

Precision in Addiction Care: Does It Make a Difference?

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This perspective article explores the possibilities of precision in addiction care — even better individually fitted or tailor-made care — and examines what changes we need to make in order to realize sensible progress in epidemiological key figures. The first part gives a short review on the development of addiction care and tries to answer the question of where we stand now and what has been achieved in addiction science through the development and evaluation of interventions in the past decades. Following this analysis, attention will be paid to what lies ahead. This second part focuses on the question of how addiction care can deal with the consequences of the emerging paradigm of personalized or precision medicine, which is based on the fundamental assumption that individual differences matter. Finally, some limitations and conditions as well as tasks and goals for progress are raised. In conclusion, it is argued that integration of addiction care in (mental) health care in the future is desirable.

INTRODUCTION

Substance use disorders abound in every country. While the numbers are mostly blurred by cultural, political, or methodological reasons, estimates indicate that a substantial proportion of the population in Western countries is addicted or demonstrates “heavy use over time” [1]. It is striking that only a minority of these users receive help, which means that considerable under-treatment occurs. On the other hand, individuals could also recover in a natural or spontaneous way without any treatment [2]. The idea that addiction is a chronic disorder, which persists throughout life, is not supported by epidemiological research. Although relapse is inherent to addiction, the same applies for maturing-out [3].

Much comorbidity with other mental disorders prevails, as well as a number of misdiagnoses, treatment at a relatively late stage (often as a result of stigmatization, lack of facilities, and professional incompetence), and, in many cases, inadequate treatments due to a lack of efficacious therapies. Combined, these factors indicate that there is room for improvement.

Addictions, or dependency on substances, encompass a specific type of mental disorder. There are many risks and vulnerabilities that can predict the emergence of

a mental disorder [4], addictive behavior [5], or a chronic addiction with all the characteristics of a disease, but this is mostly preceded by a long sequence of rewarding acts. Many adolescents experiment with drugs due to their participation in a subculture or peer group in which the substance use is part of their identity search. Adults can often gradually become addicted to alcohol after too much social drinking for 1 decade or more. Knowledge about risk factors is the starting point for prevention programs for specific groups [6,7].

Problems frequently arise after the emergence of co-existing social, legal, mental, or physical problems [8]. Prescription drugs can also become addictive, even when they are not used illegally. Regardless of the way one becomes addicted, a voluntary dimension is nearly always inherent to use and misuse, motivated by psychological patterns of learning and reinforcement. Unfortunately, this truism has frequently harmed the search for and implementation of psychological and medical treatment and unbiased social (or judicial) rehabilitation. Prejudices and/or social stigmas that make users think their misery is their own fault has frustrated addiction care for a long time.

Different countries tackle the problem of addiction differently. Individual countries face their own chal-

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†Abbreviations: AA, Alcoholics Anonymous; NNT, Number Needed to Treat

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lenges; for example, many Eastern European countries have outdated psychiatric hospitals, and the situation in developing countries is even worse. Yet despite the enormous organizational problems and challenges, there has been tangible progress in addiction care.

In order to make progress in addiction science and practice, this paper will elaborate on three major themes: the possibilities (and opportunities) for improving precision in diagnosis, prognosis, and treatment indications (preferably at an early stage). Oncology is taken as an example to discuss what can be learned regarding clinical staging, profiling, and the necessity of acquiring knowledge about individual specific mechanisms in order to best match the patient with an appropriate treatment. First, a short review of the development of addiction care will be given. The focus of this paper is on addiction to alcohol and illicit drugs; if necessary, the interrelationship with other forms of addiction will be mentioned.

WHERE DO WE STAND?

Throughout the last century, scientific knowledge about addiction has increased dramatically. We have successfully identified physiological, psychological, and social theories about crucial determinants of substance use and addiction.

The scientific basis of addiction care in the European countries was weak until the 1980s, due to a lack of research facilities and scientists' interests. Therefore, no empirically based addiction medicine science was developed. Addiction care was, at best, based on professional insights and experiences. A more positive picture was found in North America, where research facilities already existed shortly after World War II [9].

A special mention should be made of Elvin Morton Jellinek (1890-1963), who not only designed the first comprehensive medical model of addiction, but also initiated epidemiological research. He identified five subtypes of alcoholism and characterized them together in a stage model [10]. Jellinek was ahead of his time, although most of his proposals are no longer relevant.

In many developed countries, there is a broad spectrum of professional treatment facilities, including prevention programs, for different target groups. Besides alcohol and illicit drugs, treatment is also available for some legal substances, such as tobacco, and a number of addictive behaviors. For years, addiction care was comprised of a combination of "moral pedagogy," well-meant advice, and social work. A sometimes forgotten form of care is Alcoholics Anonymous (AA†), established in 1935 and still active today [11]. In many countries, AA groups function, mostly for ideological reasons, entirely on their own. In retrospect, it can be considered one of the first steps in a patient's "perspective of recovery." The 12 steps of AA that have characterized its philosophy since its foundation are, in essence, also incorporated in treatment facilities.

