitch. Oral Presentation at HIVR4P: HIV Research for Prevention; **2018**; Madrid, Spain.
9. Golub SA, Myers JE. Next-wave HIV pre-exposure prophylaxis implementation for gay and bisexual men. *AIDS Patient Care STDS*. **2019 Jun**;33(6):253–261. doi: 10.1089/apc.2018.0290
10. Myers JE, Sepkowitz KA. A pill for HIV prevention: Déjà Vu all over again? *Clin Infect Dis*. **2013**;56(11):1604–12.
11. Watkins ES. On the pill: a social history of oral contraceptives, 1950–1970. Reprint edn. Baltimore, MD: Johns Hopkins University Press; **2001**. 208 p.
12. Farley TA, Cohen DA, Kahn RH, Lolis S, Johnson G, Martin DH. The acceptability and behavioral effects of antibiotic prophylaxis for syphilis prevention. *Sex Transm Dis*. **2003**;30(11):844.
13. Willcox RR. A world look at the venereal diseases: recrudescence of the venereal diseases. *Med Clin North Am*. **1972**;56(5):1057–71.

14. Hogben M, Liddon N. Disinhibition and risk compensation: scope, definitions, and perspective. *Sex Transm Dis*. **2008**;35(12):1009.
15. Ti L, Kerr T. The impact of harm reduction on HIV and illicit drug use. *Harm Reduct J*. **2014**;11:7.
16. Wood E, Montaner JS, Kerr T. Illicit drug addiction, infectious disease spread, and the need for an evidence-based response. *Lancet Infect Dis*. **2008**;8(3):142–3.
17. Voth EA. Harm reduction drug policy. *Lancet Infect Dis*. **2008**;8(9):528.
18. Raymond EG, Weaver MA. Effect of an emergency contraceptive pill intervention on pregnancy risk behavior. *Contraception*. **2008**;77(5):333–6.
19. MacPhail CL, Sayles JN, Cunningham W, Newman PA. Perceptions of sexual risk compensation following posttrial HIV vaccine uptake among young South Africans. *Qual Health Res*. **2012**;22(5):668–78.
20. Hansen BT. No evidence that HPV vaccination leads to sexual risk compensation. *Hum Vaccines Immunother*. **2016**;12(6):1451–3.
21. Kasting ML, Wilson S, Dixon BE, Downs SM, Kulkarni A, Zimet GD. Health-care providers' beliefs and attitudes regarding risk compensation following HPV vaccination. *Papillomavirus Res*. **2016**;2:116–21.
22. Blumenthal J, Haubrich R. Risk compensation in PrEP: an old debate emerges yet again. *Virtual Mentor*. **2014**;16(11):909–15.
23. Holt M, Murphy DA. Individual versus community-level risk compensation following preexposure prophylaxis of HIV. *Am J Public Health*. **2017**;107(10):1568–71.
24. Cassell MM, Halperin DT, Shelton JD, Stanton D. Risk compensation: the Achilles' heel of innovations in HIV prevention? *BMJ*. **2006**;332(7541):605–7.
25. Eaton LA, Kalichman SC. Risk compensation in HIV prevention: implications for vaccines, microbicides, and other biomedical HIV prevention technologies. *Curr HIV/AIDS Rep*. **2007**;4(4):165–72.
26. Auerbach JD, Hoppe TA. Beyond "getting drugs into bodies": social science perspectives on pre-exposure prophylaxis for HIV. *J Int AIDS Soc*. **2015**;18 4 Suppl 3:19983.
27. Koester K, Amico RK, Gilmore H, Liu A, McMahan V, Mayer K, et al. Risk, safety and sex among male PrEP users: time for a new understanding. *Cult Health Sex*. **2017**;19(12):1301–13.
28. Milam J, Jain S, Dube MP, Daar ES, Sun XM, Corado K, et al. Sexual risk compensation in a pre-exposure prophylaxis demonstration study among individuals at risk for HIV. *J Acquir Immune Defic Syndr*. **2019**;80(1):e9–13.
29. Rojas Castro D, Fugon L, Bourgeois-Fisson E, Gall JML, Barbier F, Spire B. The "Swiss Statement": Who knows about it? How do they know? What are its effects on people living with HIV/AIDS? *AIDS Care*. **2012**;24(8):1013–9.
30. Unemo M, Bradshaw CS, Hocking JS, de Vries HJC, Francis SC, Mabey D, et al. Sexually transmitted infections: challenges ahead. *Lancet Infect Dis*. **2017**;17(8):e235–79.
31. Wasserheit JN. Epidemiological synergy. Interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. *Sex Transm Dis*. **1992**;19(2):61–77.
32. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sex Transm Infect*. **1999**;75(1):3–17.
33. UNAIDS. Miles to go. Closing gaps, breaking barriers, righting injustices [Internet]. **2018** [cited 2018 Dec 6]. Available from: http://www.unaids.org/sites/default/files/media_asset/miles-to-go_en.pdf
34. Leeman RF, Toll BA, Volpicelli JR. The Drinking-Induced Disinhibition Scale (DIDS): a measure of three types of disinhibiting effects. *Addict Behav*. **2007**;32(6):1200–19.
35. Fillmore MT, Weafer J. Alcohol impairment of behavior in men and women. *Addict Abingdon Engl*. **2004**;99(10):1237–46.
36. Wilde GJS. Target risk: dealing with the danger of death, disease and damage in everyday decisions. Toronto, Canada: PDE; **1994**.
37. Peltzman S. The effects of automobile safety regulation. *J Polit Econ*. **1975**;83(4):677–725.
38. Blomquist GC. The Regulation of Motor Vehicle and Traffic Safety. Boston, MA: Klewer Academic Publishers; **1988**. 145 p.
39. Adams J. Smeed's Law, seat belts and the emperor's new clothes. In: Evans L, Schwing R.C. (eds) editor. Human behavior and traffic safety. Springer, Boston, MA; **1985**. 193–248. p.
40. Adams J, Adams JGD. Risk and freedom: the record of road safety regulation. London: Transport Publishing Projects; **1985**.
41. Adams J. Risk homeostasis and the purpose of safety regulation. *Ergonomics*. **1988**;31(4):407–28.
42. Hedlund J. Risky business: safety regulations, risk compensation, and individual behavior. *Inj Prev*. **2000**;6(2):82–9.
43. Fishbein M, Ajzen I. Belief, attitude, intention, and behavior: an introduction to theory and research. Addison-Wesley Pub. Co., Reading, MA; **1975**. 600 p.

