



12-8-2015

## Estimated Probability of Becoming Alcohol Dependent: Extending a Multiparametric Approach

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### Repository Citation

Vsevolozhskaya, Olga A. and Anthony, James C., "Estimated Probability of Becoming Alcohol Dependent: Extending a Multiparametric Approach" (2015). *Biostatistics Presentations. 2.*  
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# Estimated Probability of Becoming Alcohol Dependent: Extending a Multiparametric Approach

## Abstract

**Background:** United States (US) epidemiological studies suggest that for every 5-8 who start drinking alcoholic beverages, at least one drinker will develop an alcohol dependence (AD) syndrome within the first 10 years after onset of drinking (Lopez-Quintero et al., 2011; Wagner & Anthony, 2002). Recently, we described a multiparametric functional analysis approach for new research to estimate these transition probabilities with a two-dimensional function (2D; Vsevolozhskaya & Anthony, 2015). Here, we demonstrate extension of this analysis to three-dimensional (3D) functions that combine information about number of recent drinking days and number of drinks on the typical drinking day (with  $Y = AD$  risk as the third dimension).

**Methods:** Data are from the United States National Survey on Drug Use and Health (NSDUH) Restricted-use Data Analysis System, 2002-2011, with nationally representative samples of newly incident drinkers and rapid-onset AD syndromes ascertained via standardized audio computer self interviews, completed for surveys of non-institutionalized civilian US citizens, age 12 years and older. Drinking history, including DSM-IV AD status, was assessed via the standardized computer-assisted interview assessments. The 3D functional estimates are based on a non-linear parametric Hill equation evaluated for (1) number of drinking days in 30 days just before NSDUH assessment, and (2) typical number of drinks on recent drinking days.

**Results:** Among newly incident drinkers with just one drink per drinking day, the estimated AD risk ranges from more or less 1% among infrequent drinkers with a single drinking day per month (95% bootstrap confidence interval, CI: 0.7, 1.0), upward to about 3% among daily drinkers (95% CI: 1.4, 3.7). Among newly incident drinkers with ~2 drinks per drinking day, estimated AD risk is much larger among daily drinkers (21.4%; 95% CI = 5, 21). Across subgroups defined by 3, 4, and 5 or more drinks per day, the estimated AD risk is larger, as can be seen clearly for those who have progressed to daily drinking: 31% for 3 drinks, 84% for 4 drinks, 90% for 5+ drinks, respectively, with some degree of CI overlap. However, among infrequent drinkers, with no more than one drinking day per month, the estimated AD risk does not appreciably differ from 1% irrespective of the number of drinks consumed per typical drinking day.

**Conclusions** Via the multiparametric functional analysis approach extended beyond the number of drinks per typical drinking day, this evidence helps clarify that AD risk apparently is relatively constant and quite limited when newly incident drinking is limited to no more than one drinking day per month. When newly incident drinkers are observed within 12 months after drinking onset, there is substantial increase in AD risk among daily drinkers, provided the typical number of drinks per day increases from 1 to 5+ drinks. This study is novel in its focus on newly incident drinkers and variations in risk of developing alcohol dependence soon after drinking onset. A new agenda for research AD risk among newly incident drinkers can be built upon this initial platform of new evidence, particularly if family history and individual-level genomic characteristics can be assessed and brought into play in future national surveys of this type.

## 2D Hill Function for AD Risk

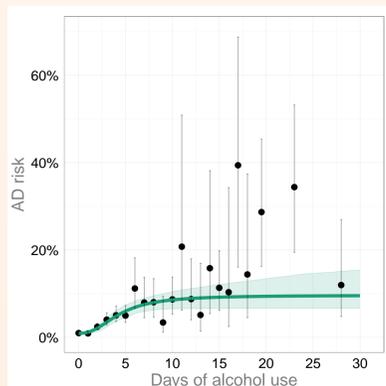


Figure 1: The estimated parameters for the AD risk are:  $P_{min} = 1\%$  (95% CI: 1%, 1%),  $P_{max} = 10\%$  (95% CI: 6%, 17%),  $PD_{50} = 4$  days (95% CI: 3, 10) and  $K = 2.48$  (95% CI: 1.47, 6.17).

The 2D estimated risk of alcohol dependence is based on the Hill equation that assumes an increasing 'S'-shaped relationship. The shape of the fitted 'S'-curve is determined by the four estimated parameters –  $P_{min}, P_{max}, PD_{50}$  and  $k$ . The estimated parameters for AD risk based on 2002-2011 NSDUH are interpreted as follows: regardless of the number of drinks per drinking occasion, among 'occasional drinkers' (with ~1 drinking day per month) about 1% are expected to develop AD disorder. Among 'frequent drinkers', about 10% of men and women are estimated to develop AD disorder. However, estimated  $PD_{50} \times 2$  for women is 14 days versus an estimated 22 days for men ( $P$ -value for the difference is 0.002).

