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Variety in alcohol use disorder relapse definitions: **is it time to stop using the term?**

1 Table included

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Opmerking [KW1]: Not sure if you like this, but I am increasingly just hating the term relapse and think it could be part of the discussion to just retire the term from our scientific and clinical speech?

Opmerking [ES2]: Yes agree, see my first title "...and could it be abandoned".

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Variety in AUD relapse definitions: is it time to stop using the term?

Wilco Sliedrecht, Hendrik Roozen, Ranne de Waart, Geert Dom, and Katie Witkiewitz

ABSTRACT

Objective: The definition of the concept of ‘relapse’ has been the subject of debate for decades and a semantic ambiguity highlighted in a 2016 paper remains. The current paper replicates and extends the 2016 findings on alcohol use disorder (AUD) relapse definitions.

Method: Based on the definition and application of relapse factors, 321 included papers (years: 2000-2019) were systematically appraised in patients with AUD. Relapse definitions were extracted and grouped together according to their content.

Results: A broad variety in the content of relapse definitions emerged from the extraction procedure. In 70 out of 321 included papers no definition of AUD relapse was given or could be reconstructed from the content of the original paper. Fifty-three papers made use of Diagnostic and Statistical Manual of Mental Disorders (DSM) related criteria, whereas the vast majority of the included papers (n=87) the ‘any alcohol use’ and the ‘any use of alcohol/drugs (n=13) criterion was used to label a ‘relapse’. However, multiple other definitions were used as well (n=97). Only twelve papers described in their definition the time-window of abstinence, after which a relapse potentially could occur. We observed relatively no meaningful intercontinental or time-related differences in the use of dichotomous and continuous drinking measures in the included papers, although the outcome measure ‘percent heavy drinking days’ was used more frequently in recent studies.

Conclusions: A wide variety of relapse definitions were identified. Despite decades of research and discussion, there is still no widely accepted consensus or definition on AUD relapse. We propose to shift the focus towards clinical continuous outcomes and quality of life-related criteria instead of using current dichotomous AUD relapse terminology. The impact of treatment or the natural course of AUD could be monitored by the use of course specifiers, the number of AUD symptoms present, but also measures of functioning in different life areas.

Keywords: Alcohol Use Disorder, relapse factors, remission, DSM 5, relapse definition, relapse, remission, recurrence, outcome measures, quality of life

1. Introduction

1.1 Alcohol use disorder: remission and relapse

The presence of an alcohol use disorder (AUD) can be diagnosed using the 5th edition of the Diagnostic and Statistical Manual of mental disorders (DSM 5) (Hasin et al., 2013; Robinson & Adinoff, 2016). Interestingly, the DSM 5 classification does not have the term relapse incorporated, nor defined, but it regards the disorder ‘in remission’, when no criteria (except ‘craving’) have been met for longer than a year. Besides this, the term ‘early remission’ is used, when the symptoms have been absent between a 3- and 12-month period. However, in the general course of AUD, 3-months periods of abstinence are very common (Schuckit et al., 1997). In the World Health Organisation’s (WHO) classification system of diseases, International Classification of Diseases (ICD-11), the terms ‘alcohol dependence’ and ‘harmful alcohol use’ do somewhat match DSM 5 AUD. Interestingly, the ICD-11 also does not mention terms such as ‘relapse’ (Saunders et al., 2019), but also has codes for remission, including ‘early full remission’, ‘sustained partial remission’, and ‘sustained full remission’. Full remission is defined by abstinence of 1-12 months (early) or more than 12 months (sustained), whereas sustained partial remission is defined by a reduction in alcohol consumption for more than 12 months and not meeting criteria for alcohol dependence.

However, ‘relapse’ in AUD has been frequently the focal point of past and present treatment research (Hendershot et al., 2011; Hunter-Reel et al., 2009; McKay, 1999; Sliedrecht et al., 2019; Witkiewitz & Marlatt, 2004). The achievement of ‘remission’ or ‘recovery’ is by most clinicians regarded as the ultimate treatment goal, which frequently is associated with stable abstinence or reductions in drinking (Cranford et al., 2014; Rosenberg et al., 2020; Witkiewitz, Wilson, et al., 2019). Nevertheless, research has indicated that in clinical populations ‘relapse’ has been identified as the most frequently used primary outcome variable (Hunt et al., 1971; Sinha, 2011) in individuals with AUD and substance use disorders (SUDs). Numerous researchers have advocated, that given the frequent presentation with cycles of remission and relapse, AUD has to be seen and treated as a “chronic relapsing condition”, highlighting the essential role of relapse into the conceptualisation of addiction (McKay & Hiller-Sturmhofel, 2011). This has been supported by several neurobiological findings in animal models examining reinstatement of alcohol and other drug use and in human neuroimaging studies (Koob and Volkow, 2016; Seo, Dongju; Sinha et al., 2015; Uhl

et al., 2019; Volkow et al., 2016).

1.2 Relapse definitions across studies

Over the last several decades the concept of AUD relapse has been the object of intensive study, and several theories and models have been postulated (Connors et al., 1996; Hendershot et al., 2011; Miller, 1996; Witkiewitz, 2011; Witkiewitz and Marlatt, 2004, 2007), as well as various outcome measures defining relapse, have been used (Maisto et al., 2016). In the literature various terms have been used to describe the course of an AUD. Semantic terms encompass: 'slip', 'lapse', 'relapse', 'relapse to heavy drinking', 'recurrence', 'recovery' and 'remission'. For example, the relapse definitions used in alcohol literature varied from 'one alcohol consumption' or 'any drinking' to 'drinking at least the former quantities'. Maisto and colleagues (2016) investigated the wide spectrum of definitions in the AUD treatment outcome literature, spanning the years 2010-2015 (Maisto et al., 2016). They included 139 papers, and found 25 different definitions to characterize alcohol relapse. In addition, it was found that only six studies made notice of a required time-window of abstinence after which a relapse could occur. Most studies made use of the cut-off point of 'any use' (alcohol or drugs) to determine when a relapse had happened. In four studies DSM symptom criteria were used to determine the occurrence of relapse. Furthermore, in this review only one of the included studies (Ramo et al., 2012) provided an empirical basis (referring to and building on earlier research) for the definition they had used to describe 'relapse' (Maisto et al., 2016). This definitional ambiguity, however, is not unique to AUD relapse, and there is also ambiguity for the concept of relapse in schizophrenia (Olivares et al., 2013).

Relapse definitions have often been derived from assessment instruments that measure daily use of alcohol, including the Timeline Follow-back (Sobell et al., 1996) and Form-90 (Miller and Del Boca, 1994). Daily drinking data is often summarized over specific time windows (e.g., past 30 days, past 3-months), such as percent heavy drinking days, percent days abstinent, drinks per drinking day, or drinks per day, and used as primary outcome variables in various studies reporting on the outcome of AUD interventions (Bach et al., 2019; Tonigan et al., 2017; Witkiewitz, 2011). Recent studies have advocated that favourable and acceptable outcome measures preferably should go beyond dichotomous ('yes/ no drinking') outcomes (Falk et al., 2019; Hasin et al., 2017; Mann et al., 2017; Roozen & van de Wetering, 2007; Witkiewitz et al., 2017, 2020; Witkiewitz, Falk, et al., 2019). A recent meta-analysis of

controlled clinical trials on patients with AUD showed that “controlled drinking, particularly if supported by specific psychotherapy, appears to be a viable option” (Henssler et al., 2020). It must be noted that recent research suggested that non-abstinent treatment options are still deemed more acceptable in Europa and Australia, as compared to Northern America (Rosenberg *et al.*, 2020).

Yet, the occurrence and recurrence of relapse is considered to be clinically important, and ‘relapse prevention’ interventions have been widely used in clinical practice all over the world (Donovan and Witkiewitz, 2012). Although for certain specific populations AUD is frequently considered a chronic relapsing disorder (Volkow, Koob et al., 2016) and stable abstinence might be very difficult or even unable to achieve. Owing to this perspective whereby addiction is viewed as a brain disease, Roozen & van de Wetering (2007) suggested to change the term ‘relapse prevention’ into ‘relapse management’, and consequently, they proposed a continuous assessment of relapse instead of a dichotomous approach (Roozen and van de Wetering, 2007).

Nevertheless, in a public health perspective for all-cause mortality and cardiovascular disease the importance of reducing use of alcoholic beverages in high-income countries is increasing (Wood et al., 2018). Based on these adverse or toxic characteristics of ethanol, national medical councils (e.g. see WHO’s European Action Plan to Reduce the Harmful Use of Alcohol 2012-2020) have concomitantly strongly recommended lower limits for alcohol than advised in previous guidelines (Goiana-da-Silva et al., 2019). Globally there exists a log-linear relationship between alcohol and cardiovascular adverse events that suggest to refrain from any alcohol consumption (Wood et al., 2018). Another study demonstrates: “the safest level of drinking is none” (Griswold et al., 2018, p1026). Although these findings are important to improve public health, they may also further impose a more binary ‘yes/ no’ perspective towards drinking alcohol, and with the binary definition comes the notion of any drinking as a failure for individuals trying to abstain from alcohol. Further, binary definitions may actually be counterproductive in that they perpetuate the stigma of AUD and also may reduce problem recognition and help seeking for AUD (Morris et al., 2020).

