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What Constitutes Prescription Drug Misuse? Problems and Pitfalls of Current Conceptualizations

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Abstract: Many medications with sedative, anxiolytic, analgesic, or stimulant properties have the potential to be inappropriately used. However, because these substances have beneficial effects, many issues pertinent to understanding prescription drug misuse may differ from those associated with other misused substances. There is currently a lack of consensus about what constitutes prescription misuse and a wide range of operational criteria have been proposed. Inappropriate medication use is frequently defined on the basis of user characteristics (i.e. any non-prescribed use), the reason for use (i.e. use for recreational purposes), the presence of clinically significant symptoms (i.e. meeting diagnostic criteria for abuse and dependence) or on the presence of any of these factors. In cases where multiple criteria are used to define misuse there is often a lack of differentiation among them, while studies that use more specific criteria tend to exclude certain types of misuse from consideration altogether. In addition, in some cases there are a number of potential ways that a single operational criterion can be met and many of these may be associated with substantially different risks, harms, and predictors. Due to considerable variability in the classification of medication misuse both within and between studies, it is currently difficult to interpret the clinical significance of existing findings or to determine the true magnitude of problems associated with any particular form of misuse. In the present review many of the problems and challenges for adequately defining prescription drug misuse will be overviewed and recommendations will be made on how to better characterize this phenomenon.

Keywords: Prescription drug misuse, drug dependence, addiction, drug abuse.

INTRODUCTION AND OVERVIEW

The inappropriate use of prescription medications is an issue of increasing concern [1-4]. Many psychiatric medications with sedative, anxiolytic, analgesic, or stimulant properties have the potential to be misused and the inappropriate use of such medications has been linked to a number of serious adverse outcomes (e.g. [5-7]). While demand for, and availability of, such medications have been rising steadily in recent years, so too have documented cases of their non-sanctioned use (e.g. [8, 9]). Despite this, prescription medication misuse remains poorly characterized and understood. Because these drugs have legitimate therapeutic benefits in addition to their potential problematic properties, many issues pertinent to defining and characterising their inappropriate use may not be adequately addressed by frameworks that have been developed to describe the use and misuse of alcohol and illicit substances.

Currently, there is no universally-accepted standard for what constitutes prescription medication misuse, and a wide range of operational criteria have been used throughout the literature. Prescription misuse has been variously defined in terms prescription status (e.g. any medication uses that occur without a prescription) [10-22], reasons for use (e.g. any intentional uses for intoxicating and/or euphoric effects) [8, 12, 16, 19, 23-26], the presence or absence of symptoms of abuse or dependence [27-31], or some combination of these factors [8-9, 32-45]. Often in cases where multiple criteria

are used, there is a lack of differentiation among them (e.g., statistics are given for the broad category of prescription drug misuse while failing to report [or often to even measure] how many individuals were so categorized according to each criterion employed). In contrast, studies that use more specific criteria tend to exclude certain types of misuse from consideration altogether. Matters are further complicated by the fact that often a single criterion will encompass several behaviours and/or patterns of use that may be associated with substantially different risks and harms and fail to distinguish among them. For example, there are numerous potential ways that a medication can be used without a prescription (e.g. use for therapeutic benefits *vs* use for intoxicating properties), for its intoxicating effects (different patterns and routes of administration), or that an individual can become dependent on a medication (e.g. using medication as prescribed for extended periods *vs* substituting medication for an illicit substance with similar pharmacologic properties). Due to the heterogeneity in individuals classified as 'misusers', both within and between studies, it is often difficult to interpret the clinical significance of existing findings or to determine the true magnitude of problems associated with any particular form of inappropriate medication use.