Scientific Progress

The last 25 years can be characterized as a quantum leap in the knowledge about addiction, especially the psychological and neural support thereof, and the discovery of a series of targets for efficacious interventions. For the most part, the neurobiology of addiction was unknown for a long time. Today, we have detailed knowledge about the neuro-circuitry of addiction, such as the reward system and the role of dopamine. We now also understand how addictive substances act on the brain and how they influence the functioning of the cognitive and affective processes [12,13,14]. This new knowledge has resulted in a rather comprehensive assessment of the mental functions and the emergence of dysfunctions, which are related to addiction processes.

The reward circuitry was discovered through experiments with rats since the 1950s. Olds and Milner identified the pleasure center of the brain [15]. The neurobiologist Wise was among the first to describe the reward circuitry in the brain and the pivotal role that dopamine plays [16]. This research laid the foundation for the neurobiological research on the effects of drugs on the brain. Wise showed that addictive drugs caused an increase in dopamine in a certain brain core, the nucleus accumbens. In addition to the neurobiological research in animals, there has been a strong development in research in the human model in recent years. The application of neuroimaging techniques created the possibility for a far more detailed picture of the structure and function of the brain and brain circuits than was available previously. It also provided insights into the effects of addictive substances on the human brain. Volkow, president of the National Institute on Drug Abuse, has set the tone for this type of research [14].

An important contribution is Robinson and Berridge's *incentive sensitization theory of addiction* [17]. It highlighted the role of affective processes in addiction and how *liking* gradually turns into *wanting*, such as craving, loss of control, and fewer natural rewards. Jentsch and Taylor [18] built upon this and provided evidence that the cognitive impulsivity related to addictive behavior is associated with dysfunction of the frontostriatal system. Later on, Koob identified the development of the aversive emotional state as the driver for the negative reinforcement of addiction [19]. He defined it as the "dark side" of addiction. Furthermore, he focused on the effect of substance abuse on the executive functions and the impairment that emerges in self-regulation. George and Koob [20] hypothesized that drug addiction involves a failure of the different subcomponents of the executive systems responsible for the mental functions with which people consciously control their behavior. These components are essential to the cognitive control of processes that are part of addiction: reward, pain, stress, emotion, habits, and decision-making. The authors assume that the differential vulnerability in one or more of the executive system's subcomponents is predictive of the individual differences in the course of addiction. These

neuropsychological theories soon will be implemented in programs that try to restore executive functions.

It is believed that dysregulation of the reward circuitry is a common factor in many addictions, including behavioral disorders such as gambling or obesity.

Progress in Therapeutic Strategies

An impressive number of evidence-based strategies for the treatment of people with a diagnosis of addiction [21,22], proven strategies for early detection and intervention [23,24], and many prevention strategies [25,26] have been found. In addition, education for physicians, psychiatrists, psychologists, nurses, and social workers who are active in this field has significantly improved. Nevertheless, we cannot boast of statistics that demonstrate an incremental decrease of the incidence or prevalence of addicted people [27,28,29]. Of course, many external determinants (e.g., national policies, drug trafficking, social-economic conditions) influence these figures.

Pharmaceutical Interventions

The repertoire of medication that can be used to treat severe addiction problems has grown over the last decades [30]. However, these medicines are only supportive, and they are not effective enough to make a big difference. Aversion drugs or aversion therapies were “en vogue” in folk medicine or so-called quackery medicine. They did not work or at best worked as a placebo. Disulfiram (thiramdisulfide), discovered in Denmark in 1947 and still in use, changed this [31]. This substance is a deterrent; it disturbs the metabolism of alcohol, not directly the desire to drink. The discoveries of naltrexone hydrochloride (for alcohol and opioid dependence) or acamprosate (for alcohol and benzodiazepine dependence) were more important. They target the addiction process directly; they change systems for motivation and how the brain controls impulsive behavior. Some other medication is available or currently being studied [32] (including those for emerging behavioral addictions [33]). These drugs support abstinence, for example, by decreasing a user’s craving. A pharmaceutical approach has many benefits, such as low costs and a potentially wide application in general practice. However, as a sole form of therapy, which is not embedded in a broader context and therapeutic relationship, these drugs risk losing their therapeutic value.

