

TWIST



Training With Stakeholders
Applying EU Addiction Research



Defining & diagnosing addiction

Jürgen Rehm

TUD Dresden, CAMH Toronto et al.

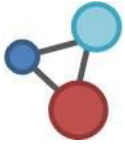
No COI for this topic, but in general support from WHO,
NIH, pharmaceutical companies (Tx for alcohol dependence)

Tuesday 24th October 2017



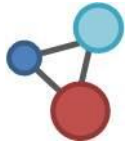
Reflections about heavy use over time

- Official definitions: DSM and WHO ICD (culturally problematic Rehm & Room, 2015; 2017)
- Research attempts (NIMH; NIH): definitions of mental disorders via brain functions (Insel: *Mental Illness Defined as Disruption in Neural Circuits*) -> often seen as future of ICD and DSM
- Epidemiological and other definitions



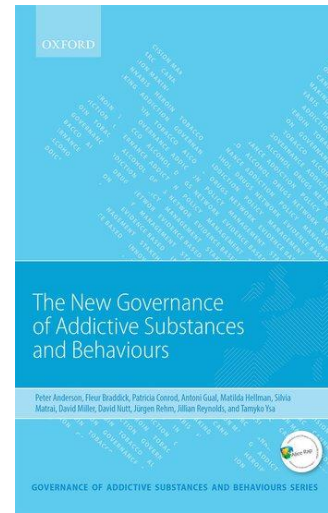
Consider the following

- Regarding alcohol dependence, Latvia has an estimated prevalence of 12.5% (national survey), Italy has a prevalence of $\ll 1\%$ (national survey)
- Regarding liver cirrhosis or *per capita* consumption, the differences are not that large (for PCA less than twofold; for Ic less than 2.5 fold)
- Other explanations: stigma? Norms for intoxication?



Basis: a joint effort!

Alcohol and Alcoholism Vol. 48, No. 6, pp. 633–640, 2013
Advance Access Publication 7 August 2013



doi: 10.1093/alcalc/agt127

FOR DEBATE

Defining Substance Use Disorders: Do We Really Need More Than Heavy Use?

J. Rehm^{1,2,3,4,5,*}, S. Marmet⁶, P. Anderson^{7,8}, A. Gual⁹, L. Kraus^{10,11}, D.J. Nutt¹², R. Room^{11,13,14}, A.V. Samokhvalov^{2,5},
E. Scafato¹⁵, M. Trapencieris¹⁶, R.W. Wiers¹⁷ and G. Gmel^{2,6,18,19}

- Interdisciplinary piece (basic research, psychology, psychiatry, public health epidemiology and sociology)
- To date several commentaries and many invitations to present



Wim van den Brink's short history in one slide

History of the concept of dependence

1. Moral model



2. Pharmacological model



3. Symptomatic model

4. Disease model



5. Learning model

6. Social model




7. Brain disease model



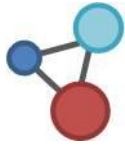
Ideological

5



1976: Edwards & Gross
Biopsychosocial model
Alcohol dependence syndrome

Empirical



Checked history of definitions: WHO 1957 habituation vs. addiction

Addiction (heroin et al.)

Drug addiction is a state of periodic or chronic intoxication produced by the repeated consumption of a drug (natural or synthetic). Its characteristics include :

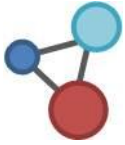
- (1) an overpowering desire or need (compulsion) to continue taking the drug and to obtain it by any means ;
- (2) a tendency to increase the dose ;
- (3) a psychic (psychological) and generally a physical dependence on the effects of the drug ;
- (4) detrimental effect on the individual and on society.

Habituation (Alcohol, tob.)

Drug habituation (habit) is a condition resulting from the repeated consumption of a drug. Its characteristics include :

- (1) a desire (but not a compulsion) to continue taking the drug for the sense of improved well-being which it engenders ;
- (2) little or no tendency to increase the dose ;
- (3) some degree of psychic dependence on the effect of the drug, but absence of physical dependence and hence of an abstinence syndrome ;
- (4) detrimental effects, if any, primarily on the individual.


Politics have been driving
definitions of addictions!