The primary purpose of this paper is to overview the problems and challenges for defining prescription drug misuse. Emphasis is placed on difficulties posed by various conceptualizations commonly found in the scientific literature (i.e. any non-prescribed use; recreational use; meeting diagnostic criteria for a substance use disorder; and the criteria used by the *American National Survey on Drug Use and Health* [A-NSDUH] [9]; a summary operational definitions used in the literature is presented in Table 1). Because there is often a lack of consistency and precision in the terminol-

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ogy used to describe inappropriate medication use, it is not always possible to coherently compare results from studies using their original language. In the present paper we will address past research on the basis of how medication misuse is operationalized rather than on the original terminology used. Throughout the paper, the terms “misuse” and “inappropriate use” will be used interchangeably to refer to the various forms of non-sanctioned or illegitimate prescription medication uses reported irrespective of how the terms are used in the literature cited. In addition, unless otherwise specified, the terms ‘abuse’ and ‘dependence’ will be strictly used in adherence to the *Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition (DSM IV)* [45] substance use disorder categories.

NON-PRESCRIBED MEDICATION USE

Prescription drug misuse has often been defined in terms of ‘any use of a target medication with-out a prescription’ [10-22]. Such definitions have been extensively used in survey research (e.g. [17]), perhaps in part, because the criterion is relatively straightforward and amenable to dichotomous classification. By definition, all non-prescribed uses of medications that require prescriptions are unsanctioned and thus constitute forms of inappropriate use. However, such conceptualizations of misuse exclude from consideration individuals that inappropriately use their own prescriptions (e.g. use of higher than recommended doses; recreation use) as well as those who have prescriptions for illegitimate reasons (e.g. procurement of a prescription to divert or for recreational purposes). Because evidence suggests that prescribed users may represent a significant proportion of cases of medication misuse [24, 25], the generalizability of findings specific to non-prescribed users might be questioned.

Motives for Non-Prescribed Medication Use

In addition, a growing body of evidence suggests that ‘non-prescribed’ medication use can involve a wide-range of behaviors and motives that might be associated with very distinct user characteristics and risks [12, 14, 16, 19, 23, 35, 36, 41, 43]. For example, non-prescribed uses of the same medication might include very hazardous uses for intoxicating purposes (e.g. use of high doses intravenously and in combination with alcohol or other drugs) as well as therapeutic use for a *bona fide* condition outside of a physician’s supervision (e.g. taking a single therapeutic oral dose of a friend or relative’s medication to treat symptoms for which the prescription is normally indicated). While each of these forms of misuse may be of clinical interest, they likely pose very different risks and have very different associated features. Because most studies that define prescription drug misuse in terms of ‘non-prescribed use’ only report on overall rates of ‘misuse’ without any attempt to separate different possible motives for use, the results of such studies may give misleading impressions about the prevalence of the problem.

Although very few studies have attempted to distinguish among different non-prescribed use motives, the evidence that does exist suggests that at least among university and college students, the most commonly endorsed reasons for the non-prescribed use of stimulants [12, 14] and opiate analgesics [19], are related to the medication’s therapeutic benefits (i.e. to improve concentration for stimulants; to help relieve pain for analgesics). A recent study using an adoles-

cent sample found that endorsed motives for non-prescribed use tended to vary by class of medication. For example while motives for non-prescribed sedative and analgesic use tended to be associated with the medication’s therapeutic effects (i.e., to help with sleep; to reduce pain), non-prescribed use of stimulant medications was more likely to be associated with recreational motives (i.e., to get high) [35]. It is important to note that non-prescribed use with therapeutic intentions may be problematic since it is not medically supervised, and often a diagnosis has not been made to support the particular treatment being administered. However, it likely does not yield the same level of risk as many forms of inappropriate recreational medication uses (discussed in detail in the ‘recreational use’ section below).

There are numerous potential quasi-legitimate reasons why an individual might chose to illicitly seek a prescription medication for its therapeutic benefits. For example, in some cases the medication may be sought from a friend or relative with a prescription for an immediate or acute need when it is not be feasible to seek a formal medical consultation. In other cases, medications may be illicitly procured due to socio-economic, geographic, or temporal barriers to access to the medical system or to a reluctance of physicians to prescribe the most efficacious medications on the grounds that they have been identified as having the potential to be mis-used (e.g. [46]).