Substitution treatment of drugs is a special case. Experiments with the prescription of methadone for opioid dependence started in New York in the early 1960s [34]. Since then, many countries have implemented methadone maintenance programs. A more radical, strongly controversial form of substitution is the medicinal prescription of heroin. In a limited number of countries, this has been legalized after well-researched (United Nations-supervised) experiments. In the Netherlands, for example, heroin is a registered medicinal drug, and addicts can use it in some strictly organized facilities on a daily basis, 3 times a day if necessary [35]. In some countries, the medically regu-

lated supply of alcohol (e.g., in sheltered housing) is another accepted form for the “regulation” and social and medical monitoring of the addictive behavior of chronically addicted people [36].

Psychological Interventions

In many respects, over the last 30 years, psychologists have been especially competent in translating theory into practice. Perhaps the most important improvement in addiction care was the arrival of the many cognitive behavioral therapies based on social learning theories. They are currently broadly implemented. Motivational interviewing [37], a counseling approach for exploring and encouraging behavioral change to rebuild a regular life, has also increased the efficacy of addiction care. It has successfully pulled addiction care within the realm of mental health.

The combination of these psychological interventions with other (social-psychological or pharmaceutical) interventions has been well researched, for example, in the COMBINE study [38].

An Evaluation

Taking all of this into consideration, scientists and professionals in addiction care can be proud of its development. Over the last 10 to 15 years, the neuro-scientific aspects of addiction, in particular the reward system and related mechanisms, have been well researched. The addiction treatment workforce has been equipped with a vast number of interventions and guidelines that can be applied to a range of diverse groups and can be directed toward specific biopsychosocially defined targets. Specific training has enabled the addiction workforce to become increasingly competent. However, an answer to the basic question of whether this has led to observable clinical-epidemiological transitions cannot be given as the figures are lacking. Furthermore, it is debatable whether the existing options for better results are actually being implemented.

Another factor to consider is that an evidence-based intervention does not mean it works for everyone or that it will work the first time. Relapse has been shown to be the key to the failure of recovery in addiction care. While that may be true, it is also a fact that, until now, we have lacked scientifically based knowledge for an effective synchronization of the range of possible interventions to a patient’s individual characteristics [39]. In addiction treatment, the timing of interventions is a huge problem: late-stage treatment is still the modus.

The available therapeutic instruments to make addiction care effective are of great importance. The question remains whether we can discern a gradual progress that is mirrored by epidemiological data. How can we make real progress?

WHAT LIES AHEAD OF US?

Personalized or individualized medicine is gaining popularity [40]. This is especially seen in oncology [41]. However, there are also great opportunities for more pre-

recision in psychiatry and addiction care. This implies a targeted focus on the patient's individual characteristics and a better selection of treatment strategies to increase positive outcomes and reduce misdiagnoses and costs. It is important that the possibilities of precision in addiction care are explored in combination with a focus on prevention, early treatment, participation of patients and relatives, and a proactive attitude from clinicians and their organizations. Clearly, addiction differs from cancer or other somatic diseases, but the addiction care field can learn from the progress of clinical oncology. For example, how did that field organize knowledge management, clinical research, a focus on early treatment and individual specific mechanisms of disease, and how did it raise funds for research? More particularly, how did oncologists and their organizations collect data to demonstrate gradual progress in the treatment of common cancer types in many developed countries?

Differences Matter

An important insight garnered from modern fundamental research is the recognition that human biosystems, not just the brains, differ from each other at every discernable level. This manifests itself in several developmental trajectories. Consequently, different disease states are the rule, not the exception. This implies that it would be a miracle if standardized treatment strategies would work for everyone at every stage and that patients with the same diagnosis would respond in the same way. In clinical research, this idea is reflected in the *Number Needed to Treat* (NNT): an epidemiological measure that estimates the number of patients who need to be treated in order to have an impact on one of them (e.g., 6 months of abstinence).

In general, addiction care and medicine share a lack of treatment strategies that work for all individuals. Clinicians cannot be blamed for this deficit; it only demonstrates the need to be more precise in our clinical research and predictions. Evidence-based guidelines derived from the results of clinical trials are still very limited. Trials mostly focus on averages of groups of patients compared to groups that receive another intervention or a placebo. In reality, however, we treat individuals, and therefore it is possible that a less effective strategy (from a group perspective) is an ideal strategy for a minority of patients. Some may even react unfavorably to the "most effective" strategy. From this perspective, many meta-analyses are misleading because they have been conducted to strictly compare the numerous types of interventions. These analyses inform us about average differences, but their predictive value for the outcome of a specific patient with very particular characteristics is insufficient. This observation does not disqualify the effectiveness of the aforementioned strategies as such. For many people, the "most effective" treatment strategy can work excellently, especially if we have additional information about dosage, timing (stage of the disease process), and other proven

predictors (e.g., age of onset, treatment history) that can support clinical or therapeutic decisions.

