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ORIGINAL ARTICLE / *ARTIGO ORIGINAL*

Critical remarks on strategies aiming to reduce drug related harm: substance misuse and HIV/AIDS in a world in turmoil

Considerações críticas sobre as estratégias de redução de danos: consumo de substâncias e HIV/AIDS em um mundo em conflito

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ABSTRACT: In the last decades, the initiatives implemented under the conceptual umbrella of Harm Reduction have gained momentum, with a vigor and scope (both from a geographic and social perspective) never seen before. A more balanced reevaluation could and should rather say such initiatives have resumed, to a large extent, ideas and actions launched much earlier, in the first decades of the 20th century. Notwithstanding, the dissemination of HIV/AIDS in recent years conferred an exceptional visibility and legitimacy to proposals formerly viewed as subsidiary or openly neglected. Nowadays, initiatives inspired by the Harm Reduction philosophy have faced an "identity crisis", not secondary (according to our perspective) to challenges faced by its concepts and operations, but rather as consequence of a world in a turmoil. Such fast-changing dynamics have reconfigured both drug scenes and the patterns and prospects of HIV/AIDS worldwide. This article briefly summarizes some of such recent, ongoing, changes, which have been deeply affecting both concepts and practices to the point of asking for a deep reformulation of most of the initiatives implemented so far.

Keywords: Substance-related disorders. HIV. Harm reduction. Hepatitis, viral, human. Psychotropic drugs. Sexually transmitted diseases.

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RESUMO: Nas últimas décadas, as iniciativas enfeixadas sob o marco conceitual da Redução de Danos se revestiram de um vigor e de uma abrangência geográfica e social jamais vistos. Embora seja mais correto afirmar que tais iniciativas retomaram, em grande medida, as estratégias propostas em períodos anteriores, a epidemia de AIDS conferiu a iniciativas antes secundarizadas uma legitimidade e uma expansão inéditas. Atualmente, as iniciativas clássicas de Redução de Danos se veem às voltas com uma crise de identidade, não tanto devido a uma anunciada crise dos seus fundamentos, mas sim devido a uma profunda reconfiguração mundial dos cenários referentes tanto ao consumo de drogas como à epidemia de AIDS. O presente texto sistematiza de forma sucinta algumas dessas transformações, ainda em curso, que vêm afetando de forma profunda os conceitos e práticas de Redução de Danos, a ponto de reclamarem uma reformulação ampla de boa parte do que têm sido proposto e implementado até então.

Palavras-chave: Transtornos relacionados ao uso de substâncias. HIV. Redução do dano. Hepatite viral humana. Psicofármacos. Doenças sexualmente transmissíveis.

INTRODUCTION

Since the 1980s and 1990s, and to a lesser extent in the first decade of the 21st century, a comprehensive series of initiatives and conceptual developments have been disseminated and implemented under the umbrella of "Harm Reduction" (HR) (or, more precisely, "programs and initiatives aiming to reduce drug-related harms and risks"). Such initiatives have gained a strength and relevance most commentators believed to be definitely lost/forgotten since the early 1930s.

To some extent, renewed concepts and strategies resume old concepts and practices, such as the ones advanced by the renowned Rolleston Report, launched in 1926, in the United Kingdom (available at: http://www.enotes.com/rolleston-report-1926-u-k-reference/rolleston-report-1926-u-k). On the other hand, contemporary initiatives have addressed brand new challenges, such as the spread of HIV/AIDS (both the infection and the clinical syndrome did not exist as such in the 1930s), as well as the dissemination of pathogens associated with viral hepatitis, e.g. the hepatitis viruses B and C. Up to the late post-War period, the latter pathogens were understood as mysterious "filterable" infectious agents rather than well-defined biological entities (see: http://rybicki.wordpress.com/2012/02/06/a-short-history-of-the-discovery-of-viruses-part-1/). Until recently, such conditions had a rather elusive etiology and pathophysiology, and a bleak medical prognosis. Recently, as the late 1980s, hepatitis C was not recognized as a well-defined condition on its own and was usually known as "non-A/non-B hepatitis".