In cases where the medication has a wide margin of safety and is used as it would be if it were to be prescribed, the actual risks and harms associated with non-prescribed use are often likely no greater than with the legitimate use of the medication. On the other hand, the non-prescribed therapeutic use of a medication in the absence of doctor’s prescription might be extremely risky, especially in circumstances where there is a lack of knowledge of appropriate dosing, potential side-effects and/or interactions, as well as precautions for use. Ironically, in contrast to medication that is used for intoxicating purposes, this form of medication ‘misuse’ often may stem from a propensity to under-medicate certain individuals or conditions with medications that have identified as having a potential for misuse. Such misuse would be expected to decrease if there was increased access to legitimate sources of medication. Because different non-prescribed medication uses may have opposing implications for policy, prevention, and treatment, it is important that investigations using ‘any non-prescribed use’ as a criterion for defining ‘misuse’, begin to systematically identify how non-prescribed medications are being used as well as unique characteristics and features associated with different motives for non-prescribed use.

RECREATIONAL USE

An alternative to defining prescription drug misuse on the basis of prescription status has been to define it on the basis of its deliberate use for recreational purposes in order to achieve intoxicating or euphoric psychoactive effects, irrespective of prescription status (e.g. [23-26]). This conceptualisation of prescription drug misuse is akin to the use of illicit substances and is how the issue of prescription misuse is often portrayed by the media. Moreover, because many forms of recreational use have also been associated with serious adverse outcomes (i.e. overdose, development

Table 1. Varied Operational Definitions for Prescription Drug Misuse

Operational Definitions	Ref.
Non-prescribed use (use without having a doctor's prescription for the medication)	Teter <i>et al.</i> (2005) [12] Teter <i>et al.</i> (2003) [15] Low & Gendasezek (2002) [16] McCabe <i>et al.</i> (2004) [20] McCabe <i>et al.</i> (2005) [13] McCabe <i>et al.</i> (2007) [19] Boyd <i>et al.</i> (2006) [35] Kaloyanides <i>et al.</i> (2007) [10] McCabe (2005) [18] Poulin (2001) [11]
NSDUH criteria: Use of any form of prescription drugs that were not prescribed for the respondent or that the respondent took only for the experience of feeling they caused (SAMSHA, 2006 [9]). DSM IV criteria for abuse and dependence are also assessed.	Kroutil <i>et al.</i> (2006) [8] Sung <i>et al.</i> (2005) [37] Wu <i>et al.</i> (2007) [38] Becker <i>et al.</i> (2007) [32] Smith & Woody (2005) [34] Arria <i>et al.</i> In press [45]
Meeting DSM-IV criteria for abuse and/or dependence.	Simoni-Wastila & Strickler, (2005) [27] O'Brien (2005) [29]
"How often do you use stimulant medications in ways not prescribed?"	White <i>et al.</i> (2006) [14]
"Individuals were asked whether they had ever used a sedative on their own, without having been prescribed one or if they had used more than the amount prescribed by the physician."	Goodwin & Hasin (2002) [33]
"...without a prescription, in greater amounts, more often, or longer than prescribed, or for a reason other than a doctor said you should use them."	Blanco <i>et al.</i> (2007) [30]
"...when you are prescribed a drug by a doctor for a specific condition, but then use the drug in a way that is not consistent with the doctor's orders, like using too much or too frequently... when you do not have a prescription, but obtain the drug from someone else..."	Arria <i>et al.</i> (2008) [44]
"...life-time non-medical use of prescription drugs that were not prescribed to them by a doctor or used in a manner not intended by the prescribing clinician (e.g. more often than prescribed, longer than prescribed or for a reason other than prescribed, such as to get high)."	McCabe <i>et al.</i> (2007) [42]
"Nonmedical use, prescription drug abuse, and/ or illicit use of prescription medications (drugs) is defined as 'the use of prescription medication to create an altered state, to 'get high,' or for reasons (or by people) other than those (or for whom) intended by the prescribing clinician.' Medical misuse and/or non-compliant use is defined as 'the use of a prescribed medication by a person (and for the purpose) intended by the prescribing clinician'; however, in the case of misuse (unlike medical use), the medication is not used in the prescribed dose and/or is not taken within a prescribed time interval"	Boyd <i>et al.</i> (2006) [35]
"...lifetime use it in a way that was not prescribed..."	Darredeau <i>et al.</i> (2007) [24]
"(1) Have you sold your prescribed medication? (2) Have you used too much of your medication? (3) Have you gotten high on your medication? (4) Have you misused your medication? (5) Have you skipped your medication to use alcohol or drugs? (6) Have you used your medication with alcohol or drugs? (7) Have you experienced a reaction with your medication and alcohol or drugs?"	Wilens <i>et al.</i> (2006) [25]
"use of any personal prescription medication used other than as prescribed by dose, frequency or route or the use of someone else's prescribed medication in any way."	Marsh <i>et al.</i> (2000) [39]
Concomitant use of methylphenidate with alcohol.	Barrett & Phil (2002) [26]
Any recreational or non-prescribed use.	Barrett <i>et al.</i> (2005) [23]
"Have you ever taken Ritalin for fun?"	Babcock & Byrne (2000) [52]
Any non-medical use, including prescribed use.	Davis & Johnson (2008) [41]
Unspecified or unclear.	Lankenau <i>et al.</i> (2007) [43] Steinmiller & Greenwald (2007) [36]