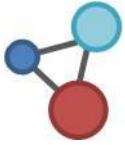


Current split

- Substance use disorders in DSM 5: 2 out of 11
- Dependence and harmful use in ICD-11

(after a relatively short period of convergence at least in the medical definition of dependence, there will be divergent developments between the US and WHO systems)

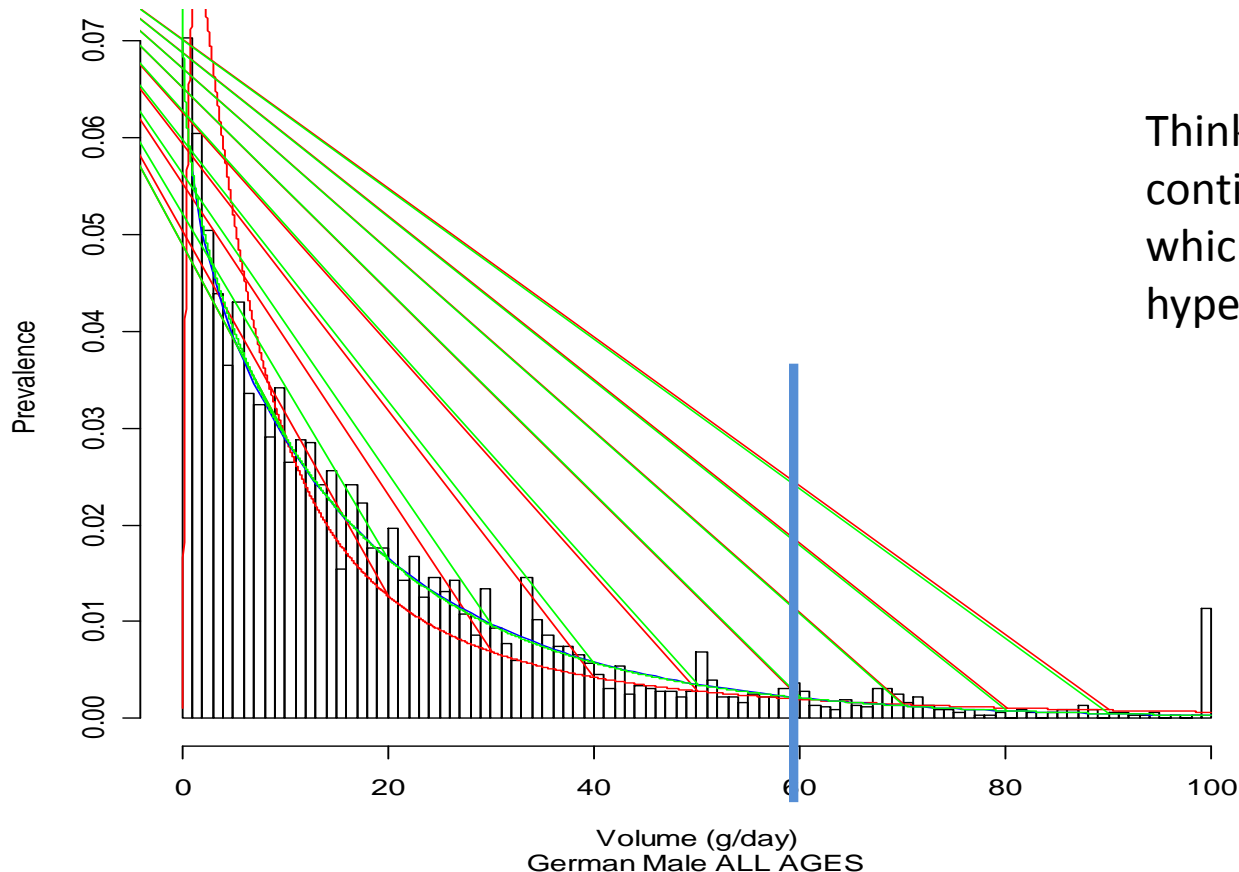
 so there is no current unified medical definition, let alone a definition which would be accepted in other systems as well (legal systems, monitoring systems: EMCDDA vs UNODC)



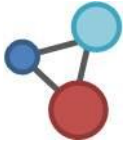
But what if...

we simply define it: **heavy use over time?**

Log-Normal (red) vs. Gamma (blue) vs. Weibull (green)



Think of blood pressure as a continuous distribution, which has been cut for hypertension