The 21st century has fortunately brought major hopes in the field of viral hepatitis management and treatment. The dramatic impact of new therapies on the subsequent spread of the hepatitis C virus (HCV), under the umbrella of what has been called "Treatment as Prevention" (TasP) has — for the first time in history — defined the eradication of HCV a concrete goal[1].

HIV/AIDS — and to a lesser extent viral hepatitis (unfortunately, a less visible public health problem[2]) — has helped to make stigmatized, unpopular and sometimes forbidden programs, such as methadone substitution, key preventative strategies, with some unfortunate exceptions such as the Russian Federation methadone substitution ban[3].

In this second decade of the 21st century, the most different programs and initiatives inspired by Harm Reduction have been under heavy criticism. We do not subscribe McKeganey's pessimistic diagnosis and harsh criticisms[4], and do not think "harm reduction" is experiencing a progressive debasement of its conceptual pillars, but have been rather adapting itself to the challenges faced by a field under rapid transition.

In Brazil, initiatives aiming to reduce drug-related harm have not be challenged by criticisms based on scientific evidence such as those advanced by McKeganey on UK drug policies. Notwithstanding, Harm Reduction in Brazil has not been spared by "its discontents" (to echo Freud's classic expression on the fate of contemporary civilization; see Laranjeira 2010 for a deeply critical appraisal of drug law reform[5]).

The present text outlines recent changes of "Harm Reduction" concepts, aims, strategies and actions. Whatever the perspective, the field of Harm Reduction has been under deep renewal, aiming to offer prompt responses to the fast-changing dynamics of drug markets, drug scenes and the new patterns of substance use and misuse.

With the implementation in recent years of new programs, strategies and norms, in Brazil as well as in most high and middle-income countries, harms and risks associated with transmissible diseases secondary to unsafe substance habits and practices must be understood under a brand new conceptual and practical perspective.

Three key examples must be cited here:

1. The full availability of antiretroviral therapy to ANY individual living with HIV (irrespectively of his/her CD4+ counts as stated by the Brazilian Minister of Health as of December 2013).
2. The new guidelines respecting testing, counselling, management and treatment of hepatitis C (see Coffin & Reynolds, 2014, on the new US guidelines[6] and the official documents on the new Brazilian guidelines[7]).
3. The dramatic impact on younger cohorts of children and adolescents of the full implementation of universal hepatitis B vaccination in Brazil[8].

METHODS

The present text does not aim to review in detail the complex inter-relationships between substance misuse and HIV and/or viral hepatitis acquisition and transmission, but rather aims to critically review selected peer-reviewed papers, as well as some recent information available in the grey literature. The most recent trends mentioned in the text have yet to be fully assessed and better understood.

RESULTS

THE NEW DRUG MARKETS AND SCENES

Drug scenes have been changing under a fast pace worldwide. The in-depth assessment of such new scenarios and trends has been addressed by recent reviews, some of them with a focus on the interface between the new drug scene and the prevention of HIV/AIDS[9].

Both in Brazil and in the vast majority of other countries, worldwide, the habit of injecting illicit drugs has experiencing a fast and pronounced decline[10]. Exception made to some "hot spots", in which the injection of illicit substances remains a relatively frequent habit, such as some countries from Southern Asia and Eastern Europe, injection has been progressively replaced by alternative ways; people use classic substances, as cocaine, snorting, smoking and by other routes (e.g. ingesting, applying dermal patches, etc.), as well as by a growing number of modified/different (many times, brand new) non-injectable substances.

Even in some places where injection was especially prevalent and had been one of the key drivers of HIV and HCV spread, such as in Estonia, Eastern Europe, injection has becoming a less frequent habit in recent years[11].

