



Identifying and Tracking Alcoholism Over the Life Course: 20 Years of Evidence

The Michigan Longitudinal Study

This high risk for alcoholism family study is a joint venture of the University of Michigan and Michigan State University that was begun in 1985. It is the developmentally earliest high risk for alcoholism and other substance use disorder prospective study currently active. The study involved three subsamples, all recruited from the same 4 county wide area and all were ascertained initially through father's diagnosis; one subset were court alcoholics (drunk driving fathers); a second were community nonalcoholic controls uncovered in canvass of the neighborhoods where court alcoholics lived (both father and mother were free of an alcohol use disorder (AUD) diagnosis in adulthood); a third subset were community alcoholics (alcoholic men uncovered in community canvass). Mothers' (wives) diagnosis was free to vary in the alcoholic groups. All families had an initially 3-5 year old son (the target child (TC)) and both were the TC's biological parents. All siblings within +/- 8 years of TC (G2s), step-parents, and now G3s (N=2,100 individuals) were also recruited. Total N = 467 families (N ~ 2,100 individuals).

The study involves assessment at 3 year waves and is currently at Wave 6 (ages 18-20) and Wave 7 (ages 21-23) for the core group of offspring.

The main study is the psychosocial characterization study (R37 AA 07065) with spin off projects involving neuropsychological assessment (R01 AA 12217), fMRIs of children prior to any drug involvement (K01 DA020088; Heitzeg) and characterization of effects of smoking on G2s and G1s (R01 DA 021032; Glass).

Goals of the Study

Identification of markers of risk for alcoholism from early childhood into adulthood for children; developing mechanistic models of risk development, increase, and dilution. Tracking clinical course, psychosocial functioning, and correlates of symptomatology for adult participants

Findings Among Children

1. Early indicators of learning about drug schemas: learning about alcohol in preschool

In order to approach and use an object, one needs to be able to label it. Precocious learning about alcohol involves the ability to identify it, know the rule structure of its use, and imagine its use in everyday situations. We developed several measures of early schema development, one involving the Appropriate Beverage Task (See Figures 2,3). Early ability to identify alcoholic beverages by name and smell was better in children of alcoholics (COAs) (Noll et al., 1990) (Fig. 4). Early use of schemas was related to parents' use (Figure 5).



Fig. 2

Knowledge Of Specific Alcoholic Beverages Among Preschooler COAs and Non-COAs

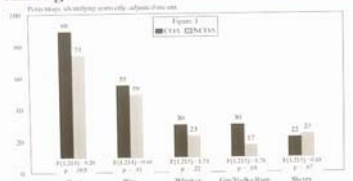


Fig. 4



Fig. 3

Child attributions of alcoholic beverage use at age 3-5: Hierarchical regressions of child's age and parental alcohol consumption on child attributions

	R ²	R ² change
Attributions to adult males		
Step 1. Child's age	0.03	0.03*
Step 2. Paternal alcohol Consumption	0.15	0.12**
Step 3. Maternal alcohol Consumption	0.16	0.01**
Attributions to adult females		
Step 1. Child's age	0.01	0.01
Step 2. Maternal alcohol Consumption	0.04	0.03*
Step 3. Paternal alcohol Consumption	0.04	0.00*

Fig. 5

2. Identifying early markers of risk for alcohol use disorder: Predicting early onset of alcohol use from precocious alcohol schema development. Both early learning and familial risk play a role in the development of alcoholism risk

Logistic regression: Early onset of drinking (≤ 14) predicted from alcohol schemas @ age 3 to 5 even when parental alcoholism is co-varied out (M+F)

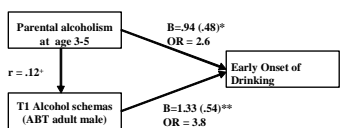


Fig. 6

When children are so young, a proxy marker of risk for later disorder is required in order to identify risky processes. We used early onset of drinking (age 14 and earlier); it is both a proxy for adolescent problem drinking, and the rate of alcohol dependence is 4Xs greater in early drinkers. Early alcohol schema development predicts early drinking above and beyond family history effects (i.e., early learning is a separate component of risk for later AUD), See Figure 6

3. Other early indicators: Preschool behavioral phenotypes in the externalizing domain predict early drinking, smoking, marijuana, and other drug involvement in early adolescence

Behavioral control is the tendency to express or contain one's impulses and behaviors. Control increases over the course of childhood and adolescence. High behavioral undercontrol in early childhood (age 4.5) predicted early onset of drinking, drunkenness by age 17, number of alcohol problems experienced in adolescence, and illicit drug use by age 17 (Wong et al., in press). In addition, rate of **change** in behavioral control also predicted these outcomes; those children whose rate of change (improvement) in behavioral control over the course of childhood was **slower** were more likely to develop all these risky alcohol and drug outcomes. (See Figure 7).