1.3 The present paper

The objective of this paper is to present an overview of current ‘relapse’ definitions, based on the secondary findings of the systematic review on AUD relapse factors (Sliedrecht et al.,

2019). The current paper is a replication and extension of the 2016 paper of Maisto et al. (Maisto et al., 2016); using a span between the years 2000-2019 including studies that reported on 'relapse'. The current review extends the Maisto paper by examining relapse definitions in the decade prior to 2010 and in the four years following 2015. Furthermore, we examined the frequency of use on 'relapse' outcomes (i.e., from dichotomous towards continuous) in this time-window. In addition, we investigated whether there were differences in relapse definitions by geographic location.

2. Method

Search strategy and data extraction

The original search algorithm is described in detail in a systematic review on AUD relapse factors (Slidrecht et al., 2019). The Slidrecht et al. (2019) review originally assessed AUD relapse determinants derived from two decades of AUD literature. Briefly, we searched three databases (PubMed, PsycINFO and the Cochrane database) with the dates of January 2000 to April 2019 for English language articles examining alcohol relapse in adult humans (18-65 years) with books and dissertations excluded. Search terms included: 'alcohol use disorder' (AUD) and relevant synonyms (e.g., alcohol dependence) were coupled with the terms 'relapse' or 'remission' using the Boolean search operators 'AND' and 'OR'. All full texts were read to extract the definition and explanation of relapse/remission/recovery terms used. We also assessed the time-window of abstinence, after which a relapse could potentially take place. In addition, we qualitatively analysed the original papers and the results on any potential difference regarding binary versus continuous outcomes among countries.

3. Results

3.1 Assessment of relapse definitions

Three hundred twenty-one papers were appraised on 'remission' or 'relapse' definitions. When no definition could be extracted, we assigned 'not applicable' (N/A). Papers were also appraised for an explanation of the given definition/description (*Supplementary material S1*). The relapse definitions were examined based on frequency, quantity, and time measures or a combination of these, and we also examined DSM III, IV or 5 definitions.

3.2 Relapse definitions

Opmerking [GD3]: I think the search needs to be updated to cover until 2020

Opmerking [WS4]: Our original review -which was the basis of the current paper- included articles from 2000-2019

Opmerking [KW5]: This isn't clear in the Table – how was abstinence versus harm reduction outcome defined? How were countries ascertained?

Opmerking [WS6]: Changed this sentence, now left out the abstinence/harm reduction remark and added S2.

An overview of the grouped relapse definitions are displayed in Table 1. An overview of the 321 distinct analysed papers, as well as a list with citations of the original research, can be found in the supplemental material (S1).

Hundred and one different definitions of relapse or remission were used in 251 (78%) of the reviewed papers. A total of 74 definitions concerned 'relapse', and 27 used the terms 'remission' or 'recovery'.

In 70 papers (22%) no definition of AUD relapse was given or could be reconstructed from the content of the paper. Several of these original papers were reviews and in several cases no overarching relapse definition was given (Castaldelli-Maia and Bhugra, 2014; Foulds et al., 2017; Garcia and Salloum, 2015; Garfield et al., 2014; Gong and Minuk, 2018; Henkel, 2011; McKay et al., 2006; Tusa and Burgholzer, 2013; Walitzer and Dearing, 2006).

In 87 papers (27%) the 'any alcohol use' criterion was used to label a 'relapse'. In addition, in thirteen papers 'any use' could also include the use of any illicit drugs.

Twelve papers reported a time-window in which a relapse could take place, but only five papers mentioned a specific number of abstinent days prior to relapse (Holt et al., 2012; Miller and Harris, 2000; Zywiak et al., 2003; Zywiak, Stout, Longabaugh, et al., 2006; Zywiak, Stout, Trefry, et al., 2006). Another 12 papers only mentioned quantity of use, and another 16 articles combined quantity and time frame.

In 26 papers one or more summary measures were used like 'percent drinking days', or 'days drinking'. Several papers explicitly used the '4 or more drinks per day for women and 5 or more drinks per day for men', or the equivalent ' ≥ 48 g/day for women and ≥ 60 g/day for men' criterion, from which the 'percent heavy drinking days' can be calculated (Tonigan et al., 1997).

In four papers readmission to a treatment service (e.g., detox clinic) or 'number of detoxifications', was used as outcome to define 'relapse'. Several papers used 'problem drinking' as outcome; but this term was not always explained. In some papers '(re) hospitalisation' or 'medical harm' criteria were considered a characteristic of a problematic drinking pattern. The severity score of the Addiction Severity Index was used to define relapse in one paper (Strakowski et al., 2005). In 53 papers (17%) that mostly had 'remission' as the outcome, authors made use of DSM related criteria. In the rest of the papers, various

other definitions were used. These definitions used for example ‘use of former quantities’, but the details of these quantities were not further specified.

In order to examine time-effects on the application of ‘relapse’ outcomes, a division of papers reporting on dichotomous and continuous outcomes was also tabulated in Table 1. We found that 26 papers reported continuous outcomes; these papers were mostly published in more recent years (from 2011-2019). ~~To assess potential differences among continents or countries we found no differences in reporting on these outcomes (see S2). We also found no indication for any potential related abstinence verse harm reduction based outcomes.~~

[INSERT TABLE 1]

4. Discussion

In line with earlier research (Maisto et al., 2016), this study confirmed that relapse definitions varied substantially. In a sizeable proportion of papers (n=69) no clear definition could be extracted from the papers nor an overarching ‘relapse definition’ (Castaldelli-Maia and Bhugra, 2014; Foulds et al., 2017; Garfield et al., 2014; Gong and Minuk, 2018; Henkel, 2011; McKay et al., 2006; Tusa and Burgholzer, 2013; Walitzer and Dearing, 2006).

It must be noted that no relapse definition was provided in almost a quarter of the included papers. Even in the remaining papers the definition varied substantially, with a range of outcomes from any use to percent days abstinent to amount of drinking to healthcare service utilization to DSM definitions of remission. Thus, we conclude that despite decades of AUD relapse research, no consensus has been reached to a uniform definition of ‘relapse’ (Maisto et al., 2016; Miller, 1996; Sliedrecht et al., 2019).

The prevalence rate of reporting the typically dichotomous drinking outcome ‘any drinking’ versus ‘abstinence’ was common (Table1). However, the binary ‘yes/no’ drinking outcome has been shown to be inadequate and may not capture substantial improvements in patient functioning that occurs with reductions in drinking (Falk et al., 2019; Witkiewitz et al., 2020). The ‘any drinking’ or ‘any use’ criteria may have some value within abstinent-only approaches (e.g., Twelve Step Facilitation, disulfiram), but it does not account for the complex and dynamic process of behaviour change (Roozen and van de Wetering, 2007; Witkiewitz et al., 2020; Witkiewitz, Wilson, et al., 2019).

Opmerking [KW7]: How are these reported in Table 1? I do not see how this is categorized

Opmerking [ES8]: Suppl. 2

Met opmaak: Engels (Groot-Brittannië)

Continuous measures, such as percent drinking days, percent heavy drinking days, attempt to capture a range of potential drinking outcomes and drinking practices. Yet, such measures were used in less than 10% of papers in the last two decades' research on relapse, while 'heavy drinking' definitions generally better predict long-term outcomes, than the 'any drinking' definition (Maisto et al., 2016). We found these measures have been more frequently used in the last 5 years as compared to the Maisto et al. paper. It must be noted that the variation in relapse descriptions could impose difficulties in the interpretation and comparison of the results among studies. Even when the criterion 'any use' after a period of abstinence is measured, this may warrant difficulties in interpretation, and in most cases the information on a preliminary abstinence period was not provided.

As our review work covered only papers written in the English language, most research originated from the western world. Although we did not find differences among countries, other research suggested such difference in the acceptance of non-abstinent treatment outcomes, where by service providers non-abstinent outcomes are deemed more acceptable in Europa and Australia compared to Northern America (Rosenberg *et al.*, 2020). Historically, this could be traced back to the dominance of abstinence based approaches like Alcoholics Anonymous and Twelve Step Facilitation Treatment in the United States, which actually seem to favour dichotomous abstinence outcomes (Kelly et al., 2020).

Interestingly, our research showed that DSM IV or 5 criteria were used in 53 papers (17 %) (compared to 2.9% in the 2016 Maisto paper), and in only two papers ICD-10 criteria were used. Consequently, a more frequent usage of DSM criteria emerged in more recent years as compared to earlier work (Maisto et al., 2016). As the DSM 5 is prominent in classifying an AUD (Carvalho et al., 2019; Hasin et al., 2013; Robinson & Adinoff, 2016), it holds promise to employ the DSM related course specifier 'remission'. The outcome 'remission' minimally spans a timeframe of three months (early remission), where no AUD criteria (besides craving) are present (Hasin et al., 2013; Robinson & Adinoff, 2016). A remission period is not interrupted by just drinking one or more alcoholic beverages, but only when this re-drinking leads to physical and/or psychosocial problems, as indicated by distinct DSM 5 criteria. In accordance with DSM 5 AUD course specifier definitions, the number of criteria present could indicate the severity of the reinstatement or impairment of the AUD. It seems that not only the remission criterion, but also the number of AUD symptoms could be used in the future. If patients exhibit a decrease in the number of AUD symptoms, this could be evaluated

as indicating progress in treatment. It has already 25 years ago been postulated that the usage of the term ‘relapse’ could even create a ‘self-fulfilling prophecy’ (Miller, 1996).