In summary, we need evidence-based strategies and predictive instruments that provide support to adequately select treatment options or prevention programs. For example, genetic tests can aid pharmacotherapy decision, and brain scans can be used to inform decisions about specific forms of counseling or therapy. If these are at our disposal, the NNT of specific interventions can become more favorable, the number of disappointed patients and therapists can be reduced, costs can be reduced, and gradually the results will increase. In the realm of addiction care, this sounds very optimistic. Evidence-based treatment interventions have become available only recently, and the rate of implementation is still rather low. From a professional point of view, this is not satisfactory. However, the strategies we have and can implement are not enough, and there are strong arguments to pursue further steps.

Improvements in Outcome

There are a number of themes that need to be discussed if a gradual improvement of addiction care outcome is our goal: precision, more data, a proactive approach, and public participation. First, we need more *precision* in our work, in how we formulate diagnoses, prognoses, and an indication for treatment. Therefore, we must collect and utilize a significant amount of general and individual data about the differential profile of addicted patients and make these available for clinical application. Of course, accuracy and a focus on the individual patient are the *sine qua non* for every form of treatment. However, the instruments and expertise that we need to be precise and predict which therapy or therapeutic principles will work in individual cases are still lacking. Trial and error based on professional experience of the therapist or clinician is the norm. We need biomarkers that can help in the selection of which pharmacotherapy should, and should not, be recommended to a given patient. This argument can be extended to other examples: the selection of specific variants of psychotherapies or psychosocial interventions or combinations of diverse treatment methods, especially when comorbidity has complicated the clinical picture. Unfortunately, our knowledge of this is not yet sufficient. If we focus our research on individual differences, effectively explore the existing databases, and develop tools that combine available information about the effectiveness of treatment with the characteristics of individuals or subgroups, personalized addiction care will be within arm's reach.

Some examples illustrate how close we are already. Data from a randomized controlled trial can be reused, which means that higher impact scores can be found. Hendriks et al. [42], for example, studied the effect of two methods for the treatment of cannabis dependence. These methods were almost equally effective at group level. However, when considering subgroups and the related moderators, they found major differences. If, in a treatment directive, a clinician would choose just one method

that is more effective or when a financier would like to reimburse only the cheapest procedure, they can completely miss the point. This calls for a more precise look at the variables on the level of sub-groups that determine the intended treatment effect. Preferably, this is even done at the individual level, to determine where and when an impact occurs — or, when it does not, to deduce that a treatment is pointless or is ultimately counterproductive.

Karpyak et al. [43] replicated the association of genetic markers with the length of abstinence in acamprosate-treated alcoholics. If these findings prove to be useful in the treatment selection and if the underlying mechanisms can be traced, this is an interesting example for personalized addiction care. Batki and Pennington [44] have given other examples related to the individualized pharmacotherapy of alcohol use disorder. Bierut et al. [45] explored the future treatment for smoking cessation, and Lee et al. showed that in order to establish a better outcome in methadone maintenance treatment programs, a personalized approach seems necessary [46].

Particularly interesting is the recent neurocognitive perspective that Noël et al. [47] used to approach addiction as an interaction of three neural systems: a system for impulsive reactions and habits; a system for the monitoring of physical states and processes; and a system for reflection, planning, and impulse control. Together, they determine the extent to which self-control is realized. The model theoretically predicts that a dysfunction of one of these three systems would indicate the need for a specific type of treatment. It also predicts which system was probably dysfunctional based on which treatment was successfully applied. It is a fine example of the way in which as much precision as possible can be achieved in substance abuse treatment.

Second, for more effective, personalized addiction care, we need more data about biological parameters that can be used as biomarkers, individual characteristics, and short- and long-term outcomes. When this is combined and well researched, it can inform clinicians about treatment decisions that make a difference in terms of outcomes. Longitudinal data is also urgently needed. Due to the many individual differences and combinations at stake, huge databases are needed to gain statistical power. Nonetheless, these can only be achieved if health care centers cooperate, preferably on an international scale, with academic research networks. Big data is needed to observe subtle (e.g., genetic) differences, which can be overlooked in relatively small samples.

Third, we need to emphasize the need for and encourage the implementation of already available evidence-based interventions for *prevention*, *early detection*, and *early intervention*. Most addicts became involved with the (excessive) use of tobacco, alcohol, or drugs during adolescence. Given the knowledge that other mental health disorders manifest themselves during early youth or adolescence, as well, this indicates that the risk for entanglement of addiction and other forms of psychopathology is

very high during that period. Therefore, it is highly important to look *proactively* for new strategies and/or possibilities to implement already proven methods in order to intervene at an early stage, preferably before a clinical disorder can fully manifest. The ongoing shift toward personalized medicine can support prevention efforts if we can better predict which individuals are at higher risk for addiction and may or may not profit from a preventive intervention.