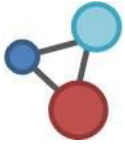
- 1. Heavy use over time is responsible for the changes in the brain, and other physiological characteristics of substance use disorders.**



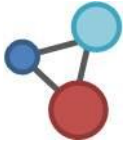
Neurobiology of use (v.d. Brink)

Function	Brain structures	Neurotransmitters
Reward deficiency	Ventral tegmental area (VTA) Nucleus accumbens (NAc)	Endorphins (μ -receptors) Dopamine
Disinhibition Impulsivity	DLPFC ACC	Noradrenalin, 5-HT GABA, glutamate
Conditioning Craving	NAc (ventral striatum) Amygdala Thalamus Prefrontal cortex (OFC, ACC)	Dynorphins (κ -receptors) Dopamine CRH Glutamate
Attentional bias/ salience	OFC VMPFC	Dopamine
Habit formation	Putamen, Nc caudatus (dorsal striatum)	Dopamine
Withdrawal	Locus coeruleus	Noradrenalin, CRH Glutamate

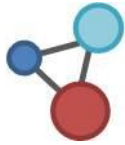
Increase in use over time with successive labels



2. Heavy use is responsible for intoxication, and for the withdrawal and tolerance phenomena regarded as central to current definitions of addiction or dependence.



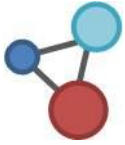
- 3. Heavy use over time is responsible for the main social consequences of substance use disorders such as problems in fulfilling social roles.**



The relation between heavy use over time and conventional criteria

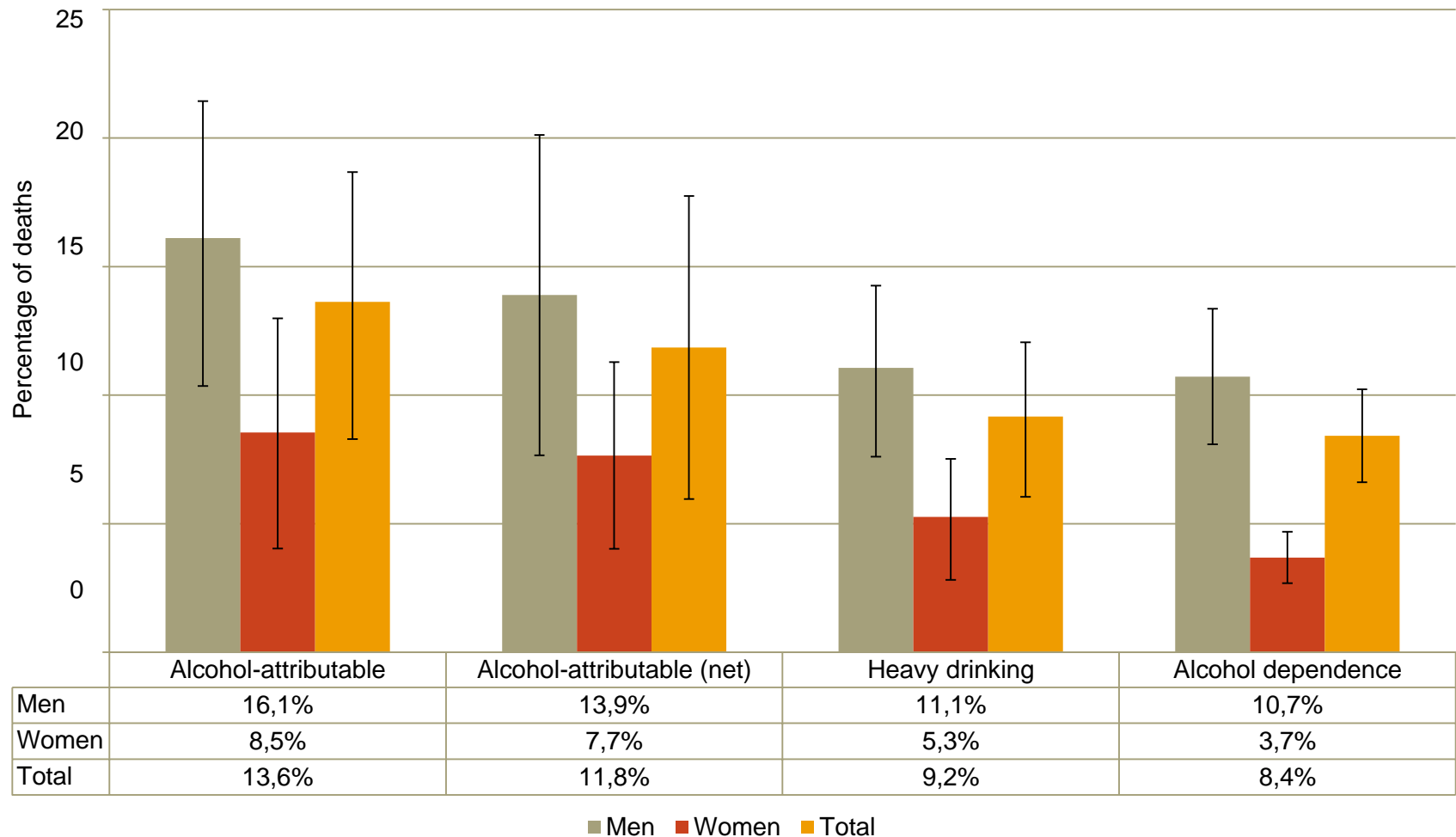
Table 1. Average alcohol intake in grams per day by number of DSM-IV criteria fulfilled for alcohol dependence (last year), by whether treated in lifetime: from data of the US National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)