It has recently been advocated that besides ‘drinking measures’ also measures like ‘psychosocial functioning, employment, life satisfaction and mental health’, should be taken into account (Witkiewitz, Wilson, et al., 2019). In those patients that persist in some heavy drinking in the year following treatment, nevertheless half of these patients appear to maintain high levels of psychosocial functioning; even up to 3 years following treatment (Pearson et al., 2020). Moreover, recent research has also shown the relevance of lowering ‘World Health Organisation (WHO) risk drinking levels’, which is associated with better functioning (Witkiewitz et al., 2020). These risk levels are defined by grams of alcohol used per day (very high risk: >101 gram for males/ >61 gram for females, high risk: 61–100 gram for males/41–60 gram for females, low risk: 1–40 gram for males/1–20 gram for females, medium risk: 41–60 gram for males/21–40 gram for females) (Witkiewitz et al., 2020). Interestingly, in recent years a similar recovery/rehabilitation based approach has been postulated in the broader context of psychiatry, appraising a broader perception of the distinct psychiatric disorder (Rössler & Drake, 2017; Rössler, 2006; Vita & Barlati, 2019).

The term ‘relapse’ has now for decades been used as a well-known concept and has been studied intensively. We suggest to make use of contentious assessment such as DSM 5 (remission) criteria. That said, we would suggest that a future expert panel might come to an evidence- and practice-based construct of AUD relapse, or any other related construct if this future panel would choose to rename ‘relapse’, and perhaps the panel would decide to not use the term at all. This would probably provide the means of ‘leaving the wagon’ of over 40 years of semantic controversy (Miller, 1996).

Opmerking [KW9]: Love this line

5. Conclusions

A wide variety of relapse definitions were identified and consequently, and consistent with prior work by Maisto et al. (2016) we found lack of consensus in operationalizations of AUD relapse in the AUD literature. Despite decades of research and discussion, there is still no widely accepted definition of AUD relapse. We propose to shift the focus from dichotomous AUD relapse terminology towards continuous outcome and quality of life related criteria. Outcomes like psychosocial functioning, life satisfaction and mental health, should also be taken into account. The clinical use of the DSM-5 criteria might be tempting, as one could

distinguish AUD being present or being 'in (partial) remission'. The impact of treatment or the (natural) course of AUD could be monitored by the use of course specifiers (the number of AUD symptoms present), but also measures of functioning in different life areas. Taken together, the great variability as shown in our review and its broad, negative, impact on the development of the AUD field, highlights the urgency for an international (Delphi-consensus) project in view of developing a general accepted and theoretically well embedded definition of relapse in AUD, or a consensus decision to stop using the term.

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Table 1

Relapse definition/ continuous	Paper
PDD/ PHD & DDD measures	
days drinking & drinks per day past 28 days	Brower, 2003
percent days alcohol consumed, average daily number of drinks	Prisciandaro, 2012
percent days drinking (PDD)	Gillihan, 2011; Zandberg, 2016
4 or more drinks per day for women and 5 or more drinks per day for men (PHDD)/ ≥ 48 g/day for women and ≥ 60 g/day for men	Witkiewitz, 2011; Janu, 2012; Bujarski, 2013; Witkiewitz, 2015; Possemato, 2017/ Jorde, 2014, Bach, 2015; Zois, 2016; Field, 2017; Zois, 2017; Bach, 2019a; Bach, 2019b
average number of drinks per day	Lehavot, 2014
drinks per drinking day (DDD), PDD and PHDD	Witkiewitz, 2009; Witkiewitz, 2013; Maisto, 2018
percent days abstinent (PDA), mean number of DDD or PHDD	Davis, 2016
PDD and DDD	Roos, 2015; Karpyak, 2016; Maisto, 2017
PDA and DDD	Tonigan, 2017
DDD	Adinoff, 2017
Relapse definition/ dichotomous	
Any use	
any alcohol use	Curran, 2000; Gulliver, 2000; Tómasson, 2000; Bellamy, 2001; Brower, 2001; Driessen, 2001; Gann, 2001; Gish, 2001; Schmidt, 2001; Vielva, 2001; Gann, 2002; Lucht, 2002; Junghanns, 2003; Schadé, 2003; Walton, 2003; Wiesbeck, 2003; Bottlender, 2004; Mann, 2004; Miguet, 2004; Pfefferbaum, 2004; Bottlender, 2005a; Friend, 2005a; Björnsson, 2005; Junghanns, 2005a; Bottlender, 2005b; Friend, 2005b; Junghanns, 2005b; Bowden-Jones, 2005; Jorge, 2005; Perney, 2005; Turkcapar, 2005; Verheul, 2005; Walter, 2006a; Walter, 2006b; Demmel, 2006; Gordon, 2006; Sander, 2006; Terra, 2006; Bartels, 2007; Diehl, 2007; Feige, 2007; Schmidt, 2007; Sterling, 2007; Edens, 2008; Krampe, 2008; Müller, 2008; Pinto, 2008; Rus- Makovec, 2008; Terra, 2008; Witkiewitz, 2008; Wojnar, 2008; Oslin, 2009; Pitel, 2009; Wojnar, 2009; Farren, 2010; Müller, 2010; Berking, 2011; Cardenas, 2011; Costa, 2011; Dahlgren,

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	2011; Durazzo, 2011; Lejoyeux, 2011; Rando, 2011; Sinha, 2011; Suter, 2011; Garland, 2012; Schneekloth, 2012; Deruytter, 2013; Dolan, 2013; Jakubczyk, 2013; Oberleitner, 2013; Smith, 2014; Weinberger, 2015; Budzyński, 2016; Engel, 2016; Law, 2016; Manning, 2016; McHugh, 2016; Mo, 2016; Shaw, 2016; Durazzo, 2017a; Durazzo, 2017b; Hufnagel, 2017; Wang, 2018; Wu, 2018; Zou, 2018; Ledda, 2019
any use of alcohol or illicit drugs	Strowig, 2000; Walton, 2000; Bauer, 2001; McKay, 2006; Tate, 2008; Heffner, 2011; McKee, 2011; Bauer, 2012; Camchong, 2013; De Wilde, 2013; Sau, 2013; Trocchio, 2013;
alcohol or substance use, excluding caffeine and tobacco, but including the intake of “nonalcoholic beer”	Rupp, 2016; Rupp, 2017
Various	
various: any drinking, a drinking binge, three consecutive days of drinking	Kushner, 2005
not occasional but continuous re-drinking	Haraguchi, 2009
drinking -but improved-or drinking unimproved	Long, 2000
any episode of problematic drinking, however brief or limited	Ercan, 2003
number of drinking days and number of heavy drinking days	Conroy, 2006
first day of heavy drinking [6 or more drinks for men], percent drinking days over 3 months, and number of drinks per drinking day over 3 month	Gelernter, 2007
problem drinking: (1) drinking five or more drinks per day at least once a month for men or three or more drinks per day weekly for women, (2) one or more alcohol-related social consequences in the past year (from a list of eight), and/or (3) one or more alcohol dependence symptoms in the past year (from a list of nine)	Mericle, 2018
excessive drinking (regularly drank more than 70 g of pure ethanol); hospitalization (reinstitutionalized primarily for alcohol-related problems); unable to drink due to	Noda, 2001

illness (remained abstinent at home because of illness)	
more than 4 drinks/ day, more than 4 days drinking/ week, situations requiring detoxification	Noël, 2002
recurrence of an addictive drinking pattern which results in a premature termination of treatment or cessation of post-treatment follow-up visits	Wagner, 2004; Krampe, 2006
(1) Need for hospitalization, or emergency department attendance, due to alcohol consumption (2) Positivity of a urine screening. (3) Clinical detection, according to patient's medical record, of any alcohol consumption	Barrio, 2017
recurrence of alcoholic disease	Platz, 2000
(harmful) drinking with recorded medical or social harm, or drinking above 140 g ethanol/week / harmful relapse: associated with medical or social harm or a return to daily consumption of alcohol or in excess of 140 g of ethanol/week	Kelly, 2006/ Wiggs, 2017
relapse to problem use	Mertens, 2012
repeated drinking after initial lapse/ repeated alcohol consumption	Papachristou, 2014/ Nalpas, 2018
Only timeframe	
time to first drink	Pagano, 2004; Ludwig, 2013; Seo, 2013; Zakiniaez, 2017
drinking lapse: the first drink recorded after a period of at least 7 days of abstinence	Holt, 2012
consumption of any alcohol on at least three consecutive days	Demirbas, 2012; Wiers, 2015
heavy drinking after at least 4 days abstinence	Miller, 2000
a day of drinking preceded by at least 4 days of abstinence	Zywiak, 2003b; Zywiak, 2006b
alcohol consumption after at least 2 weeks abstinence	Zywiak, 2006a
1 or more weeks of substance use after the 26th week of remission from use	Aharonovich, 2005
Only quantity	
≥ 5 drinks on one occasion	Aguiar, 2012
3 (+) standard drinks women, 5 (+) standard	Greenfield, 2000; Greenfield, 2002;