of symptoms of abuse or dependence), it has also garnered considerable clinical interest [30, 32]. Unfortunately, however, there is no single universally-accepted means of assessing the use of prescription medications for recreational purposes developed to date. Instead, there is considerable variation in the operational criteria used throughout the literature as well as inconsistencies in the terminology used to describe the phenomenon (e.g. the term 'abuse' is often used to refer to any recreational use of a medication (e.g. [10, 29]), but is

also sometimes used specifically in reference to *DSM* diagnostic criteria (e.g. [8, 32, 48]). To complicate matters further, it is not uncommon for findings to be discussed in terms of recreational use when they are based on operational definitions that are not specific to this form of misuse (i.e. inferring recreational use from broad operational definitions of misuse that encompass various forms of prescribed and non-prescribed medication use).

Notwithstanding issues related to discrepancies in how recreational prescription drug use is defined and discussed in the literature, there appears to be considerable variability in the ways that various medications are used for their intoxicating or euphoric effects. Although many misused medications fall into the same pharmacological classes as misused illicit substances, when they are used as prescribed, their rate of onset of action and dosages are generally thought to be insufficient to produce psychoactive effects that are desirable for recreational use [48], and it is often necessary for users to alter a substance's normal rate of delivery and/or availability to the brain when using it recreationally. Ingestion of a substance through injection, smoking, or inhalation results in a much more rapid entry of a drug into the brain than oral administration, and there have been numerous reports of medications with stimulant, analgesic, anxiolytic, or sedative properties being recreationally used through alternative routes of administration.

There have also been several reports of recreational oral use of medications from different classes being co-administered with alcohol and/or other substances [26, 49-52]. The simultaneous use of multiple substances can lead to: pharmacokinetic changes that affect a substance's metabolism, concentration and/or rate of delivery to the brain; pharmacodynamic changes that affect its actions in the brain; and/or the production of new psychoactive metabolites (e.g. the production of ethylphenidate following alcohol-methylphenidate co-administration [53]) that might have different effects than the individual or additive effects of the parent compounds. Polysubstance users often appear to seek medications that have particular pharmacologic actions that will complement the actions of the other substances they are using, and different combinations of substances might be deliberately sought to achieve specific purposes. For example, medications may be mixed with other substances to augment desirable psychoactive effects (e.g. the co-administration of opiates and stimulants has been reported to produce greater euphoric effects than either drug alone (e.g. [50]), counteract or diminish certain undesirable effects (e.g. sedatives have been reported to be mixed with stimulants to reduce insomnia [49]) or to facilitate continuous consumption (e.g. methylphenidate has been reported to be used to prolong alcohol drinking sessions [26, 52]). While there are often different motives for co-administering prescription drugs and other substances for recreational purposes, different combinations of substances are likely to be associated with very different levels of risk. For example, a normally therapeutic dose of a sedative or anxiolytic medication might have lethal consequences when used in combination with some other substances (e.g. increased risk of overdose with heroin or alcohol (e.g. [5, 6]), while it might help mitigate an adverse reaction to another substance (e.g. decreased amphetamine- or cocaine-induced agitation (e.g. [29, 32])).