However, the deep and fast transition of drug markets and scenes in recent years is much broader than the changes associated with new/renewed routes people may use substances. First of all, the very nature and composition of substances have been reconfigured and (re)designed. Some of these changes correspond to different presentations of a single or related group of substances, such as the increase of smoked crack cocaine in detriment of snorted powder cocaine in contemporary Brazil[12]. From a different, maybe complementary perspective, markets and drug scenes have been flooded by brand new drugs, most of them undetectable by current toxicological analyses. Due to the illicit nature of such markets and the very fact such substances are specifically designed to evade detection, it is very difficult and many times impossible to track their dissemination and to better understand the profile, habits and risks faced by their consumers.

Anyway, sooner or later, substances initially regarded as local, sometimes idiosyncratic, have become global commodities, as happened to ecstasy over the last decade, a substance which is nowadays the "lubricant" of the disco party scenes all over the world.

To the best of our knowledge, exception made to compounds based on *salvia divinorum*, a plant which is native to many different Brazilian regions, there is no sound information on the putative misuse of such different substances, which may or may not be used in Brazil. These new substances may include: bath salts and other cathinones[13], untraceable amphetamine-like substances[14], new synthetic cannabinoids[14] etc. Such vast and highly heterogeneous group of substances has been studied under the conceptual umbrella of "legal highs", i.e. substances with psychoactive effects which do not belong to the classic lists of substances under control, are virtually untraceable, and are not amenable to any modality of medical or legal surveillance[15].

Despite the undeniable relevance of such substances in the American, Western European and Australian markets, as recently summarized by UNODC, in its 2012 Annual Report (http://www.unodc.org/documents/data-and-analysis/WDR2012/WDR_2012_web_small.pdf), there is no clear information about the putative association of their use and misuse with the acquisition and transmission of HIV and/or other sexually transmitted infections, either as mind-altering substances that might compromise the consistent use of condoms or substances that may be eventually injected, as have been seldom reported[16].

One thing is pretty clear to experts and policy-makers: the markets and scenes of drug trafficking and use will be deeply impacted by such new substances, as well as by alternative modes of administration and habits, many of them navigating "under the radar" of surveillance systems worldwide.

THE CHALLENGE OF PHARMACOTHERAPY

Since the Rolleston Report, the parsimonious use of different therapeutic alternatives has been one of the pillars of Harm Reduction. For didactic purposes, we may roughly classify such therapeutic alternatives as follows:

a. substitution therapies;
b. *stricto sensu* pharmacotherapies;
c. assisted prescription of illicit substances.

In the Brazilian context, some confusion has emerged between items "a" and "b". The prevailing confusion between pharmacotherapy and substitution therapy refers, first of all, to anecdotal reports from health services, as well as to some empirical observations from the field about the use of cannabis as a way to mitigate anxiety and psychomotor agitation among powder/crack cocaine users. Although, different empirical evidence points to the role of cannabis and similar products, as substance with "anxiolytic" properties, such as those described for "pitilho", among users of snorted/smoked cocaine in Bahia (i.e. the smoking of smashed crack powder sparkled over cannabis), Northeastern Brazil. Such informal strategies should not be understood as a modality of "substitution therapy". Coca/cocaine in their most different presentations are stimulants and as such cannot be "substituted" by substances such as cannabis that have not only different, but opposed, effects on thought, perception, memory etc.

Cocaine might be "substituted", in the long term, by legally approved medicines such as metylphenidate (Ritalin®), other amphetamine-like substances and/or modafinil[17]. By now, such attempts have been tentative, and none of such medicines are currently approved by national regulatory agencies, such as the US-based FDA (Food and Drug Administration) or its Brazilian equivalent, ANVISA. In case of such strategies can be scientifically documented in the near future as safe, effective and — ideally — cost-effective alternatives, they might constitute invaluable tools in terms of moderating cocaine craving, to provide comprehensive management and care for drug-dependent people, and — last but not least — to avert new by HIV infections and other STI's that may be associated with snorted, smoked or injected cocaine.