44. Sheppard BH, Hartwick J, Warshaw PR. The theory of reasoned action: a meta-analysis of past research with recommendations for modifications and future research. *J Consum Res*. 1988;15(3):325–43.
45. Ajzen I. The theory of planned behavior. *Organ Behav Hum Decis Process*. 1991;50(2):179–211.
46. Ajzen I, Fishbein M. Understanding attitudes and predicting social behavior. Englewood Cliffs, NJ: Prentice-Hall; 1980.
47. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. *Am J Health Promot AJHP*. 1997;12(1):38–48.
48. Fisher JD, Fisher WA. Changing AIDS-risk behavior. *Psychol Bull*. 1992;111(3):455–74.
49. Fisher WA, Fisher JD. A general social psychological model for changing AIDS risk behavior. In: Pryor JB, Reeder GD (eds). *The social psychology of HIV infection*. Hillsdale, NJ, US: Lawrence Erlbaum Associates Inc; 1993. 127–153 p.
50. Fisher WA, Fisher JD. Understanding and promoting sexual and reproductive health behavior: theory and method. *Annu Rev Sex Res*. 1998;9(1):39–76.
51. Fuller R. A conceptualization of driving behaviour as threat avoidance. *Ergonomics*. 1984;27(11):1139–55.
52. Naeetaenen R, Summala H. Road-User Behaviour And Traffic Accidents. *Publ N-Holl Publ Co [Internet]*. 1976 [cited 2019 Jan 22]; Available from: <https://trid.trb.org/view/46118>
53. Molen HHVD, Bötticher AMT. A hierarchical risk model for traffic participants. *Ergonomics*. 1988;31(4):537–55.
54. Wilde GJS. The theory of risk homeostasis: implications for safety and health. *Risk Anal*. 1982;2(4):209–25.
55. Adams J. The risk compensation theory and bicycle helmets. *Inj Prev*. 2001;7(2):89–91.
56. Wilde GJS. Does risk homeostasis theory have implications for road safety. *BMJ*. 2002;324(7346):1149–52.
57. Hoyes TW, Stanton NA, Taylor RG. Risk homeostasis theory: a study of intrinsic compensation. *Saf Sci*. 1996;22(1):77–86.
58. Taylor-Gooby P, Zinn JO. Current directions in risk research: new developments in psychology and sociology. *Risk Anal*. 2006;26(2):397–411.
59. O'Neill B, Williams A. Risk homeostasis hypothesis: a rebuttal. *Inj Prev*. 1998;4(2):92–3.
60. Thompson DC. Risk compensation theory should be subject to systematic reviews of the scientific evidence. *Inj Prev*. 2001;7(2):86–8.
61. Trimpop RM. Risk homeostasis theory: problems of the past and promises for the future. *Saf Sci*. 1996;22(1):119–30.
62. Schleinitz K, Petzoldt T, Gehlert T. Risk compensation? The relationship between helmet use and cycling speed under naturalistic conditions. *J Safety Res*. 2018;67:165–71.
63. Esmailikia M, Radun I, Grzebieta R, Olivier J. Bicycle helmets and risky behaviour: a systematic review. *Transp Res Part F Traffic Psychol Behav*. 2019;60:299–310.
64. Underhill K. Study designs for identifying risk compensation behavior among users of biomedical HIV prevention technologies: balancing methodological rigor and research ethics. *Soc Sci Med*. 2013;94:115–23.
65. Crepaz N, Hart TA, Marks G. Highly active antiretroviral therapy and sexual risk behavior: a meta-analytic review. *JAMA*. 2004;292(2):224–36.
66. Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012;367(5):399–410.
67. Thigpen MC, Kebaabetswe PM, Paxton LA, Smith DK, Rose CE, Segolodi TM, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *N Engl J Med*. 2012;367(5):423–34.
68. Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S, et al. Preexposure prophylaxis for HIV infection among African women. *N Engl J Med*. 2012;367(5):411–22.
69. Guest G, Shattuck D, Johnson L, Akumatey B, Clarke EEK, Chen P-L, et al. Changes in sexual risk behavior among participants in a PrEP HIV prevention trial. *Sex Transm Dis*. 2008;35(12):1002–8.
70. Richens J, Imrie J, Copas A. Condoms and seat belts: the parallels and the lessons. *Lancet*. 2000;355:400–3.
71. Ortblad KF, Harling G, Chimbindi N, Tanser F, Salomon JA, Barnighausen T. Does incident circumcision lead to risk compensation? Evidence from a population cohort in KwaZulu-Natal, South Africa. *J Acquir Immune Defic Syndr*. 2019 Mar 1;80(3):269–275. doi: 10.1097/QAI.0000000000001912
72. Westercamp N, Agot K, Jaoko W, Bailey RC. Risk compensation following male circumcision: results from a two-year prospective cohort study of recently circumcised and uncircumcised men in Nyanza Province, Kenya. *AIDS Behav*. 2014;18(9):1764–75.
73. Kelly JA, Otto-Salaj LL, Sikkema KJ, Pinkerton SD, Bloom FR. Implications of HIV treatment advances for behavioral research on AIDS: protease inhibitors and new challenges in HIV secondary prevention. *Health Psychol*. 1998;17(4):310–9.