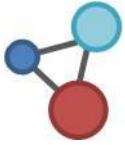
Gender	Number of criteria of DSM-IV for alcohol dependence							
	0	1	2	3	4	5	6	7
For people who have never been in treatment								
Men	9.1	27.1	35.9	56.5	73.6	88.0	107.4	189.0
Women	4.1	13.6	19.8	23.6	48.5	56.7	108.8	114.5
Total	6.6	21.6	29.5	45.4	64.7	77.5	107.8	170.3
For people who have been in treatment in their lifetime								
Men	20.6	35.2	98.2	75.2	109.1	124.2	119.8	214.1
Women	10.1	20.3	23.5	19.8	37.9	55.5	275.1	230.4
Total	17.5	31.7	77.9	61.5	91.2	104.7	165.1	218.3



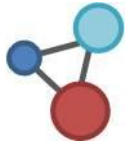
- 4. Heavy use over time is responsible for the majority of the substance-attributable burden of disease and mortality.**

How many deaths are attributable to heavy drinking?





- 5. Heavy use over time as a definition better fits the empirical data and will eliminate some of the current problems with definitions and operationalizations.**

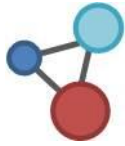


Correlations of prevalence of AD (explained variance often < 10%)

Table 2. Correlations between the prevalence of AD and variables hypothesized to be associated with AD (EU countries, Iceland, Norway, and Switzerland, 2010)

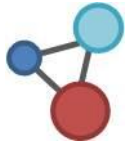
	Women			Men			Total		
	r ¹	95% CI	p value	r ¹	95% CI	p value	r ¹	95% CI	p value
Gross domestic product (purchasing power parity)	0.07	-0.30-0.42	0.710	-0.22	-0.54-0.15	0.245	-0.16	-0.49-0.21	0.404
Per capita consumption	0.17	-0.21-0.50	0.383	0.25	-0.12-0.56	0.179	0.24	-0.13-0.56	0.192
Unrecorded consumption ²	-0.02	-0.38-0.34	0.922	-0.06	-0.41-0.31	0.772	-0.06	-0.41-0.31	0.763
Patterns of drinking score ³	0.27	-0.10-0.58	0.145	0.63	0.35-0.81	0.000	0.59	0.29-0.78	0.001
Prevalence of heavy alcohol consumption ⁴	0.24	-0.13-0.55	0.199	0.18	-0.19-0.51	0.333	0.23	-0.14-0.55	0.219
Liver cirrhosis mortality	0.08	-0.33-0.46	0.713	0.25	-0.16-0.59	0.234	0.21	-0.21-0.56	0.324
Injury mortality	0.62	0.30-0.82	0.001	0.39	0.01-0.68	0.054	0.45	0.07-0.72	0.024
Alcohol-attributable liver cirrhosis, cancer and injury deaths	0.21	-0.20-0.56	0.304	0.47	0.09-0.73	0.018	0.39	0.00-0.68	0.053

¹ Pearson product-moment correlation coefficients. ² Unrecorded consumption in liters adult per capita (see above and WHO [21]). ³ Pattern of drinking score (see Methods above and Rehm et al. [44, 120]). ⁴ On average a consumption of alcohol ≥ 60 g/day for men and 40 g/day for women.