Fitted hazard function for age of onset of alcohol use among MLS children with low, normal, and high levels of behavioral control (BC)

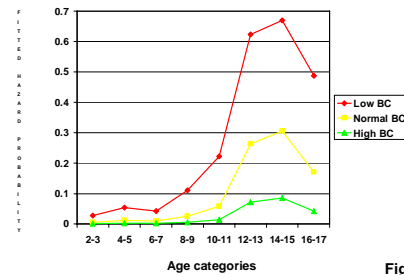


Fig. 7

Other early appearing phenotypes that independently predict these outcomes include **child conduct symptoms**, and an **executive function measure, poor response inhibition** (as measured by the tracking version of the Stopping Task). Poor response inhibition predicted alcohol involvement onset, alcohol problems, and number of other drugs used. This relationship existed over and above the contribution of low IQ, paternal alcoholism, paternal antisocial personality disorder, child ADHD or conduct disorder symptoms, or shared family history. The

predictive models explained 20-40% of residual variance in outcome scores. (Nigg et al., in press).

4. Early sleep problems are an indicator of another pathway into AUD risk.

Sleep problems have been known to predict relapse among alcoholic patients, sleep problems in adolescence are related to problem alcohol use, and sleep problems in middle childhood are known to be related to a number of child behavior problems of that era. However, no prior work has examined the possibility that the sleep difficulties precede and anticipate these difficulties. Wong et al. (2004) examined the relationship of early reports of sleep difficulties by mothers to alcohol and drug outcomes in adolescence.

Sleep problems at age 3 to 5 predicted an early onset of any use of alcohol, marijuana, and illicit drugs, as well as an early onset of occasional or regular use of cigarettes by age 12 to 14. (Figure 8). Although sleep problems in early childhood also predicted attention problems and anxiety/

Percentage of Ss having Childhood Sleep Problems as Related to Onset of Adolescent Alcohol and Other Drug Use

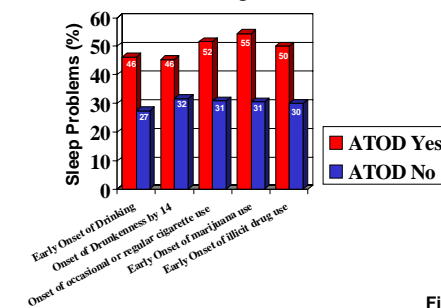


Fig. 8

5. Pathways of risk from childhood to adolescence: Multiple trajectories and nonlinearity of risk as a function of family adversity.

Although externalizing behavior problems are one well established risk factor for early alcohol use, problem use, and risk for later AUD, variation in level of that behavior varies both with age and as a function of level of family adversity. The normative pattern is for a decrease from early to middle childhood, followed by an increase occurring at the childhood to adolescent transition. Zucker et al (2003) examined variation in level of this risk factor as a function of initial level of risk (behavioral problems at 3 to 5) and amount of family adversity. Family adversity was based on amount and currency of parental alcoholism (0 vs. 1 vs. 2 parents alcoholic; alcoholism current or past) and whether or not a parent also was antisocial (antisocial personality disorder diagnosis). This cross classification produced 4 different groups on the basis of child and family functioning in early life (Fig 9). Although the adversity index is at least partially a marker for genetic risk, it also is a marker of adverse socialization experiences (Loukas et al, 2003).

Two subsets of children are of special interest, both in the off-diagonal categories. These are the "resilient" group (low initial psychopathology within a high adversity family) and the "troubled" group (the obverse). Trajectories of externalizing and internalizing behavior were plotted for the 2X2 matrix of familial and child phenotypic risk. Externalizing decreases over the course of childhood, then increases at the childhood to adolescent transition (Fig 10). This transition is both a social (the move to middle school) and a biological (pubertal onset) turning point. The main effect for all 4 groups following the transition is for increased deviance proneness. There is also a significant interaction between group and change in level of externalizing, involving divergence in the rate of emergence of undercontrolled as well as socially deviant behavior. Internalizing behavior (Figure 11) continues to maintain its place among 3 risk

groups, but the resilient group's negative affect level increases starting after school entry, and proceeds to a level that is indistinguishable from the vulnerable (Hi/Hi) and troubled (Hi initial risky phenotype embedded in a family of low adversity) groups. The resilient group also starts to show differences in self esteem at age 9-11.