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drinks men	Greenfield, 2003; Trucco, 2007
consumption of > 60 grams of alcohol in men or > 40 grams of alcohol in women	Wrase, 2008; Charlet, 2013; Charlet, 2014; Garbusow, 2016; Sebold, 2017; Quoilin, 2018
relapse to heavy drinking: consumption of $\geq 60/48$ (male/female) grams of alcohol in 1 drinking occasion	Bernhardt, 2017
Quantity & timeframe: alcohol + drugs	
21 units (12 gram per unit) of alcohol per week at least one week and/or any use of illegal provided drugs and/or any use of benzodiazepines (prescribed or illegal)	Pedersen, 2009
3 or more consecutive days of drug use and/or heavy drinking operationalized as six or more drinks per day for men and four or more drinks per day for women	Tate, 2005
Quantity & timeframe: alcohol	
> 4 standard drinks (1 standard drink = 10 g of pure alcohol) on 1 day/ ≥ 5 drinks on one day	Nieva, 2011/ Oslin, 2002
drinking more than 30 grams of ethanol (2 standard drinks) in 24 h	Haver, 2001
31 standard drinks or more in 3 days or less	Allsop, 2000
≥ 4 standard drinks for women and ≥ 5 standard drinks for men at least once in the past 30 days	Mojarrad, 2014
relapse spectrum: minor lapse (1 use) - very heavy relapse (> 4 uses/week, > 6 weeks)	Humke, 2005
five or more standard drinks of alcohol three or more days a week	Marquenie, 2006
>3 drinks per day for at least 1 month	Sorg, 2012
heavy drinking (i.e. consumption of at least 5 alcoholic beverages on one day), or intoxication with alcohol during two consecutive days a week	Schellekens, 2015
relapsers to alcohol abuse: women consuming ≥ 4 drinks daily for 1 day, men consuming ≥ 5 drinks daily for 1 day, or any adult consuming ≥ 3 drinks daily for ≥ 7 consecutive days	Wilens, 2011
consumption of ≥ 5 units of alcohol on one occasion and ≥ 4 such occasions in 1 week, or ≥ 12 units on one or more occasions	Willinger, 2002
3 or more consecutive days of drinking operationalized as six or more drinks per	Durazzo, 2010a; Durazzo, 2010b

day for men and four or more drinks per day for women	
5 or more drinks per day for men and 4 or more drinks for women; or 5 or more consecutive days of slips for men and 4 or more days for women	Zikos, 2010
Abstinent: less than one drink (0.5 ounces of ethanol) a month for a year	Vaillant, 2003
Return to previous levels	
resumption of frequent use or a return to previous levels of alcohol use	Pelc, 2002
return to drinking, consuming alcohol regularly at least in the amount of prior use	Evren, 2012
return to alcohol consumption rates at or near the level of their pre-detoxification use	Matheus-roth, 2016
relapse into pretreatment drinking levels	Snelleman, 2018
Readmission/ detoxification measures	
re-admission detox unit	Callaghan, 2002
number of previous detoxifications	Baars, 2013
number of alcohol-related hospital readmissions and the days to first readmission	Weinland, 2017; Weinland, 2019
Problems	
experiencing one or more items of the 'Drinking Problems Index'	Schutte, 2003; Schutte, 2009
drug- or alcohol-related problems at both follow-up and over the preceding year	Landheim, 2006
DSM/ ICD criteria	
recurrence of any DSM-IV AUD symptoms	Dawson, 2007
reinstallation of a state of alcohol dependence according to DSM-IV criteria	Spruyt, 2013
returning to drinking after a period of abstinence accompanied by reinstatement of dependence symptoms	Paulino, 2017
two or more DSM-5 AUD symptoms following remission	Tuithof, 2014
fulfilling DSM-III-R criteria for alcohol dependence 3 months after hospital admission	Tatsuzawa, 2002
problem drinkers > reported any criteria for a diagnosis of "alcohol abuse" or "dependence" during 12 months	Russell, 2001
DSM-IV, ICD-10 and CWM criteria at 1	De Bruijn, 2006

and 3 year follow up (relapse to abuse of dependence)	
≥ 1 week with any DSM-IV dependence or abuse symptom after 26 weeks of remission	Samet, 2013
Recurrence: at least 1 week of new symptom severity scores greater than 3 (no dependence criteria, but the ASI rater severity score greater than 3)	Strakowski, 2005
Recurrence: number of assessment ages at which a DSM (III, III-R, IV) AUD was diagnosed	Milne, 2009
Recurrence: presence of a CIDI diagnosis of Alcohol Dependence (DSM-IV) at any time during the 2-year follow-up	Boschloo, 2012
Persistence: maintaining full criteria for DSM-IV alcohol dependence (i.e. chronicity/persistence) throughout 3 years	Elliott, 2016
Recovery: abstinent or no last year DSM-IV criteria abuse/ dependence, no risk drinker	Dawson, 2005; Dawson, 2006
Recovery: abstinent or no last year DSM-IV criteria abuse/ dependence, no severe headaches when getting over drinking, no risk drinker	Dawson, 2012
Recovery: past 3-year interval of no diagnosis, characterizing <i>securely</i> abstinent former abusers	McAweeney, 2005
Recovery: no DSM-III-R abuse and dependence criteria over at least the final 5-year follow up period	Schuckit, 2011; Haller, 2014
Remission: did not meet criteria for any substance use disorder in the past year	Karno, 2008
Remission: a minimum of 6 months with either no use of alcohol or some use of alcohol but no symptoms of dependence or abuse (DSM-III-R), and the criteria for dependence (or abuse) not met	Knop, 2007; Penick, 2010
Remission: no DSM-III criteria abuse/ dependence for 12 months	Sher, 2004
Remission: no DSM-III-R criteria dependence for 6 months or more	Gilder, 2008
Remission: absence of full criteria for abuse or	Xie, 2010

Dependence (DSM-III-R)	
Remission: no DSM-IV criteria abuse/dependence for 12 months	Ojesjö, 2000; Bischof, 2001; Bischof 2005; Bischof, 2007; Damian, 2017
Remission: no DSM-IV or ICD-10 criteria last 12 months	Rumpf, 2002; Degenhardt, 2018
Remission: at least six months without evidence of abuse or dependence	Brunette, 2003
Remission: no DSM-IV criteria dependence for 12 months	Pirkola, 2006
Remission: no DSM-IV criteria dependence	Lopez-Quintero, 2011
Remission: at least 1 year none of DSM-5 AUD criteria	McCutcheon, 2014
Remission: did not meet DSM-IV criteria for AUD in any subsequent follow-up	Trim, 2013
Remission: no criteria for dependence or abuse during the last year but reported using drugs or alcohol during the past year at least once; or abstinent, no longer criteria for dependence or abuse and reported no substance use during the last year	Arndt, 2010
Remission: one or none of: (1) drinking five or more drinks a day at least once a month for men (three or more drinks a day for women); (2) one or more alcohol-related social consequences (from a list of eight); and (3) one or more alcohol dependence symptoms (from a list of nine)	Matger, 2005
Remission: cessation of alcohol use and the absence of any pre-existing DSM-IV abuse or dependence symptoms for at least 1 year	Silviera, 2011
Remission: the cessation of alcohol use and the absence of any symptoms (DSM-IV) for at least two years	Kalaydjian, 2009; Lee, 2009; Suliman, 2010; Abdin, 2014
Remission: at least 1 year absence of DSM-V AUD- symptoms	McCutcheon, 2012; McCutcheon, 2017
Remission: abstinence, 3 or less ounces on a drinking day, no alcohol related problems	Moos, 2003
Remission: abstinence or moderate drinking in each of the past 6 months, no intoxication and consumption of no more than 3 oz. of ethanol on drinking days in the past month, and no drinking problems in the past 6 months	Moos, 2005; Moos, 2006a; Moos, 2006b; Moos, 2007
Remission: either past-year abstinence from both alcohol and drug use, or past-year non-problem substance use	Tsoh 2011; Satre, 2012
Remission: no longer meeting DSM-IV	Grella, 2013

criteria for an alcohol or drug dependence disorder (past 12 months)	
NO definition	<p>Markianos, 2001; Schutte, 2001; Zywiak, 2003a; Hufford, 2003; Fein, 2004; Tapert, 2004; Garbutt, 2005; Ilgen, 2005; Krahn, 2005; McKay, 2005; Bradizza, 2006; Brady, 2006; Hammerbacher, 2006; Hingson, 2006; Jackson, 2006; Rask, 2006; Walitzer, 2006; Arnedt, 2007; Cooney, 2007; Di Sclafani, 2007; Levin, 2007; Waldrop, 2007; Becker, 2008; Tucker, 2008; Hunter- Reel, 2009; Mattoo, 2009; Romo, 2009; Udo, 2009; Borders, 2010; Gamble, 2010; Kalman, 2010; Loeber, 2010; North, 2010; Henkel, 2011; Higley, 2011; Kelly, 2011; Schepis, 2011; Copeland, 2012; Dakwar, 2012; Fein, 2012; Kelly, 2012; O'Daly, 2012; Abulseoud, 2013; Connolly, 2013; Farren, 2013; Gross, 2013; Khan, 2013; Preuss, 2013; Schepis, 2013; Tuithof, 2013; Vito Agosti, 2013; Castaldelli-Maia, 2014; Chiappetta, 2014; Cosgrove, 2014; Cranford, 2014; Garfield, 2014; Huntley, 2014; Jessup, 2014; Segobin, 2014; Flórez, 2015; Garcia, 2015; Conde, 2016; Czapla, 2016; Weinberger, 2016; Zahr, 2016; Blaine, 2017; Foulds, 2017; Gong, 2018; Karriker-Jaffe, 2018</p>