One may hypothesize that one day such strategies may have a key role in the management of stimulant substances misuse, and its associated harms and risks. In a similar way, methadone and related substances currently have in the management of opiate misuse and its complex inter-relationships with different medical conditions, among them HIV infection and overdoses, as well as crime and marginalization of opiate dependent people[18].

Many different attempts (not related to substitution) have been made to improve the complex management of stimulant-dependent people. The most successful trials carried so far have comprised the use of topiramate[19] and acamprosate[20]. In the moment such text is being written (September 2014), none of such medications were cleared by national or international regulatory agencies. New clinical trials are on the way, and results have been mixed and only partially successful.

Last but not the least, one must observe assisted prescription has no concrete relevance in the Brazilian context due to the fact all trials carried out so far have highlighted the prescription under medical supervision of heroin, a substance which is rare and very expensive in the Brazilian context. Similarly, due to the very modest role of opiates in Brazil, substitution therapies using methadone or analogues (e.g. buprenorphine, LAAM [levo-alpha-acetyl-methadol], etc.) have no practical relevance in Brazil, except for a few cases of opiate dependent patients under follow-up in private clinics.

TREATMENT AS PREVENTION AND BIOMEDICAL PROPHYLAXIS FOR PEOPLE WHO USE/INJECT DRUGS

HIV risk management in recent years has incorporated a series of initiatives which have been profiting from new biomedical interventions, being them implemented as isolated protocols or integrated packages combining "classic" and new interventions. More recently, a broad series of papers have been assessing such interventions, using mathematical modeling and the piloting of large-scale trials (as documented in detail in a recent paper by Eaton et al. cross-comparing the findings from 12 different mathematical models)[21], under the broad denomination of "treatment as prevention" (or TasP), as comprehensively defined by the CDC in a recent statement (available at: http://www.cdc.gov/hiv/prevention/research/tap/). A whole supplement of *PLOS Medicine* has targeted ongoing initiatives as well as the challenges they have been facing (available at: http://www.ploscollections.org/article/browse/issue/info%3Adoi%2F10.1371%2Fissue.pcol.v07.i18;jsessionid=570EB76AF358A20E9013A9B08610BCC6).

Many different protocols using anti-retrovirals as a prophylaxis respecting the acquisition of HIV have been successfully completed in recent years. Key examples include the iPrEx protocol targeting gay men (http://www.niaid.nih.gov/news/QA/Pages/iPrExQA.aspx).

People who misuse illicit drugs have been seldom targeted by such protocols, with some very rare exceptions, such as the comprehensive intervention targeting men who have sex with men who misuse meta-amphetamines, combining behavioral therapy and pre-exposure prophylaxis with anti-retrovirals[22]. Very recently, an ambitious intervention targeting injection drug users was completed in Bangkok, Thailand[23], with the use of Tenofovir as a prophylaxis. The protocol faced many difficulties, such as the high drop-out rates, and the accompanying comments published in a recent issue of *The Lancet*[24] were considered far from conclusive and not solid enough to provide the necessary evidence for guidelines for interventions targeting this population.

Some authors have criticized the systematic exclusion of an especially vulnerable population — drug-dependent people and/or heavy users of different substance facing serious harms and risks — from the vast majority of intervention and treatment protocols worldwide. Such exclusion may be understood as a violation of the basic rights of this population and a serious limitation of the efforts to curb the spread of HIV and viral hepatitis in different contexts such as Southern Asia and Eastern Europe, where their role as drivers of the local epidemic dynamics is especially relevant. This exclusion seems to be secondary to deeply entrenched prejudices and has been called "addictophobia"[25].