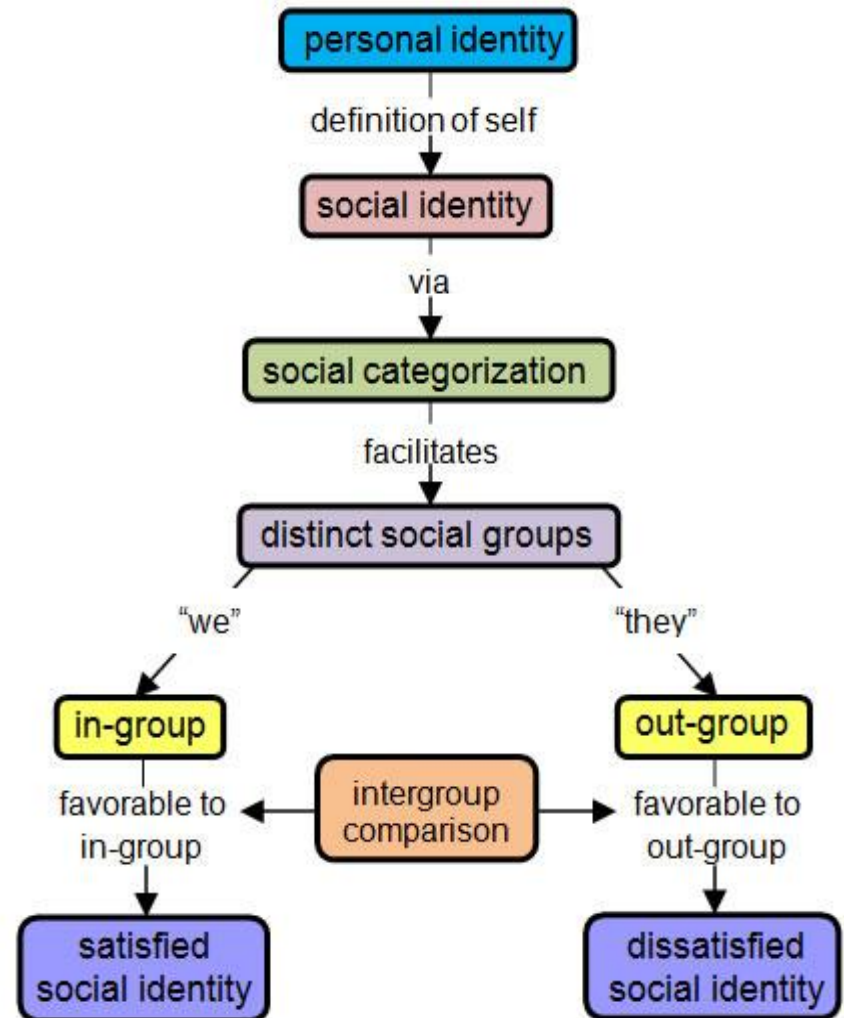
Classification need a purpose

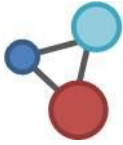
- For any kind of epidemiology including establishing causal relationships, heavy use over time is better
- This includes biological correlations.
- What about clinical? Necessity of a dichotomous outcome (sick vs. not sick)
 - Consider the example of blood pressure/hypertension



Stigmatization and thresholds

- The problem of groups (Nominal Group Theory Tajfel)
- It is harder to stigmatize against a continuum where we are all part of
- The key is to stress the continuum and de-emphasize the thresholds!





Thank you!

TWIST  **Training With Stakeholders**
Applying EU Addiction Research

www.twist-train.eu



The TWIST project is co-funded by grant N° 759685 under the European Union's Justice Programme – Drugs Initiatives. The content of this presentation represents the views of the author only and is his/her sole responsibility. The European Commission does not accept any responsibility for use that may be made of the information it contains.