Supplemental material Table S1 & references original systematic review

Study, year	Relapse definition	Explanation definition
Allsop, 2000	time to heavy drinking was defined as 31 standard drinks or more in 3 days or less	N/A
Curran, 2000	any return to drinking	N/A
Greenfield, 2000	3 (+) women, 5 (+) men	Yes (earlier work)
Gulliver, 2000	any drinking post treatment	N/A
Long, 2000	drinking but improved or drinking unimproved	N/A
Miller, 2000	heavy drinking after at least 4 days abstinence (blood alcohol level 200 mg% in few hours drinking)	Yes (earlier work)
Ojesjö, 2000	Remission: no DSM-IV criteria abuse/dependence for 12 months	N/A
Platz, 2000	recurrence of alcoholic disease	N/A
Strowig, 2000	any use of alcohol or illicit drugs	N/A
Tómasson, 2000	any drinking (not abstinent)	N/A
Walton, 2000	any use of alcohol or illicit drugs	N/A
Bauer, 2001	any use of alcohol or illicit drugs	N/A
Bellamy, 2001	any alcohol use	N/A
Bischof, 2001	Remission: no DSM-IV criteria abuse/dependence for 12 months	N/A
Brower, 2001	any alcohol use	N/A
Driessen, 2001	having consumed alcohol on 1 or more days	N/A
Gann, 2001	any consumption of alcohol	N/A
Gish, 2001	any alcohol consumption	N/A
Haver, 2001	drinking more than 30 g of ethanol (2 standard drinks) in 24 h	Yes (common drinking pattern women Sweden)
Markianos, 2001	N/A	N/A
Noda, 2001	excessive drinking (regularly drank more than 70 g of pure ethanol); hospitalization (reinstitutionalized primarily for alcohol-related problems); unable to drink due to illness (remained abstinent at home because of illness)	N/A
Russel, 2001	problem drinkers > reported any criteria for a diagnosis of “alcohol abuse” or “dependence” during the 12 months prior to interview	Yes (Sobell)
Schmidt, 2001	any alcohol use	N/A
Schutte, 2001	N/A (long term remission & abstention)	N/A
Vielva, 2001	relapse vs. abstinence	N/A

Met opmaak: Engels (Groot-Brittannië)

Callaghan, 2002	re-admission to the Detox Unit during the 3-year course of the study	N/A
Gann, 2002	any reported consumption of alcohol	N/A
Greenfield, 2002	three or more standard drinks per drinking day for women and five or more drinks per drinking day for men	N/A
Lucht, 2002	relapse vs abstinence (one year no alcohol)	N/A
Noël, 2002	more than 4 drinks/ day, more than 4 days drinking/ week, situations requiring detoxification	N/A
Oslin, 2002	5 or more drinks on a single day	Yes (multiple pharmacotherapy trials)
Pelc, 2002	resumption of frequent use or a return to previous levels of alcohol use	N/A
Rumpf, 2002	Remission: no DSM-IV or ICD-10 criteria last 12 months	Yes (DSM-IV criteria)
Tatsuzawa, 2002	fulfilling DSM-III-R criteria for alcohol dependence 3 months after hospital admission	N/A
Willinger, 2002	consumption of ≥ 5 units of alcohol on one occasion and ≥ 4 such occasions in 1 week, or ≥ 12 units on one or more occasions	N/A
Zywiak, 2003a	N/A (probably any alcohol drinking)	N/A
Brower, 2003	Days drinking & drinks per day past 28 days	N/A
Brunette, 2003	Remission: at least six months without evidence of abuse or dependence	N/A
Zywiak, 2003b	a day of drinking preceded by at least 4 days of abstinence	N/A
Ercan, 2003	any episode of problematic drinking, however brief or limited	N/A
Greenfield, 2003	3 (+) standard drinks women, 5 (+) standard drinks men	N/A
Hufford, 2003	N/A	N/A
Junghanns, 2003	consumption of at least one alcoholic beverage since discharge from the hospital	N/A
Moos, 2003	Remission: abstinence, 3 or less ounces on a drinking day, no alcohol related problems	N/A
Schadé, 2003	any drinking	N/A
Schutte, 2003	experiencing one or more items of the 'Drinking Problems Index'	N/A
Vaillant, 2003	Abstinent: less than one drink (0.5 ounces of ethanol) a month for a year	N/A
Walton, 2003	any alcohol use	N/A
Wiesbeck, 2003	relapse vs. abstainers; any alcohol use	N/A

Met opmaak: Engels (Groot-Brittannië)

Bottlender, 2004	any alcohol intake	Yes (Feuerlein, 1989)
Fein, 2004	N/A	N/A
Mann, 2004	any amount or form of alcohol intake	N/A
Miguet, 2004	any alcoholic beverage after liver transplant	N/A
Pagano, 2004	time to first drink from the nominal end of treatment at month 3	Yes (Match data (Babor, 2003))
Pfefferbaum, 2004	abstainers (no alcohol use) vs relapse	N/A
Sher, 2004	Remission: no DSM-III criteria abuse/dependence for 12 months at year 7 follow up	Yes (DSM-III criteria)
Tapert, 2004	N/A	N/A
Wagner, 2004	recurrence of an addictive drinking pattern which results in a premature termination of treatment or cessation of post-treatment follow-up visits	N/A
Bottlender, 2005a	any alcohol intake	Yes (criteria Feuerlein, W., Kuefner, H., 1989)
Friend, 2005a	consuming any drink during follow-up period	N/A
Aharonovich, 2005	1 or more weeks of substance use after the 26th week of remission from use	N/A
Junghanns, 2005a	at least one standard alcoholic drink since discharge from the hospital	N/A
Bottlender, 2005b	any alcohol intake	Yes (criteria Feuerlein, W., Kuefner, H., 1989)
Friend, 2005b	Absence of sobriety	N/A
Bischof, 2005	Remission: no DSM-IV criteria abuse/dependence for 12 months	N/A
Björnsson, 2005	any alcohol use	N/A
Junghanns, 2005b	at least one alcoholic beverage since discharge from the hospital	N/A
Bowden- Jones, 2005	no explicit definition: relapse vs. abstinence	N/A
Dawson, 2005	Recovery: abstinent or no last year DSM-IV criteria abuses/ dependence, no risk drinker	Yes (but complex)
Garbutt, 2005	N/A	N/A
Humke, 2005	relapse spectrum: minor lapse (1 use) - very heavy relapse (>4 uses/week, > 6 weeks)	Yes (Walton, 1994)
Ilgen, 2005	N/A (deterioration)	N/A
Jorge, 2005	no explicit definition: relapse vs.	N/A

	abstinence	
Krahn, 2005	N/A (relapse vs. abstinence??)	N/A
Kushner, 2005	any drinking, a drinking binge, three consecutive days of drinking	N/A
Matzger, 2005	Remission: one or none of: (1) drinking five or more drinks a day at least once a month for men (three or more drinks a day for women); (2) one or more alcohol-related social consequences (from a list of eight); and (3) one or more alcohol dependence symptoms (from a list of nine)	N/A
McAweeney, 2005	Recovery: past 3-year interval of no diagnosis, characterizing <i>securely</i> abstinent former abusers	Yes (Finney and Moos, 1991; Vaillant, 1995).
McKay, 2005	N/A (alcohol use outcomes)	N/A
Moos, 2005	abstinence or moderate drinking in each of the past 6 months, no intoxication and consumption of no more than 3 oz. of ethanol on drinking days in the past month, and no drinking problems in the past 6 months	N/A
Perney, 2005	any alcohol use after liver transplantation	N/A
Strakowski, 2005	Recurrence: at least 1 week of new symptom severity scores greater than 3 (no dependence criteria, but the ASI rater severity score greater than 3)	N/A
Tate, 2005	3 or more consecutive days of drug use and/or heavy drinking operationalized as six or more drinks per day for men and four or more drinks per day for women	Yes (MATCH, 1997)
Turkcapar, 2005	any alcohol consumption during 6 months following discharge	Yes (reliable measure)
Verheul, 2005	no continuous abstinence (ABST)	Yes
Moos, 2006a	relapse = non- remission (abstinence from alcohol or moderate drinking in each of the past 6 months, no drinking problems in the past 6 months and no intoxication or consumption of more than 3 ounces of ethanol on drinking days in the past month)	N/A
Walter, 2006a	any alcohol consumption during 6 month follow up	N/A
Zywiak, 2006a	alcohol consumption after at least 2 weeks abstinence	Yes (MATCH)
Moos, 2006b	abstinence or moderate drinking in each of the past 6 months, no intoxication and consumption of no more than three ounces	N/A

	of ethanol on drinking days in the past month, and no drinking problems in the past 6 months	
Bradizza, 2006	N/A (varied across included studies)	N/A
Brady, 2006	N/A	N/A
Walter, 2006b	any alcohol during 12-month follow-up period	N/A
Zywiak, 2006b	a (posttreatment initiation) drinking day preceded by at least four consecutive days of abstinence	Yes (Miller & Marlatt, 1996)
Conroy, 2006	number of drinking days and number of heavy drinking days	N/A
Dawson, 2006	no past- year criteria of either alcohol abuse or dependence, including severe headaches due to drinking and their past-year alcohol consumption lay within the low-risk drinking guidelines stipulated in the NIAAA <i>Health Practitioner's Guide</i>	Yes (but complex)
De Bruijn, 2006	DSM-IV, ICD-10 and CWM criteria at 1 and 3 year follow up (relapse to abuse of dependence)	N/A
Demmel, 2006	at least one drink during follow up period	N/A
Gordon, 2006	reporting any alcohol use	N/A
Hammerbacher, 2006	N/A	N/A
Hingson, 2006	N/A	N/A
Jackson, 2006	N/A	N/A
Kelly, 2006	(harmful) drinking with recorded medical or social harm, or drinking above 140 g ethanol/week	N/A
Krampe, 2006	recurrence of an addictive drinking pattern that resulted in a premature termination of treatment or cessation of posttreatment follow-up visits	N/A (see: Wagner, 2004)
Landheim, 2006	drug- or alcohol-related problems at both follow-up and over the preceding year	N/A
Marquenie, 2006	five or more standard drinks of alcohol three or more days a week	N/A
McKay, 2006	any alcohol or drug use	Yes (review several definitions)
Pirkola, 2006	Remission: no DSM-IV criteria dependence for 12 months, criteria were present before	N/A
Rask, 2006	N/A (“positive drinking”)	N/A
Sander, 2006	any alcohol during 1 year follow up	N/A
Terra, 2006	any alcohol use (no explicit definition)	N/A
Walitzer, 2006	N/A (review: definition in original papers)	N/A
Arnedt, 2007	N/A (any dinking?)	N/A