Despite the variability in behaviours considered to be recreational prescription drug use as well as in their associated risks, most studies that address recreational use fail to distinguish among them. To date, most information about the different ways prescription medications are recreationally used comes from studies that have used targeted sampling methods [23-25] or that have relied exclusively on anecdotal reports [26, 49, 52, 54]. Although such investigations have been very valuable for documenting various possible forms

of misuse, they are typically not able to provide reliable estimates of their relative rates of occurrence or relative risks. In addition, it is also possible that different forms of recreational medication use require different targets for prevention. For example, the use of tamper-proof formulations may be effective in preventing use of medications through different routes of administration (e.g. [55]) but may be less effective in preventing polysubstance users from inappropriately using medications to alter or enhance certain other substance-related effects.

DSM CRITERIA

A third method for defining prescription drug misuse that has been employed in the extant literature has been to make use of established criteria for diagnosing a disorder of clinical significance associated with use of these medications [8, 32, 34]. Most often, such definitions make use of the diagnostic criteria for substance use disorders available in the DSM. The most recent version of this manual is the *DSM Fourth edition, text revision (DSM-IV-TR*; American Psychiatric Association, 2000). Most mental health professionals and psychopathology researchers use the classification system contained in the *DSM-IV-TR* [47]. It is the official system for classification of mental health and addictive disorders in North America and it is a system used widely around the world. While the International Classification of Disease [56] has a comparable system of classification of problematic substance use, to date, the bulk of the research that has defined problematic prescription drug use in terms of diagnostic criteria has utilized the DSM criteria. Use of the diagnostic criteria within a system like the *DSM* allows for consistency in assessment, facilitates communication between scientists/practitioners, and assists with the advancement of knowledge [57]. The *DSM-IV-TR* recognizes two forms of substance use disorders – abuse and dependence – which vary in severity. Dependence is the more severe of the two types of disorder.

Abuse

The DSM defines substance abuse as a pattern of maladaptive substance use that is associated with recurrent and significant adverse consequences. A diagnosis of substance abuse requires meeting at least one of the following four criteria due to recurrent substance use: 1) failure to fulfill obligations at home/school/work; 2) use in situations that are physically hazardous; 3) legal problems; and/or 4) social or interpersonal problems [47]. Although numerous studies purport to discuss prescription medication abuse (e.g. [7, 10, 14, 28, 34, 49-50, 54]), few actually assess it. And those that have assessed it according to *DSM* criteria suggest that it is actually a relatively rare occurrence. For example, fewer than 4% of individuals reporting past year misuse of stimulant medications (using the A-NSDUH criteria discussed below) met the diagnostic criteria for abuse [8], and less than 10% of past year sedative and anxiolytic misusers met the criteria for either abuse or dependence [32]. Unfortunately data was not separately reported for each diagnosis or for each class of drug so it is impossible to know the exact rates of abuse vs dependence (see next section for discussion of prescription drug dependence). It is important to note however that because a user must perceive their behaviour as dangerous or problematic to receive a diagnosis of abuse,

many potentially hazardous medication uses (e.g. infrequent medication use in a polysubstance context) may not be adequately assessed with these criteria.

Dependence

According to the *DSM-IV* [47], substance dependence is defined as a compulsive pattern of substance use characterized by a loss of control over substance use and continued use despite the significant substance-related problems. The diagnostic criteria for dependence require the presence of three or more of the following symptoms: tolerance (i.e., the need to use increased amounts of substance for effect or a diminished effect with use of same amount), withdrawal, taking the substance in greater amounts or over a longer period of time than intended, unsuccessful attempts to cut back use, spending excessive time procuring, using, or recovering from the effects of the substance, giving up important activities in order to use the substance, and continued use of the substance despite evidence that it is causing serious physical and/or psychological problems. When the diagnostic criteria for dependence are met and symptoms of either withdrawal or tolerance are present, the dependence diagnosis can be further specified as involving 'physical dependence' on the substance.