74. Van de Ven P, Prestage G, Crawford J, Grulich A, Kippax S. Sexual risk behaviour increases and is associated with HIV optimism among HIV-negative and HIV-positive gay men in Sydney over the 4 year period to February 2000. *AIDS Lond Engl*. 2000;14(18):2951–3.
75. Remien RH, Wagner G, Carballo-Diéguez A, Dolezal C. Who may be engaging in high-risk sex due to medical treatment advances? *AIDS Lond Engl*. 1998;12(12):1560–1.
76. Chen SY, Gibson S, Katz MH, Klausner JD, Dilley JW, Schwarcz SK, et al. Continuing increases in sexual risk behavior and sexually transmitted diseases among men who have sex with men: San Francisco, Calif, 1999–2001, USA. *Am J Public Health*. 2002;92(9):1387–8.
77. Katz MH, Schwarcz SK, Kellogg TA, Klausner JD, Dilley JW, Gibson S, et al. Impact of highly active antiretroviral treatment on HIV seroincidence among men who have sex with men: San Francisco. *Am J Public Health*. 2002;92(3):388–94.
78. Stolte IG, Dukers NH, de Wit JB, Fennema JS, Coutinho RA. Increase in sexually transmitted infections among homosexual men in Amsterdam in relation to HAART. *Sex Transm Infect*. 2001;77(3):184–6.
79. Vernazza P, Hirschel B, Bernasconi E, Flepp M. Les personnes séropositives ne souffrent d'aucune autre MST et suivant un traitement antirétroviral efficace ne transmettent pas le VIH par voie sexuelle. *Bull Médecins Suisses*. 2008;89(05):165–9.
80. Doyle JS, Degenhardt L, Pedrana AE, McBryde ES, Guy RJ, Stooé MA, et al. Effects of HIV antiretroviral therapy on sexual and injecting risk-taking behavior: a systematic review and meta-analysis. *Clin Infect Dis*. 2014;59(10):1483–94.
81. Gafos M, Horne R, Nutland W, Bell G, Rae C, Wayal S, et al. The context of sexual risk behaviour among men who have sex with men seeking PrEP, and the impact of PrEP on sexual behaviour. *AIDS Behav*. 2019 Jul;23(7):1708–1720. doi: 10.1007/s10461-018-2300-5
82. Rivierez I, Quatremer G, Spire B, Ghosn J, Rojas Castro D. Lessons learned from the experiences of informal PrEP users in France: results from the ANRS-PrEPPage study. *AIDS Care*. 2018;30 Suppl 2:48–53.
83. Fonner VA, Dalglish SL, Kennedy CE, Baggaley R, O'Reilly KR, Koechlin FM, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. *AIDS Lond Engl*. 2016;30(12):1973–83.
84. Traeger MW, Schroeder SE, Wright EJ, Hellard ME, Cornelisse VJ, Doyle JS, et al. Effects of pre-exposure prophylaxis for the prevention of human immunodeficiency virus infection on sexual risk behavior in men who have sex with men: a systematic review and meta-analysis. *Clin Infect Dis*. 2018;67(5):676–86.
85. Jenness SM, Weiss KM, Goodreau SM, Gift T, Chesson H, Hoover KW, et al. Incidence of gonorrhea and chlamydia following human immunodeficiency virus preexposure prophylaxis among men who have sex with men: a modeling study. *Clin Infect Dis*. 2017;65(5):712–8.
86. Kofman A, Adashi EY. Pre-exposure prophylaxis for the primary prevention of HIV in at-risk women: empowerment and equity revisited. *AIDS Rev*. 2014;16(3):134–43.
87. Mayer KH, Krakower DS. Editorial commentary: uncoupling epidemiological synergy: new opportunities for HIV prevention for men who have sex with men. *Clin Infect Dis*. 2015;61(2):288–90.
88. Morel S. Promoting sexual health through community education and activism: How community involvement could improve sexual health access & STI test regularity. Presentation at: STI 2018: Understanding and Addressing the HIV and STI Syndemics; 2018; Amsterdam, The Netherlands.
89. Wall KM, Khosropour CM, Sullivan PS. Offering of HIV screening to men who have sex with men by their healthcare providers and associated factors. *J Int Assoc Physicians AIDS Care (Chic)*. 2010;9(5):284–8.
90. Underhill K, Morrow KM, Collier C, Holcomb R, Calabrese SK, Operario D, et al. A qualitative study of medical mistrust, perceived discrimination, and risk behavior disclosure to clinicians by U.S. male sex workers and other men who have sex with men: implications for biomedical HIV prevention. *J Urban Health*. 2015;92(4):667–86.
91. Mayer KH. Do ask, do tell: clinicians and the U.S. National AIDS strategy. *AIDS Lond Engl*. 2014;28(8):1233–5.
92. ANRS. L'étude ANRS Prévenir démarrage [Internet]. 2017 [cited 2019 Jan 7]. Available from: <http://www.anrs.fr/fr/actualites/313/letude-anrs-prevenir-dema>
93. Whitfield THF, John SA, Rendina HJ, Grov C, Parsons JT. Why I quit Pre-Exposure Prophylaxis (PrEP)? A mixed-method study exploring reasons for PrEP