Bartels, 2007	no abstinence	N/A
Bischof, 2007	Remission: no DSM-IV criteria abuse/dependence for 12 months	N/A
Cooney, 2007	N/A	N/A
Dawson, 2007	recurrence of any DSM-IV AUD symptoms	N/A
Di Sclafani, 2007	N/A	N/A
Diehl, 2007	any alcohol consumption	N/A
Feige, 2007	relapse vs. abstinence	N/A
Gelernter, 2007	first day of heavy drinking [6 or more drinks for men], percent drinking days over 3 months, and number of drinks per drinking day over 3 month	N/A
Knop, 2007	Remission: a minimum of 6 months with either no use of alcohol or some use of alcohol but no symptoms of dependence or abuse (DSM-III-R), and the criteria for dependence (or abuse) not met	Yes (DSM-III-R)
Levin, 2007	N/A (9 DSM-III-R correlated items)	N/A
Moos, 2007	Remission: abstinence from alcohol or moderate drinking in each of the past 6 months, no drinking problems in the past 6 months, and no intoxication or consumption of more than three ounces of ethanol on any day in the past month	N/A
Schmidt, 2007	any consumption of alcohol	N/A
Sterling, 2007	renewed alcohol use	N/A
Trucco, 2007	three or more standard drinks on a drinking day for women, and five or more on a drinking day for men	Yes (O'Malley, 1992)
Waldrop, 2007	N/A (any alcohol use?)	N/A
Becker, 2008	N/A (several definitions from cited studies)	N/A
Edens, 2008	abstention vs. other categories	Yes
Gilder, 2008	having no symptom of alcohol dependence for 6 months or longer (DSM-III-R)	N/A
Karno, 2008	Remission: did not meet criteria for any substance use disorder in the past year	Yes (NESARC criteria)
Krampe, 2008	any (signs of) alcohol consumption	N/A
Müller, 2008	started to drink again, even for only 1 day	N/A
Pinto, 2008	relapse vs abstinence	N/A
Rus- Makovec, 2008	relapse vs abstinence	N/A
Tate, 2008	first alcohol or drug use	N/A
Terra, 2008	non- abstinent	N/A
Tucker, 2008	N/A (abstinent, low- risk/ high- risk)	N/A
Witkiewitz, 2008	first drinking (lapse)	Yes (literature)
Wojnar, 2008	any drinking in the follow-up period	Yes (Sobell)
Wrase, 2008	consumption of more than 60 grams of	Yes (standard

	alcohol in men or more than 40 grams of alcohol in women during the assessment period	clinical trials)
Haraguchi, 2009	not occasional re-drinking but continuous re-drinking	N/A
Hunter- Reel, 2009	N/A	N/A
Kalaydjian, 2009	Remission: the cessation of alcohol use and the absence of any symptoms (DSM-IV) for at least two years before interview	N/A
Lee, 2009	Remission: cessation of use and the absence of any pre-existing symptom (of abuse and dependence) for at least two years before interview	
Mattoo, 2009	N/A (vs. abstinence?)	N/A
Milne, 2009	Recurrence: number of assessment ages at which a DSM (III, III-R, IV) AUD was diagnosed	N/A
Oslin, 2009	any drinking	N/A
Pedersen, 2009	21 units (12 gram per unit) of alcohol per week at least one week during the six-month period after discharge from treatment and/or any use of illegal provided drugs and/or any use of benzodiazepines (prescribed or illegal)	N/A
Pitel, 2009	relapse vs abstinence	N/A
Romo, 2009	N/A (total days abstinent)	N/A
Schutte, 2009	one or more drinking problems	N/A
Udo, 2009	N/A (abstainer, moderate, or heavy drinker)	N/A
Witkiewitz, 2009	Drinks per drinking day (DDD), Percent drinking days (PDD), percent heavy drinking days (PHD)	N/A
Wojnar, 2009	any drinking	Yes (Sobell)
Durazzo, 2010a	3 or more consecutive days of drinking operationalized as six or more drinks per day for men and four or more drinks per day for women	Yes (project MATCH criteria)
Arndt, 2010	Remission: no criteria for dependence or abuse during the last year but reported using drugs or alcohol during the past year at least once; or abstinent, no longer criteria for dependence or abuse and reported no substance use during the last year	N/A
Durazzo, 2010b	3 or more consecutive days of drinking operationalized as six or more drinks per day for men and four or more drinks per	Yes (project MATCH criteria)

	day for women	
Borders, 2010	N/A (remission)	N/A
Dom, 2010	N/A	N/A
Farren, 2010	relapse to alcohol vs. abstinent	N/A
Gamble, 2010	N/A	N/A
Kalman, 2010	N/A	N/A
Loeber, 2010	N/A (relapse vs. abstinence?)	N/A
Müller, 2010	relapse vs. abstinence	N/A
North, 2010	N/A	N/A
Penick, 2010	Remission: a minimum of at least 6 months with “either no use of the substance, or some use of the substance and no symptoms of dependence” (DSM-III-R)	Yes (DSM-III-R)
Suliman, 2010	Remission: cessation of alcohol use and the absence of any (DSM-IV) symptoms for at least 2 years before the interview	N/A
Xie, 2010	Remission: absence of full criteria for abuse or Dependence (DSM-III-R)	Yes (DSM-III-R)
Zikos, 2010	5 or more drinks per day for men and 4 or more drinks for women; or 5 or more consecutive days of slips for men and 4 or more days for women	N/A
Berking, 2011	consuming any alcohol vs abstinent	N/A
Cardenas, 2001	relapse vs abstinent	N/A
Costa, 2011	relapse vs abstinent	N/A
Dahlgren, 2011	any drinking	Yes (Flannery, 1999; Strowig, 2000)
Durazzo, 2011	any alcohol use	N/A
Gillihan, 2011	percent days drinking	Yes (outcome ‘parent study’)
Heffner, 2011	any use of alcohol or illicit drugs during the study	N/A
Henkel, 2011	N/A (literature review)	N/A
Higley, 2011	N/A	N/A
Kelly, 2011	N/A	N/A
Lejoyeux, 2011	relapse vs abstinence	N/A
Lopez-Quintero, 2011	Remission: no DSM-IV criteria dependence	Yes (AUDADIS)
McKee, 2011	any alcohol or drug use in the past 3 months	N/A
Nieva, 2011 (2010)	more than 4 standard drinks (1 standard drink = 10 g of pure alcohol) on 1 day	N/A
Rando, 2011	any alcohol use; relapse to heavy drinking =5 drinks for men and 4 drinks for women	N/A
Schepis, 2011	N/A (recurrence of AUD)	N/A
Schuckit, 2011	Recovery: no DSM-III-R abuse and	N/A

	dependence criteria over at least the final 5-year follow up period	
Silveira, 2011	Remission: cessation of alcohol use and the absence of any pre-existing DSM-IV abuse or dependence symptoms for at least 1 year before the interview	N/A
Sinha, 2011	first alcoholic drink	N/A
Suter, 2011	abstinence vs first drink	N/A
Tsoh, 2011	Remission: (past year) either self-reported past-year abstinence from both alcohol and drug use, or past-year non-problem substance use. <i>Non-problem use: 1) no days of drinking five or more drinks in a day, and drinking no more than four times per month in the past year; or using marijuana no more than once per month in the past year; 2) had no other drug use in the past year; 3) had no problems with friends of family, violent behavior, or suicidal ideations in the prior month, and 4) had no arrests, jail/prison, electronic home surveillance, or visits to a probation or parole officer in the prior year.</i>	Yes (Moos, 2003 & Ouimette, 2000 & Mertens, 2008)
Wilens, 2011	relapsers to alcohol abuse: women consuming ≥ 4 drinks daily for 1 day, men consuming ≥ 5 drinks daily for 1 day, or any adult consuming ≥ 3 drinks daily for ≥ 7 consecutive days	Yes (“consistent with standard definitions”)
Witkiewitz, 2011	4 or more drinks per day for women and 5 or more drinks per day for men (PHD)	Yes
Aguiar, 2011	heavy relapse: consumption of five or more standard drinks in one occasion. A standard drink containing 10 g of alcohol.	Yes (Greenfield, 1998; Rubio, 2001; Guardia, 2002; Johnson, 2003; De Sousa, 2004, 2005; Kiefer, 2005; Laaksonen, 2007)
Bauer, 2012	relapse vs abstinence (alcohol, cocaine, amphetamine, marijuana, or heroin)	N/A
Boschloo, 2012	Recurrence: presence of a CIDI diagnosis of Alcohol Dependence (DSM-IV) at any time during the 2-year follow-up	Yes (CIDI= Composite International Diagnostic