Fourth, the aforementioned proactive approach among professionals has to be combined with more public *participation* in prevention and programs for early intervention and client participation (including relatives) in care centers. It is an illusion that salient progress in epidemiological key figures can be made if depending on professional responsibility only. It is certainly true that participation, especially in this subject, cannot be easily increased. Many young people have “good reasons” to stay involved in peer groups that take drugs for the expression of their identity. More generally, drug use and alcohol addiction are substantially stigmatized or discriminated. This keeps many from being open about their issues, which increases the risk of waiting too long before asking for help or considering taking measures. Personalized medicine is more likely to be realized if patients are prepared to collaborate with data sampling. Moreover, if a personalized approach becomes the rule, we can expect that individuals will be more willing to ask for help, preferably at an earlier stage.

In addiction care, more precision (and participation) could imply higher average treatment effects, even with the existing repertoire of interventions, if we can better predict which person in which situation will profit from which type of intervention, or a mix thereof. It could increase compliance and hopefully the willingness to ask for help at an earlier stage. Predictors for success could be a rise of substance abusers in addiction care facilities at an earlier stage, shorter treatment duration, more compliance with the proposed treatment options, and a decrease in resistance to treatment.

Limitations and Conditions for Progress

However, the previously mentioned possibilities will not happen automatically. One can think of many obstacles that will emerge when we take precision in addiction care seriously, we try to act at an early stage, and promote participation of clients, relatives, and the general public in the implementation of health objectives related to alcohol and illicit drugs.

We stand, in scientific respect, at the start of a struggle to adapt research programs in such a way that they generate clinically relevant knowledge for specific individuals with complex problems. This means that the design and organization of trials have to be adjusted. Multi-center research should become the norm, so that greater databases can be created. The research populations must be narrowly specified in order to enrich the validity of the outcomes. Finally, we have to analyze the data in

such a way that we gain some deeper understanding of the responses of subgroups, or even specific individuals. Knowledge about significant differences between types of interventions is not enough to inform clinicians of what to do in specific cases. It is plausible that the continued participation in (abstinence-oriented) rehabilitation programs is an unintentional result of lack of understanding regarding who has or has not had an opportunity to become abstinent. Besides, the risks of possible physiological damage when detoxing (kindling effect [48]) or binge drinking [49] repeat themselves again and again. Moreover, an addict can perceive every relapse as a disappointment that decreases his or her self-confidence.

Hurdles to Clear

Besides these scientific and therapeutic issues, there are political, juridical, and financial obstacles varying from country to country to be cleared before personalized addiction care will be realized in the future. In some cases, law enforcement is so dominant that people scrupulously hide their drug use, while an open approach is indispensable for prevention, crisis management (overdoses), and early intervention. It could be argued that a strong prohibitive policy has prevented many people from getting involved in drug use, while at the same time the minority of heavy users face severe health risks because they are isolated and stigmatized and risk criminal penalties [50]. An important solution to this is to differentiate between the involvement in production and trade versus the possession of drugs for personal consumption. A similar policy has been enforced in The Netherlands since the 1970s [51]. Factors that hinder regular addiction care now may be even greater obstacles for a personalized approach.

At the conceptual level, there is an ongoing debate on the nature of addiction. The definition of addiction has had very strong moral connotations, although a medical definition of addictive behavior (including references to hereditary aspects) is nothing new. What is new is the definition, since the end of the 20th century, of addiction as a brain disease. It is probable that with an article in *Science*, Alan I. Leshner [52] has created a new “neuro-paradigm,” which has resulted in a switch in many (especially medical-biological) research programs. The possible disadvantage of this focus on the brain and other biological aspects, such as genetic factors, is that it did not motivate addicts to ask for help or therapy on time. Demotivation is risked when people believe that their habit is biologically determined. Addiction care must take biological aspects into consideration, but this has to be complemented with a focus on psychological, social, cultural, and other aspects. Addiction is, moreover, an atypical brain disorder, as many addicts have successfully demonstrated an ability to overcome their disorder after they have decided to do so. Humans think, feel, act purposefully, are active in social and cultural domains, and potentially achieve a high level of self-regulation. If we want to create solutions for addictive behaviors and addicts, we have to take all of

these levels into account. Reductionism to one specific level is insufficient.

The public message about the nature of addiction should be adapted in such a way that it increases the chance of a personalized approach.