discontinuation and potential re-initiation among gay and bisexual men. *AIDS Behav.* **2018**;22(11):3566–75.

94. Coy KC, Hazen RJ, Kirkham HS, Delpino A, Siegler AJ. Persistence on HIV preexposure prophylaxis medication over a 2-year period among a national sample of 7148 PrEP users, United States, 2015 to 2017. *J Int AIDS Soc.* **2019**;22(2):e25252.

95. Krakower D, Maloney KM, Powell VE, Levine K, Grasso C, Melbourne K, et al. Patterns and clinical consequences of discontinuing HIV preexposure prophylaxis during primary care. *J Int AIDS Soc.* **2019**;22(2):e25250.

96. Molina J-M, Charreau I, Chidiac C, Pialoux G, Cua E, Delaugerre C, et al. Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial. *Lancet Infect Dis.* **2018**;18(3):308–17.

97. Bolan RK, Beymer MR, Weiss RE, Flynn RP, Leibowitz AA, Klausner JD. Doxycycline prophylaxis to reduce incident syphilis among HIV-infected men who have sex with men who continue to engage in high-risk sex: a randomized, controlled pilot study. *Sex Transm Dis.* **2015**;42(2):98–103.

98. Siguier M, Molina J-M. Doxycycline prophylaxis for bacterial sexually transmitted infections: promises and perils. *ACS Infect Dis.* **2018**;4(5):660–3.

99. Traeger MW, Cornelisse VJ, Asselin J, Price B, Roth NJ, Willcox J, et al. Association of HIV preexposure prophylaxis with incidence of sexually transmitted infections among individuals at high risk of HIV infection. *JAMA.* **2019**;321(14):1380–90.

100. Low N, Broutet N, Adu-Sarkodie Y, Barton P, Hossain M, Hawkes S. Global control of sexually transmitted infections. *Lancet.* **2006**;368(9551):2001–16.

101. Fee E. Sin vs. science: venereal disease in Baltimore in the twentieth century. *J Hist Med Allied Sci.* **1988**;43(2):141–64.