		Interview, DSM-IV)
Copeland, 2012	N/A (persistence DSM-IV AUD)	N/A
Dakwar, 2012	N/A (AUDADIS-IV)	N/A
Dawson, 2012	Recovery: abstinent or no last year DSM-IV criteria abuse/ dependence, no severe headaches when getting over drinking, no risk drinker (NIAAA- criteria)	N/A
Demirbas, 2012	consumption of any alcohol on at least three consecutive days	N/A
Evren, 2012	return to drinking during 12 month follow up, consuming alcohol regularly at least in the amount of their prior use	N/A
Fein, 2012	N/A	N/A
Garland, 2012	one or more occasions of drinking any quantity of alcohol.	Yes (due to treatment facility)
Holt, 2012	drinking lapse: the first drink recorded after a period of at least 7 days of abstinence	N/A
Janu, 2012	consumption of 5 or more drinks (alcohol units) for men and 4 or more drinks for women per one occasion (drinking day)	Yes (O'Malley, 1992)
Kelly, 2012	N/A (measures: PDA & DDD)	N/A
McCutcheon, 2012	Remission: at least 1 year absence of DSM-V AUD- symptoms at the time of interview and was conditional on the presence of lifetime AUD	Yes (Knop, 2007; Gilder, 2008; Penick, 2010)
Mertens, 2012	relapse to problem use <i>(Non-problem use: (a) used alcohol, but had no days of drinking five or more drinks in a day, and drank only four times per month or less in the past year; or used marijuana, but not more than once per month in the past year; (b) had no other drug use in the past year; (c) had no problems with friends or family, violent behavior, or suicidal ideations in the month prior to interview; and (d) had not been arrested, in jail/prison, under electronic home surveillance, or been to a probation or parole officer in the year prior to interview)</i>	Yes (Moos, 2003, Ouimette, 2000)
O'Daly, 2012	N/A	N/A
Prisciandaro, 2012	percent days alcohol consumed, average daily number of drinks	N/A
Satre, 2012	Remission: abstaining in the past year or those who were non-problem users <i>((a) used alcohol but had no days of</i>	Yes (Mertens, 2008, Moos, 2003)

	<i>drinking five or more drinks in a day and drank only four times per month or less in the past year, or used marijuana but not more than once per month in the past year; (b) had no other drug use in the past year; (c) had no problems with friends or family, violent behavior, or suicidal ideations in the month before the interview; and (d) had not been arrested, in jail/prison, under electronic home surveillance, or to a probation or parole officer in the year before the interview)</i>	
Schneekloth, 2012	any consumption of alcohol after discharge	N/A
Sorg, 2012	more than three drinks per day for at least 1 month during the 6-month follow-up	N/A
Abulseoud, 2013	N/A	N/A
Baars, 2013	number of previous detoxifications	Yes
Bujarski, 2013	relapse to heavy drinking (operationalized as five or more drinks in a day for men and four or more drinks in a day for women).	N/A
Camchong, 2013	any use of alcohol or other substance (except nicotine) during any time after participating in the study	N/A
Charlet, 2013	days of abstinence and days of binge drinking (alcohol intake >60 g/day in male participants, >40 g/ day in female participants)	N/A
Connolly, 2013	N/A	N/A
De Wilde, 2013	substance use (apart from caffeine and nicotine)	N/A
Deruytter, 2013	any alcohol consumption after LT	Yes (Pageaux, 2003; Gish, 2001; Dimartini, 2001)
Dolan, 2013	relapsers vs abstainers	N/A
Farren, 2013	N/A (vs. abstinence?)	N/A
Grella, 2013	Remission: no longer meeting DSM-IV criteria for an alcohol or drug dependence disorder (past 12 months)	N/A
Gross, 2013	N/A (vs. abstinence?)	N/A
Jakubczyk, 2013	any drinking during the follow-up period	N/A
Khan, 2013	N/A	N/A
Ludwig, 2013	time to first alcohol use	N/A
Oberleitner, 2013	any breathalyzer result above .000	N/A
Preuss, 2013	N/A	N/A
Samet, 2013	relapse to dependence could occur only	Yes

	after the 26 th week of remission, and was defined as ≥ 1 week with any DSM-IV dependence or abuse symptom	(DSM IV-TR)
Sau, 2013	return to even a single usage of a substance or process of which they had previously established abstinence	N/A
Schepis, 2013	N/A (recurrence)	N/A
Seo, 2013	time to first drink (and time to heavy drinking relapse (5 or more drinks/occasion in men; 4 or more drinks/occasion in women))	Yes ("frequently used measures")
Spruyt, 2013	reinstallation of a state of alcohol dependence according to DSM-IV criteria	Yes (Wiers, 2011)
Trim, 2013	Remission: did not meet DSM-IV criteria for AUD in any subsequent follow-up	N/A
Trocchio, 2013	any use of alcohol and/or any drug use was coded as non-abstinent	N/A
Tuithof, 2013	N/A	N/A
Tusa, 2013	N/A (review)	N/A
Vito Agosti, 2013	N/A	N/A
Witkiewitz, 2013	Drinks per drinking day (DDD), Percent drinking days (PDD), percent heavy drinking days (PHD)	N/A
Abdin, 2014	Remission: cessation of alcohol use and the absence of any symptoms for at least 2 years before interview	Yes (Kalaydjian, 2009)
Castaldelli-Maia, 2014	N/A (review)	N/A
Charlet, 2014	alcohol consumption more than 60 g in men or more than 40 g in women	Yes (Beck, 2012)
Chiappetta, 2014	N/A (presence DSM-IV alcohol abuse/dependence)	N/A
Cosgrove, 2014	N/A	N/A
Cranford, 2014	N/A (Drinks per Drinking Day, trajectories)	N/A
Garfield, 2014	N/A (review)	N/A
Haller, 2014	Recovery: no DSM-III-R abuse and dependence criteria over at least the final 5-year follow up Period (remission > past year)	Yes (Sobell, 2000)
Huntley, 2014	N/A	N/A
Jessup, 2014	N/A (relapse vs. abstinent?)	N/A
Jorde, 2014	≥ 48 g/day for women and ≥ 60 g/day for men (relapse to heavy drinking)	Yes (Kiefer, 2011)
Lehavot, 2014	average number of drinks per day	N/A
McCutcheon, 2014	Remission: at least 1 year none of DSM-5 AUD criteria	Yes (DSM-5)

		sustained remission)
Mojarrad, 2014	heavy alcohol use: ≥ 4 standard drinks for women and ≥ 5 standard drinks for men at least once in the past 30 days	N/A
Papachristou, 2014	repeated drinking after initial lapse	N/A
Segobin, 2014	N/A	N/A
Smith, 2014	taken any alcoholic drink since discharge	N/A
Tuithof, 2014	reported two or more DSM-5 AUD symptoms	N/A
Bach, 2015	relapses to heavy drinking: ≥ 48 g per day for women & ≥ 60 g per day for men	N/A
Flórez, 2015	N/A (mentioned some outcome measures)	N/A
García, 2015	N/A (review sleep)	N/A
Roos, 2015	percent drinking days (PDD) and drinks per drinking day (DDD)	N/A
Schellekens, 2015	heavy drinking (i.e. consumption of at least 5 alcoholic beverages on one day), or intoxication with alcohol during two consecutive days a week	Yes (Potgieter, Fureman)
Weinberger, 2015	having consumed at least 1 drink at any time in the previous year	Yes (Grant, 1995)
Wiers, 2015	drinking alcohol within the last 12 months for at least 3 days in a row	Yes (Gladwin, 2015; Wiers, 2011)
Witkiewitz, 2015	process of returning to heavy drinking (often defined as 4+/5+ drinks per occasion for women/ men) after a period of abstinence or reduced alcohol use	N/A
Budzyński, 2016	relapse vs. abstinence	N/A
Conde, 2016	N/A (recovery, DSM-5)	N/A
Czapla, 2016	N/A	N/A
Davis, 2016	percent days abstinent (PDA), mean number of drinks per drinking day (DDD), and proportion of heavy drinking days (HDD)	
Elliott, 2016	Persistence: maintaining full criteria for DSM-IV alcohol dependence (i.e. chronicity/persistence) throughout 3 years	N/A
Engel, 2016	relapse vs abstinence. (a severe relapse was defined as any alcohol consumption of >60 g/day in males and >48 g/day in females for 2 days)	N/A
Garbusow, 2016	$\geq 60/48$ (male/female) gram of alcohol per occasion	N/A
Karpyak, 2016	number of drinks per drinking day, and the number of drinking days	N/A
Law, 2016	Lapse: any amount of alcohol	N/A