Development of dependence typically requires prolonged and sustained exposure to a substance. In many cases this can occur when the medication is taken exactly as prescribed and in the absence of intentional misuse (e.g., opioid pain management during hospital care [58]; use of benzodiazepines for the management of anxiety disorders [31]). Alternatively, many individuals who develop tolerance to the same psychotherapeutic medications do so completely outside of a legitimate context. For example, illicit drug users may habitually use a prescribed opiate medication as a substitute for an illicit drug that is more expensive or difficult to obtain, such as heroin. Individuals who become dependent on a medication during the course of treatment for a *bona-fide* medical or psychiatric condition might be expected to differ from those developing dependence through varied forms of illicit use in terms of their risk factors, and symptom expressions. Evidence suggests that individuals who develop symptoms of dependence during the course of a legitimate treatment appear to be particularly prone to the development of some symptoms (e.g. use for longer periods than intended; withdrawal upon cessation) but not others (e.g. dose escalation due to tolerance), while this different susceptibility to symptoms does not appear to occur in recreational users [29, 59]. Moreover, although past research has linked dependence on analgesic and anxiolytic medications to distinct diagnostic [31, 32], personality [59], and demographic features [27], due to the existence of distinct pathways to dependence, it is not clear to what extent these factors are associated with the pathologies the medications are intended to treat or with the propensity to deliberately misuse the medications. Because different pathways to dependence may be associated with distinct risk factors and symptom expressions as well as having different optimal targets for treatment, information about the pathogenesis of symptom development is of considerable clinical importance. Unfortunately, to date, the vast majority of studies of prescription drug dependence fail to distinguish among different possible trajectories to symptom onset.

A-NSDUH CRITERIA

Perhaps the most widely cited source of datum used to define and describe inappropriate medication misuse in the Americas is the National Survey on Drug Use and Health (A-NSDUH). The A-NSDUH is an annual epidemiological study that, in part, documents the non-medical use of prescription stimulant, analgesic, anxiolytic, and sedative medications in a civilian, non-institutionalized American population aged 12 years or older [9]. It is important to note that the A-NSDUH was formerly known as the National Household Survey of Drug Abuse (NHSDA); however they represent two different surveys and thus cannot be directly compared]. The data collected through this survey is publicly available for research purposes and it has been used extensively in recent years to describe the prevalence and patterns of prescription drug misuse in the United States [8, 27-28, 30, 32, 34, 45]. For A-NSDUH purposes, prescription drug misuse is defined as "use of the target medication (or class of medications) without a prescription or that was taken only for the experience or feeling the medication causes", while DSM IV criteria for substance abuse and substance dependence are used to infer problematic use. Thus, the A-NSDUH criteria encompasses each of the more specific criteria discussed in detail above.

Unfortunately, however, although broader in its overall coverage, the A-NSDUH retains perhaps the most serious limitation of more specific conceptualisations of prescription medication use in that it does not adequately distinguish between inappropriate medication uses for therapeutic *vs* recreational purposes, or among most forms of recreational use (the A-NSDUH currently collects limited data about the intravenous use of some substances but no information is collected about other routes of administration or about simultaneous polysubstance use). In addition, because A-NSDUH prevalence data is typically reported in terms of 'any use' during a particular timeframe, vastly different behaviors and patterns of use can be given the same weight for determining overall rates of misuse (e.g. a solitary non-prescribed therapeutic oral dose of codeine is treated in the same way as chronic intravenous administration of OxyContin when determining the rates of analgesic misuse) making it difficult to interpret the clinical significance of the findings. Interpretation of A-NSDUH data may also be limited by a degree of ambiguity in exactly what constitutes "use of the medication for the experience or feeling it causes" as the A-NSDUH does not specify what it includes [36]. Does it include using a prescribed medication at a higher than recommended dose, or using a medication to counteract the effects of another substance? What about using a medication appropriately to "experience" relief from a condition for which it is prescribed or to "feel" better? The A-NSDUH leaves it for respondents to decide.