## 3D Hill Function for Alcohol Dependence Risk

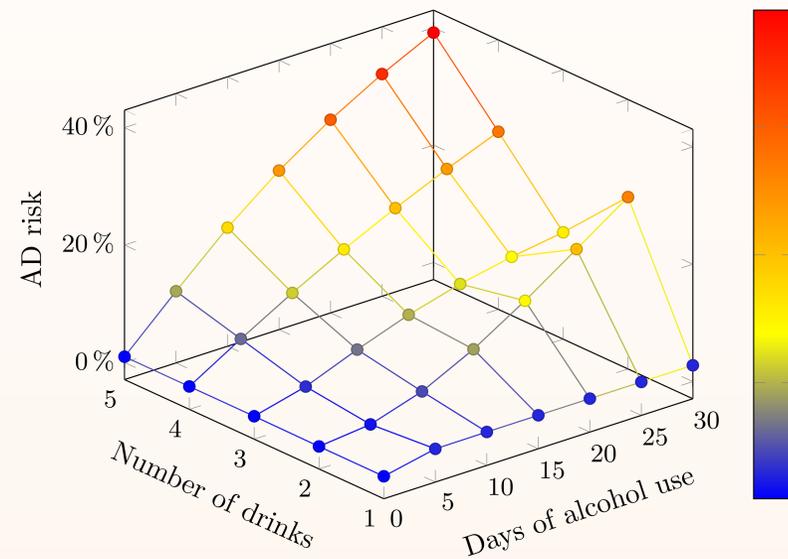


Figure 2: Estimated non-linear 3D Hill function for the predicted probability of newly incident drinkers with AD syndrome, as observed soon after onset of alcohol use. Data from the R-DAS United States National Surveys on Drug Use and Health, 2002-2011.

The 3D Hill function accounts for both the frequency of drinking and the number of drinks per drinking occasion. In the table, the row-wise Hill function parameter estimates are with number of drinks per drinking occasion as shown. The figure is a plot of the predicted probability of observing an AD syndrome based on this 3D Hill function approach.

	Parameters (95% Bootstrap Confidence Intervals)			
	$P_{min}$	$P_{max}$	$PD_{50}$	$k$
1 drink	1% (0.7, 1%)	3.5% (1.4, 11%)	3 days (1, 12)	5.00 (1.53, 5.00)
2 drinks	1% (0.7, 1%)	70% (8.1, 100%)	33 days (9, 138)	2.29 (1.05, 19.48)
3 drinks	1% (0.9, 1%)	29% (6.1, 100%)	20 days (4, 1000)	1.91 (0.70, 20.38)
4 drinks	1% (0.9, 1%)	100% (12, 100%)	48 days (4, 1923)	1.18 (0.51, 4.18)
5+ drinks	1% (0.8, 1%)	89% (29, 100%)	35 days (8, 58)	1.17 (0.99, 1.66)

Table 1: Comparative estimates of Hill function parameters characterizing probability of developing alcohol dependence soon after first occurrence of newly incident alcohol use. Data from the United States National Surveys on Drug Use and Health, 2002-2011.

## Discussion of Findings

Evaluated for newly incident drinkers with ~1 drinking day per month, the model-based probability of observing an AD syndrome is roughly 1%, irrespective of the number of drinks consumed. This estimate is consistent with 1% value from the 2D Hill function.

As the frequency of drinking increases, this 'AD risk' estimate begins to depend on the amount of alcohol consumed per drinking occasion. Specifically, among daily drinkers with 4+ drinks per drinking occasion we see a marked increase in AD risk relative to those with one drink per occasion. Also, the highest lower bound of the estimated AD risk for newly incident drinkers is seen among daily heavy episodic drinkers, with 5+ drinks consumed per drinking occasion, at least 30% of whom are observed with an AD syndrome.

In terms of the expected number of the consecutive drinking days, after which half of the expected maximum proportion of people develop AD (i.e.,  $PD_{50}$ ), we see no marked variation among drinkers with at least 2 drinks per drinking occasion (although there is variation in the respective expected maximums or  $P_{max}$ ). Also, the quantity  $PD_{50} \times 2$  leads us to predict that very high AD risk values will be seen for newly incident drinkers after about two months of daily drinking of two or more drinks per occasion, all else being equal.

## Limitations

Of special concern is the self-report interview survey data from NSDUH. However, in the context of nationally representative sample surveys on this scale, there are few logistically feasible and affordable alternatives to self-report. In addition, cross-sectional data always will be inferior to longitudinal data when fitting Hill functions of this type. Nonetheless, these cross-sectional estimates provide novel evidence of the distribution of estimated 'AD risk' in relation to indicators of both frequency and "dose" of drinking. Finally, feedback loops might be present (Anthony, 2010) as can be seen in a monotonic increase in the typical number of drinks per drinking occasion association with a non-monotonic increase in the AD risk. However, a restriction on the Hill parameter estimates can be enforced to ensure a monotonic increase in AD risk associated with the monotonic increase in the number of drinks.

## Funding Source and Disclosure

### Disclosure

There are no relevant financial interests to disclose.

### Funding Source

Supported via a National Institute on Drug Abuse Senior Scientist Award JCA: K05DA015799.