Committed researchers and clinicians who work with drug dependent people on a daily basis knows this is a particularly marginalized, stigmatized and hard-to-reach population. Notwithstanding, such challenges should not be translated into viewing such individuals as members of a population who does not deserve to be treated with compassion and respect, benefiting from initiatives tailored to their special needs and demands.

SURVEILLANCE SYSTEMS UNDER TRANSITION

The different National Surveillance Systems, even those which track HIV infections (unlike Brazil's Surveillance System, which focus on AIDS cases, besides HIV among newborns and women from "sentinel" maternities), do not monitor HIV and viral hepatitis among people who misuse illicit drugs, other than those who inject them.

Whereas Injection Drug Users (IDUs) constitute a well-defined exposure category since the late 1980s worldwide, very modest (or most of the time, none at all) progress has been made respecting the surveillance of new infections or AIDS or Hepatitis cases among non-injectors. Some specific studies, such as pooled analyses of data from non-injecting drug users, have brought new information about this population[26], but such advances have not been incorporated into standard surveillance systems.

In the context of the abovementioned fast and deep transitions, and considering the sustained decline of the habit of injecting in parallel with the increase in the use of new substances and/or new self-administration routes, current surveillance systems should be reevaluated and carefully tailored to the needs and challenges of a world under transition.

In the absence of tools provided by surveillance systems information about the inter-relationship between substance misuse and the spread of different pathogens, data have been inferred from pooled analyses/meta-analyses of local and regional studies, aiming to estimate the fraction of overall risk that could be attributed to the misuse of substances in the acquisition and transmission of HIV and other STIs.

As brand new substances that may evade detection by standard toxicological analyses have gained momentum and scope, the very concept of what is/what is not a mind-altering substance becomes problematic. The most recent World Reports issued by the UNODC have explicitly addressed these new challenges.

Feasible and useful alternatives comprise the thorough triangulation of data from the most different sources, as have been attempted by the European Union Observatory (see publications available for download at: http://www.emcdda.europa.eu/). Nothing short of innovative methods, exception made to a deep reform of the drug legislation and global treaties (something currently beyond the horizon of policy reform), would help to monitor and evaluate such brand new trends. Without the progressive, concerted development of methods that may help to reach hard-to-reach populations and/or to probe the deepest strata of a multi-layered illicit market, national surveillance systems will remain fragmentary and insufficient.

In the unlikely event (at least in the short-term) of a comprehensive reform of national and international legislations and treaties substances nowadays defined as illicit, which are exempt from any regulation mandated by commercial agreements, consumer rights agencies or pharmaceutical regulatory bodies will not be under the scrutiny of health and social institutions and advisory boards.

DISCUSSION

HARM REDUCTION: CONCEPT AND INITIATIVES UNDER REFORM

The conceptual benchmark of "Harm Reduction" is much broader than its visible face targeting people who inject drugs and their associated harms and risks. Harms associated with substances as diverse as tobacco and alcohol have been targeted by HR. Notwithstanding, in the eyes of the public, as well as on the minds of many policymakers, activists and health professionals, initiatives such as needle and syringe exchange programs (NSEP) are frequently viewed as exclusive.

In this sense, the coming reformulations and renewed proposals will be far from simple or straightforward and much likely will face strong resistance, denial or a priori criticism. There is no plausible reason ideas, such as the provision of safer devices for crack smoking, that would not face the same harsh opposition NSEP experienced in the 1980s and 1990s.

Initiatives aiming to reduce harms related to crack cocaine have been sparse and, in a large extent, hampered by political opposition to the point some attempts, as the pilot program implemented in Vancouver, Canada[27], had had no real chance to be evaluated with the necessary detail. Its mixed results cannot be attributed to any single factor or dimension, but should be rather viewed in the context of confusing and contradictory policies, such as equipment confiscation, harassment by the police, underfunded programs and heavy criticisms by legislative bodies, as well as by local and regional administrations. The same difficulties and challenges have compromised any attempt to launch supervised facilities for the personal use of non-injectable drugs[28].