Despite its limitations, the A-NSDUH provides perhaps the most comprehensive definition for inappropriate medication use currently found in the literature, and it enables estimates of both the overall prevalence of any form of misuse medication, as well as of the prevalence of medication abuse and dependence. In addition, recent versions of this survey have begun to collect more details about certain forms of hazardous use (e.g. intravenous administration) for at least some substances (e.g. methamphetamine). Although such

efforts have not been exhaustive, and information regarding motives for misuse is currently entirely lacking, the A-NSDUH appears to have the potential to provide both vast coverage as well as some insight into more specific forms of prescription medication misuse. Because it would likely not be feasible for the A-NSDUH to systematically examine every possible form of inappropriate medication use, it is important that the most prevalent, pervasive, and/or harmful forms of misuse are identified through examining targeted populations so that their inclusion in larger scale studies can be justified.

CONCLUSIONS

Given the wide range of behaviors and characteristics that can be considered inappropriate medication uses, as well as the ever-growing array of psychoactive medications that may be liable for misuse, it may prove difficult to achieve both complete coverage and specificity for all potentially clinically relevant forms of misuse within the same assessment instrument. There are innumerable potential ways a medication can be misused in a polysubstance context by an individual. And for each combination of substances there may be variations in the routes of administration as well as in the user characteristics (e.g. prescribed users *vs* non-prescribed users) and in the motives for use (e.g. to increase intoxication *vs* medication of unpleasant side-effects). Thus it may not always be feasible to systematically examine all possible combinations of medications, administration patterns, user characteristics, and motives for use in the same investigation. Moreover since certain methods of data collection do not easily lend themselves to delineating such details (e.g. self-report questionnaires) and other approaches may be time and/or cost prohibitive (e.g. in-depth semi-structured interviews), it may not be reasonable to expect that all investigations will be able to provide the same degree of coverage or specificity. However, it is important, irrespective of the approach used, that all operational definitions are clearly stated, that the precise meaning of the terms used in the study are specified, and that the limits to the generalizability and specificity of findings be clearly and directly acknowledged.

Because many inappropriate medication uses may include non-sanctioned therapeutic usage as well as use for recreational/intoxicating purposes, it is also important that, whenever possible, efforts be made to distinguish between these potentially distinct clinical populations. Knowledge of why an individual is misusing a specific type of prescription medication can be critical for targeting prevention efforts as well as for designing the most effective interventions. An individual who developed dependence on a prescription anxiolytic in the context of treatment for an anxiety disorder presumably has a very different trajectory to dependence as well as very different treatment needs for discontinuing this medication [60] than does an individual who developed dependence on a prescription anxiolytic in the context of polysubstance abuse (e.g., use of the anxiolytic to manage unpleasant side effects of stimulant drugs). In fact, recent research suggests that matching treatments to the underlying motivations for substance misuse improves treatment outcomes for those with substance use disorders, including for those with prescription drug abuse/dependence [61, 62].

Another issue, which is beyond the scope of this review, although pertinent to note, is the health care system's contribution to prescription drug misuse. Misuse of psychoactive medications, particularly in the case of prescribed users, may not only stem from individual factors, but from a lack of quality health care service. According to the *Agency for Health Care Research and Quality*, quality health care means, "doing the right thing at the right time, in the right way, for the right person-and having the best possible results" [63]. Health care providers may play a role in prescription drug misuse behaviors through disregard for this quality of care (e.g., failing to recognize a patients' potential for developing a substance abuse/dependence disorder, misdiagnosing the patient, over-prescribing the medication; see a journal article by Chasin and colleagues [64] for a broad description of the problems surrounding provision of quality health care). In acknowledging the health care system as an additional contributing factor to prescription drug misuse, in addition to the extensive conceptualization problems involved in defining individuals' prescription drug misuse addressed in this review, prescription drug misuse clearly emerges as a complex phenomenon that requires much additional research attention.

Key Learning Objectives:

1. To become familiar with different commonly used operational definitions for prescription medication misuse.
2. To gain knowledge about the different user characteristics, and medication-related behaviors and problems that are sometimes used to define prescription drug misuse.
3. To identify strengths and limitations of different conceptualizations of inappropriate prescription drug use.
4. To understand the clinical importance of assessing different potential motives for non-sanctioned medication use.

Future Research Questions:

1. In what ways can one achieve both breadth and depth of coverage when attempting to define and characterize prescription drug misuse?
2. What are the clinical implications of different forms of misuse?
3. To what extent would systematically identifying the reasons for misuse improve prognosis and treatment planning?

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