Manning, 2016	abstinence vs. relapse	N/A
Matheus-roth, 2016	return to alcohol consumption rates at or near the level of their pre-detoxification use	N/A
McHugh, 2016	any alcohol use	Yes Witkiewitz, 2015/ COMBINE)
Mo, 2016	any alcohol use	N/A
Rupp, 2016	alcohol or substance use, excluding caffeine and tobacco, but including the intake of “nonalcoholic beer”	N/A
Shaw, 2016	any alcohol: time to first drink and number of drinks	N/A
Weinberger, 2016	N/A (“AUD persistence”)	N/A
Zahr, 2016	N/A (relapse vs. abstinence?)	N/A
Zandberg, 2016	Percentage Days Drinking (PDD)	N/A
Zois, 2016	relapse to heavy drinking: 48 g ethanol/day for women and 60 g ethanol/day for men (≥ 4 drinks per day for women and ≥ 5 drinks for men)	Yes (Jorde, 2014)
Adinoff, 2017	drinks per drinking day (DDD)	N/A
Durazzo, 2017a	any alcohol consumption	N/A
Barrio, 2017	(1) Need for total or partial (day hospital) hospitalization, or emergency department attendance, due to alcohol consumption. (2) Positivity of a urine screening (performed with ethanol). (3) Clinical detection, according to patient’s medical record, of any alcohol consumption. (This could be in the form of patient selfreport, significant others report or clinician report.)	N/A
Durazzo, 2017b	any alcohol use	N/A
Bernhardt, 2017	relapse to heavy drinking: consumption of $\geq 60/48$ (male/female) grams of alcohol in 1 drinking occasion	N/A
Blaine, 2017	N/A (first alcohol consumption?)	N/A
Damian, 2017	Remission: having a history of DSM-IV alcohol abuse or dependence, but not within the past 12 months	Yes (DSM-IV criteria)
Field, 2017	PHDD: percentage of days in which participants reported consuming in excess of eight (men) or six (women) units of alcohol, for which one unit equals 8 g of	Yes (Fertig, 2012; Garbutt, 2010; Gual, 2013;

	alcohol	Litten, 2013; Witkiewitz, 2014)
Foulds, 2017	N/A (review; definitions original papers)	Yes
Hufnagel, 2017	any alcohol use since discharge from the facility's detoxification unit.	N/A
Maisto, 2017	percentage of days when drinking occurred (PDD), and drinks per drinking day (DDD)	N/A
McCutcheon, 2017	Remission: as the absence of all 10 DSM-V AUD criteria, other than craving, for at least 12 months	
Paulino, 2017	returning to drinking after a period of abstinence accompanied by reinstatement of dependence symptoms	N/A
Possemato, 2017	"heavy" drinking days (≥ 5 drinks per day for men and ≥ 4 drinks per day for women) in 8-week periods	N/A
Rupp, 2017	any alcohol or substance use, excluding caffeine and tobacco, but including the intake of "nonalcoholic beer"	N/A
Sebold, 2017	consumption of 60/40 (male/female) gram of alcohol on any occasion	N/A
Tonigan, 2017	percent days abstinent (PDA) and drinks per drinking day (DPDD)	N/A
Weinland, 2017	number of alcohol-related hospital readmissions and the days to first readmission	N/A
Wigg, 2017	harmful relapse: associated with medical or social harm or a return to daily consumption of alcohol or in excess of 140 g of ethanol/week	Yes (NIAAA, Vanlemmens, 2009)
Zakinaeiz, 2017	first day of return to alcohol use during 90-day follow-up period	N/A
Zois, 2017	≥ 48 g/day for women and ≥ 60 g/day for men = 4 or more drinks per day for women and 5 or more drinks per day for men	Yes (earlier research)
Degenhardt, 2018	Remission: absence of all DSM-IV disorder related symptoms for more than 12 months	N/A
Gong, 2018	N/A (review of literature)	N/A
Karriker-Jaffe, 2018	N/A (relapse/ recurrence)	N/A
Maisto, 2018	percent drinking days (PDD), percent heavy (4/5 drinks in a day for women/men) drinking days (PHDD), and drinks per drinking day (DDD)	Yes (Form-90, Witkiewitz, 2015)
Mericle, 2018	problem drinking: (1) drinking five or more drinks per day at least once a month	Yes (Delucchi, 2010;

	for men or three or more drinks per day weekly for women, (2) one or more alcohol-related social consequences in the past year (from a list of eight), and/or (3) one or more alcohol dependence symptoms in the past year (from a list of nine)	Karriker-Jaffe, 2017)
Nalpas, 2018	repeated alcohol consumption	N/A
Quoilin, 2018	consumed at least 60 g alcohol (male; 40 g for a female) on a single occasion during the past year	Yes (standard clinical trials: Sass, 1996; Seo, 2015; Charlet, 2014)
Snelleman, 2018	relapse into pretreatment drinking levels	N/A
Wang, 2018	consumed at least one drink (a drink contains 13.6 grams of pure alcohol)	
Wu, 2018	relapse vs abstainers	N/A
Zou, 2018	any alcohol use	N/A
Bach, 2019a	relapse to heavy drinking: ≥ 48 g per day for women and ≥ 60 g per day for men	Yes (previous work: Bach, 2015)
Bach, 2019b	categorized into heavy relapse, if alcohol consumption exceeded 48 g per day for women or 60 g for men	Yes (Kiefer, 2011; Jorde, 2014)
Ledda, 2019	any alcohol use	N/A
Weinland, 2019	alcohol related readmission, days to first readmission	N/A

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S2 table outcome/ countries

<u>PDD/ PHD & DDD measures (US)</u>	<u>PDD/ PHD & DDD measures (Europe)</u>
Witkiewitz, 2015 (US/ UK)	Witkiewitz, 2015 (US/ UK)
Adinoff, 2017 (US)	Bach, 2015 (Germany)
Brower, 2003 (US)	Bach, 2019a (Germany)
Bujarski, 2013 (US)	Bach, 2019b (Germany)
Davis, 2016 (US)	Field, 2017 (UK)
Gillihan, 2011 (US)	Janu, 2012 (Czech)

Karpyak, 2016 (US) Lehavot, 2014 (US) Maisto, 2017 (US) Maisto, 2018 (US) Possemato, 2017 (US) Prisciandaro, 2012 (US) Roos, 2015 (US) Tonigan, 2017 (US) Witkiewitz, 2009 (US) Witkiewitz, 2011 (US) Witkiewitz, 2013 (US) Zandberg, 2016 (US)	Jorde, 2014 (Germany) Zois, 2016 (Germany) Zois, 2017(Germany)
<p><u>Any alcohol use</u> <u>(US, Brazil, Asia & Australia)</u></p>	<p><u>Any alcohol use</u> <u>(Europe)</u></p>
Bellamy, 2001 (US) Brower, 2001 (US) Cardenas, 2011 (US) Curran, 2000 (US) Dolan, 2013 (US) Durazzo, 2011 (US), Durazzo, 2017a (US), Durazzo, 2017b (US) Edens, 2008 (US) Friend, 2005a (US), Friend, 2005b (US) Garland, 2012 (US) Gish, 2001 (US) Gordon, 2006 (US) Gulliver, 2000 (US) Jorge, 2005 (US) McHugh, 2016 (US) Oberleitner, 2013 (US) Oslin, 2009 (US) Pfefferbaum, 2004 (US) Rando, 2011(US) Schneekloth, 2012 (US) Shaw, 2016 (US) Sinha, 2011 (US) Sterling, 2007 (US) Walton, 2003 (US) Weinberger, 2015(US) Witkiewitz, 2008 (US) Zou, 2018 (US)	Bartels, 2007 (Germany) Berking, 2011(Germany) Björnsson, 2005 (Sweden) Bottlender, 2004 (Germany) Bottlender, 2005a (Germany), Bottlender, 2005b (Germany) Bowden- Jones, 2005 (UK) Budzyński, 2016 (Poland) Costa, 2011 (France) Dahlgren, 2011 (Sweden) Demmel, 2006 (Germany) Deruytter, 2013 (Belgium) Diehl, 2007 (Germany) Driessen, 2001 (Germany) Engel, 2016 (Germany) Farren, 2010 (Ireland) Feige, 2007 (Germany) Gann, 2001 (Germany) Gann, 2002 (Germany) Hufnagel, 2017 (Germany) Jakubczyk, 2013 (Poland) Junghanns, 2003 (Germany) Junghanns, 2005a (Germany), Junghanns, 2005b (Germany) Krampe, 2008 (Germany) Ledda, 2019 (Italy) Lejoyeux, 2011 (France, multicenter; 10 countries) Lucht, 2002 (Germany) Mann, 2004 (Germany) Miguet, 2004 (France, Switzerland, Slovakia) Müller, 2008 (Germany)
Law, 2016 (Australia) Mo, 2016 (Australia) Terra, 2006 (Brazil), Terra, 2008 (Brazil)	

<p><u>Turkcapar, 2005 (Turkey)</u> <u>Manning, 2016 (Singapore)</u> <u>Wang, 2018 (China)</u></p>	<p><u>Müller, 2010 (Germany)</u> <u>Perney, 2005 (France)</u> <u>Pinto, 2008 (Belgium)</u> <u>Pitel, 2009 (France)</u> <u>Rus- Makovec, 2008 (Slovenia)</u> <u>Sander, 2006 (Germany)</u> <u>Schadé, 2003 (Netherlands, review)</u> <u>Schmidt, 2001 (Germany)</u> <u>Schmidt, 2007 (Germany)</u> <u>Smith, 2014 (UK)</u> <u>Suter, 2011 (Switzerland)</u> <u>Tómasson, 2000 (Iceland)</u> <u>Verheul, 2005 (Netherlands, Europe multi-center)</u> <u>Vielva, 2001(Spain)</u> <u>Walter, 2006a (Germany), Walter, 2006b (Germany)</u> <u>Wiesbeck, 2003 (Germany)</u> <u>Wojnar, 2008 (Poland), Wojnar, 2009 (Poland)</u> <u>Wu, 2018 (Belgium)</u></p>
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