Tasks and Goals for Progress

We need to reach local, national, and, if possible, international consensus on achievable targets for making progress in addiction care. These can be divided into long-term, short-term, and medium-term goals. First, we have to define long-term goals that relate to what we, in cooperation and agreement with a range of partners, think can be achieved in terms of the improvement of addiction (e.g., general numbers on incidence and prevalence of addictions, the reduction of number of people with Korsakoff’s syndrome, the limitation of somatic or psychological comorbidity, etc.) It is the specialists’ task to formulate realistic but ambitious targets. This can succeed only when entrepreneurial institutions consult with researchers, governments, funders, patients’ organizations, and other stakeholders to set realistic goals (for the next 15 years). Laws and regulations may need to be adjusted, while the structure and working methods of the institutions also should be drastically changed.

Second, we need short-term goals. Here, the aim is to give meaning to the often very abstract notions about more exact, more personal, and more focused work and how we can quickly lay the practical foundation for the arrival of new working methods such as more precise diagnostics and forecasting or predictive methods for treatment indication. It is quite possible that we will not be able to indicate this very specifically. We do not know what we would initially need to achieve this. For this reason, it is important to directly exploit all available opportunities. The field should make a database of the new possibilities for precision in addiction care, which will gradually occur. Much can already be achieved when the dropout rates (and no-show rates) are significantly reduced.

Third, we need medium-term goals aimed at creating the conditions and creating or raising the resources to enable the long-term goals to be reached. Developing these resources, collecting essential data, and conducting experimental research is partly a task for regional institutions. It is also partly a matter of waiting and seeing what other professionals develop and test. The scientific literature hints at new interventions and more precise diagnostic and prognostic methods. Still, the practical application of such knowledge can often take years.

Integration in (Mental) Health Care

A specific medium-term goal that can be achieved is the integration of addiction care in mental health and integration of mental health in health care. In the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders*, addiction is classified as a mental disorder and therefore deserves to be approached as such. Addiction

disorders and mental disorders are primarily separated theoretically, and there are many arguments and growing evidence in favor of the integration of care centers and their specific treatment strategies [53]. The relative separation of addiction care from mental health care systems has historical roots, while scientific insights argue for integration [54,55].

Mental disorders (including addiction) are health issues. Therefore, they cannot be separated from somatic processes [56]. Most international organizations and professionals have accepted this point of view. Of course, medical care is part of addiction care or mental health guidelines. Nevertheless, a separated development has had some disadvantages. It has unintentionally maintained the under-funding of mental health programs, separated the mind from the body, and continued the dramatic stigmatization of people with mental disorders or addictions. Mental disorders may not be reduced to somatic illnesses; they have unique characteristics that need specific approaches. However, somatic comorbidities are frequent in patients with mental health problems, so integration of mental health and addiction care with medical care is essential [57].

This does not mean that the medical profession (physicians, psychiatrists, nurses) supplies the most ingredients for effective addiction care. On the contrary, psychologists and social workers are very important in making a difference to the outcome of addiction care. Therefore, the suggestion of integrating addiction in mental health care and mental health care in medical care does not underestimate the many social implications of mental or addictive disorders. In a biopsychosocial approach, facilities for social work should form an integral part of the care system, as should the cooperation with self-help organizations and the involvement of families.

CONCLUSION

In more than 100 years, much has been achieved in addiction care. A number of evidence-based interventions have been discovered, and the understanding of the neurobiological and neuropsychological mechanisms of addiction has increased. Despite this, the key epidemiological figures have not changed. We are faced by new challenges today: to achieve better results that are epidemiologically measurable and show that more specific addiction care contributes to our general health. This indicates a need for more precise and personalized treatments, in which evidence-based interventions can be better tailored to the individual characteristics of addicted people. In addition, we need efficacious prevention and early intervention programs that make a difference. In order to accomplish this, we need to reach a consensus about goals and specific programs.