NEW TIMES, RENEWED RISKS AND HARMS

In parallel, new as well as long-term vulnerable populations have (re)emerged in recent times. For instance, a brand new generation of young gay men have been affected by increasing rates of gonorrhea (including rectal gonorrhea) in recent years (which is a clear marker of unprotected sex), what seems to be associated with a series of factors such as prevention fatigue; the clash between the worldview espoused and promoted by the "heroic" generation of the 1980s/90s, when HIV (as well as the less noticed hepatitis B) dissemination peaked; treatment optimism; and the role of the Internet and other social media as a way of socializing, establishing virtual communities and finding affective and sexual partners, among others.

Such changes also comprise deep transformation in the renewed gay scenes, including the emergence of new lifestyles and attitudes, as well as the use and misuse of new substances, as different modalities of amphetamines and design drugs[29].

Stimulant drugs have been on the rise worldwide, whereas the specific "portfolio" of stimulant substances varies in a pronounced way according to different social strata, settings and societies. For instance, some varieties of amphetamine, such as Crystal meth, are on the rise in the US, but are not relevant in Brazil. On the other hand, crack cocaine, which emerged in the US in the early 1980s, remains a key drug in certain deprived inner-city communities in that country, whereas in Brazil been reported all over the country[30,31].

In this sense, the growing "share" of stimulant drugs, old and new, in the portfolio of psychoactive substances seems to be a global trend, with local specificities. Such stimulant drugs, usually in combination with alcohol (which, depending on the dose, individual characteristics and settings, may function as a selective inhibitor of inhibition), have been strongly associated with the acquisition of HIV and hepatitis B (and to a less extent with the transmission of HCV) worldwide[32-34]. In this sense, they markedly differ from opiates, cannabis derivates and mixed hallucinogenic drugs, both old (LSD) and new (e.g. synthetic cannabinoids), in which the association with different STIs is much less relevant or rather absent.

CONCLUSION

In agreement with McKeganey's diagnosis, but in frank opposition to his underlying reasoning, we do agree HR is in a crossroad. However, differently from the author's perspectives, we rather think:

1. We do not believe the "long forgotten emphasis on abstinence" should be recovered, first of all because it had never fade out or forgotten. For the vast majority of health professionals and policymakers, abstinence was and is the dominant paradigm and pervasive goal. By the way, as the privileged path to be free of any kind of drug-related harm, abstinence never was, is or should be in conflict with HR. Notwithstanding, to the extent, it may be viewed as a short-term goal for all patients, as well as an

all-encompassing concept for both individuals and societies it seems not only far from real-life conditions, but a proposal close to coercion and empty proselytism.

2. Concepts and practices that seem to us innovative may become old and even counterproductive over the years, especially when such years become decades, as have happened to AIDS and viral hepatitis. In this sense, such ideas may be hurdles to effective progress and even prejudices. Concepts and practices should and must be renewed and reformed. From this perspective, to be situated in a crossroad is not only challenging but means a relevant boost toward real innovation.

There is a long confusion involving the Chinese ideogram for Crisis that has been applied for the most different misguided purposes, from motivational speeches to party politics. The Chinese ideogram for "Crisis" combines the concepts of "danger" and "turning point", what is usually mistranslated as "opportunity". Maybe, but not necessarily, turning points may translate into brand new opportunities. Anyway, crises are moments in which change become mandatory, paving the way for cautious, but concrete, actions (see the subtleness of such debate at: http://en.wikipedia.org/wiki/Chinese_word_for_%22crisis%22).

This seems to be the moment experienced by HR worldwide. A moment not to be viewed as conducive to easy solutions, a moment not to be viewed either as condoning or fostering indifference, lenience or inertia. There is too much at stake, above all, human lives. Dynamic environments and new challenges have been the drivers of evolution over the eons. There is no single reason it should be different in our times.

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