REFERENCES

1. Rehm J, Marmet S, Anderson P, Gual A, Kraus L, Nutt DJ, et al. Defining substance use disorders: do we really need more than heavy use? *Alcohol Alcohol*. 2013;48(6):633-40.
2. Schippers GM, Broekman TG. The course of alcohol dependence; the course of drug dependence. State of the art reports for ZonMw Program Addiction. Den Haag: ZonMw; 2006.
3. Heyman GM. Quitting drugs: quantitative and qualitative features. *Annu Rev Clin Psychol*. 2013;9:29-59.
4. Risks to mental health: an overview of vulnerabilities and risk factors. Background paper by WHO secretariat for the development of a comprehensive mental health action plan. World Health Organization [Internet]. 2012 Aug 27. Available from: http://www.who.int/mental_health/mhgap/risks_to_mental_health_EN_27_08_12.pdf.
5. Stone AL, Becker LG, Huber AM, Catalano RF. Review of risk and protective factors of substance use and problem use in emerging adulthood. *Addict Behav*. 2012;37(7):747-75.
6. Drugs, Brains, and Behavior: The Science of Addiction. National Institute on Drug Abuse [Internet]. 2014. Available from: <http://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/preface>.
7. World Drug Report. United Nations Office on Drugs and Crime [Internet]. 2015. Available from: https://www.unodc.org/documents/wdr2015/World_Drug_Report_2015.pdf.
8. Comorbidity: Addiction and Other Mental Illnesses. Research Report Series. National Institute on Drug Abuse [Internet]. 2010. Available from: <https://www.drugabuse.gov/sites/default/files/rcomorbidity.pdf>.
9. Smith DE. The evolution of addiction medicine as a medical specialty. *Virtual Mentor*. 2011;13(12):900-5.
10. Jellinek EM. The disease concept of alcoholism. New Haven: Hillhouse; 1960.
11. White WL. Slaying the dragon: the history of addiction treatment and recovery in America. Bloomington, IL: Chestnut Health Systems; 2014.
12. Koob GF, Simon EJ. The Neurobiology of addiction: where we have been and where we are going. *J Drug Issues*. 2009;39(1):115-32.
13. Wise RA, Koob GF. The development and maintenance of drug addiction. *Neuropsychopharmacology*. 2014;39(2):254-62.
14. Volkow ND, Baler RD. Addiction science: uncovering neurobiological complexity. *Neuropharmacology*. 2014;76 Pt B:235-49.
15. Olds J, Milner P. Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. *J Comp Physiol Psychol*. 1954;47(6):419-27.
16. Wise RA. Addictive drugs and brain stimulation reward. *Annu Rev Neurosci*. 1996;19:319-40.
17. Robinson TE, Berridge KC. Review. The incentive sensitization theory of addiction: some current issues. *Philos Trans R Soc Lond B Biol Sci*. 2008;363(1507):3137-46.
18. Jentsch JD, Taylor JR. Impulsivity resulting from frontostriatal dysfunction in drug abuse: implications for the control of behavior by reward-related stimuli. *Psychopharmacology (Berl)*. 1999;146(4):373-90.
19. Koob GF. Negative reinforcement in drug addiction: the darkness within. *Curr Opin Neurobiol*. 2013;23(4):559-63.
20. George O, Koob GF. Individual differences in prefrontal cortex function and the transition from drug use to drug dependence. *Neurosci Biobehav Rev*. 2010;35(2):232-47.
21. Marsch LA, Dallery J. Advances in the psychosocial treatment of addiction: the role of technology in the delivery of evidence-based psychosocial treatment. *Psychiatr Clin North Am*. 2012;35(2):481-93.
22. Van den Brink W. Evidence-based pharmacological treatment of substance use disorders and pathological gambling. *Curr Drug Abuse Rev*. 2012;5(1):3-31.
23. Pilowsky DJ, Wu LT. Screening instruments for substance use and brief interventions targeting adolescents in primary care: a literature review. *Addict Behav*. 2013;38(5):2146-53.
24. Harris SK, Louis-Jacques J, Knight JR. Screening and brief intervention for alcohol and other abuse. *Adolesc Med State Art Rev*. 2014;25(1):126-56.

25. Borsari B. Universal prevention for alcohol use disorders: 1940-2014. *J Stud Alcohol Drugs Suppl.* 2014;75 Suppl 17:89-97.
26. Faggiano F, Minozzi S, Versino E, Buscemi D. Universal school-based prevention for illicit drug use. *Cochrane Database Syst Rev.* 2014;12:CD003020.
27. Epidemiologic Trends in drug Abuse. Proceedings of the Community Epidemiology Work Group. Volume I Highlights and Executive Summary. U.S. Department of Health and Human Services National Institutes of Health. National Institute on Drug Abuse [Internet]. 2009. Available from: https://www.drugabuse.gov/sites/default/files/cewgjune09vo11_web508.pdf.
28. Merikangas KR, McClair VL. Epidemiology of substance use disorders. *Hum Genet.* 2012;131(6):779-89.
29. Rehm J, Allamani A, Aubin HJ, Della Vedova R, Elekes Z, Frick U, et al. People with alcohol use disorders in specialized care in eight different European countries. *Alcohol Alcohol.* 2015;50(3):310-8.
30. Liechti M. Novel psychoactive substances (designer drugs): overview and pharmacology of modulators of monoamine signaling. *Swiss Med Wkly.* 2015;145:w14043.
31. Suh JJ, Pettinati HM, Kampman KM, O'Brien CP. The status of disulfiram: a half of a century later. *J Clin Psychopharmacol.* 2006;26(3):290-302.
32. Lin SK. Pharmacological means of reducing human drug dependence: a selective and narrative review of the clinical literature. *Br J Clin Pharmacol.* 2014;77(2):242-52.
33. Marazziti D, Presta S, Baroni S, Silvestri S, Dell'Osso L. Behavioral addictions: a novel challenge for psychopharmacology. *CNS Spectr.* 2014;19(6):486-95.
34. Kreek MJ, Vocci FJ. History and current status of opioid maintenance treatments: blending conference session. *J Subst Abuse Treat.* 2002;23(2):93-105.
35. Uchtenhagen AA. Heroin maintenance treatment: from idea to research to practice. *Drug Alcohol Rev.* 2011;30(2):130-7.
36. Podymow T, Turnbull J, Coyle D, Yetisir E, Wells G. Shelter-based managed alcohol administration to chronically homeless people addicted to alcohol. *CMAJ.* 2006;174(1):45-9.
37. Miller WR, Rollnick S. Motivational interviewing: helping people change. 3rd ed. New York: Guilford Press; 2013.
38. Anton RF, O'Malley SS, Ciraulo DA, Cisler RA, Couper D, Donovan DM, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. *JAMA.* 2006;295(17):2003-17.
39. Miller WR. Are alcoholism treatments effective? The Project MATCH data: response. *BMC Public Health.* 2005;5:76.
40. Fischer T, Langanke M, Marschall P, Michl S, editors. Individualized medicine. Ethical, economical and historical perspectives. Springer; 2015.
41. Jain KK. Textbook of personalized medicine. Dordrecht: Springer; 2009.
42. Hendriks V, van der Schee E, Blanken P. Matching adolescents with a cannabis use disorder to multidimensional family therapy or cognitive behavioral therapy: treatment effect moderators in a randomized controlled trial. *Drug Alcohol Depend.* 2012;125(1-2):119-26.
43. Karpayak VM, Biernacka JM, Geske JR, Jenkins GD, Cunningham JM, Rüegg J, et al. Genetic markers associated with abstinence length in alcohol-dependent subjects treated with acamprosate. *Transl Psychiatry.* 2014;4:e462.
44. Batki SL, Pennington DL. Toward personalized medicine in the pharmacotherapy of alcohol use disorder: targeting patient genes and patient goals. *Am J Psychiatry.* 2014;171(4):391-4.
45. Bierut LJ, Johnson EO, Saccone NL. A glimpse into the future: personalized medicine for smoking cessation. *Neuropharmacology.* 2014; 76 Pt B: 592-9.
46. Lee HY, Li JH, Sheu YL, Tang HP, Chang WC, Tang TC, et al. Moving toward personalized medicine in the methadone maintenance treatment program: a pilot study on the evaluation of treatment responses in Taiwan. *Biomed Res Int.* 2013;2013:741403.
47. Noël X, Brevers D, Bechara A. A triadic neurocognitive approach to addiction for clinical interventions. *Front Psychiatry.* 2013;4:179.
48. Becker HC. Kindling in alcohol withdrawal. *Alcohol Health Res World.* 1998;22(1):25-33.
49. Stephens DN, Duka T. Review. Cognitive and emotional consequences of binge drinking: role of amygdala and prefrontal cortex. *Philos Trans R Soc Lond B Biol Sci.* 2008;363(1507):3169-79.
50. Bewley-Taylor DR. International drug control: consensus fractured. Cambridge: Cambridge University Press; 2012.
51. Uitermark J. The origins and future of the Dutch approach towards drugs. *J Drug Issues.* 2004;34:511-32.
52. Leshner AI. Addiction is a brain disease, and it matters. *Science.* 1997;278(5335):45-7.
53. Mueser KT, Gingerich S. Treatment of co-occurring psychotic and substance use disorders. *Soc Work Public Health.* 2013;28(3-4):424-39.
54. Torrens M, Rossi PC, Martinez-Riera R, Martinez-Sanvisens D, Bulbena A. Psychiatric co-morbidity and substance use disorders: treatment in parallel systems or in one integrated system? *Subst Use Misuse.* 2012;47(8-9):1005-14.
55. Morisano D, Babor T, Robaina KA. Co-occurrence of substance use disorders with other psychiatric disorders: implications for treatment services. *Nordic Studies on Alcohol and Drugs.* 2014;31:5-25.
56. Ehrlich C, Kendall E, Frey N, Kisely S, Crowe E, Crompton D. Improving the physical health of people with severe mental illness: boundaries of care provision. *Int J Ment Health Nurs.* 2014;23(3):243-51.
57. Van der Stel J. Evolution of mental health and addiction care systems in Europe. In: Dom G, Moggi F, editors. Co-occurring addictive and psychiatric disorders. Heidelberg: Springer; 2015. p 13-26.