The different adaptation groups during the preschool years

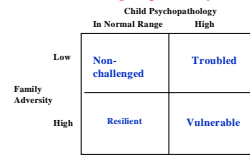
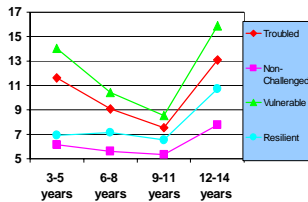
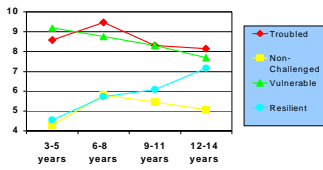


Fig. 9



Stability and change in externalizing symptoms during the transition into high school

Fig. 10



Internalizing symptoms

Fig. 11

6. Social environmental factors that enhance risk development: Differential environmental effects as a function of trajectory of behavioral risk

The trajectories just described involve the broadband factors of externalizing and internalizing, the two broadest indicators of undercontrol and negative affectivity. The potential for heterogeneity of content within factors defined so broadly might explain the weak evidence for environmental effects. To pursue this issue, Jester et al (2005) focused on the externalizing factor and examined trajectory variation over the age 7-16 interval for the externalizing subdomains of aggression and inattention/hyperactivity /disorganization. Jester et al. suggested that (a) because these behaviors frequently co-occur, their overlapping content is confounded in analyses that do not disaggregate them. (b) The literature also suggests they have different etiologies that map onto different neurological substrates, and (c) there is also some suggestion that different social environmental variables may influence their course. Initial analyses using a parallel process latent growth model found aggressive behavior decreasing throughout childhood and adolescence, whereas inattentive/hyperactive behavior levels were constant. Growth mixture modeling found two classes for inattention/hyperactivity and two for aggressive behavior, resulting in a total of four trajectory classes. Different influences of the family environment predicted development of the two types of behavior problems when the other behavior problem was held constant. **Lower emotional support and lower intellectual stimulation** by the parents in early childhood predicted membership in the high problem class of inattention/hyperactivity when the trajectory of aggression was held constant. Conversely, **family conflict and low cohesiveness** predicted membership in a worse developmental trajectory of aggressive behavior when the inattention/hyperactivity trajectories were held constant.

PATHWAYS AND FINDINGS AMONG ADULTS and IN THE FAMILIES

7. The importance of antisocial comorbidity as a differentiator of the alcoholic phenotype

For at least a generation, subtyping of alcoholism based on the presence/absence of a comorbid diagnosis of antisocial personality disorder has shown itself to be a powerful differentiator of symptomatic severity, course, and familiarity of alcoholism. Analyses of family functioning within the MLS continue to indicate this is an important differentiating set of characteristics, including being a powerful differentiator of offspring characteristics. Thus, AAL offspring show the precursive risk characteristics suggested by the adult studies, and these characteristics are identifiable in early childhood (Zucker et al., 1996; Puttler et al, 1998). AAL COAs have greater externalizing and internalizing behavioral risk vis a vis nonantisocial COAs, who in turn have more of these behavioral risks than control children (Puttler et al., 1998). Where evaluated, maternal alcoholism, or antisociality, sometimes provides an incremental, albeit small contribution to the differentiation.

In another set of analyses examining couple functioning, Floyd et al, (2005) behaviorally coded videotaped marital interactions of the G1 (parent) participants and evaluated whether and how the marital interactions of alcoholic couples might differ across alcoholic subtypes. They also examined the role of the wife's alcoholism status on couples' problem-solving interactions. They found that couples with an antisocial alcoholic husband had **more hostile behaviors** than control couples, but wife's alcoholism showed no effect (Fig 12). Why do couples with an antisocial alcoholic husband have more hostile behaviors than control couples? Compared to non-antisocial alcoholics, the antisocial alcoholics have an earlier onset of drinking and more severe alcohol-related problems. They also have higher levels of other forms of psychopathology, including depressed mood. They also have larger deficits in executive-cognitive functioning that may produce poorer problem-solving skills. All of these factors increase the likelihood of escalation of marital conflict.

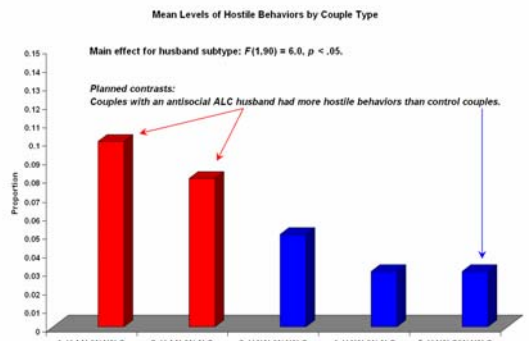


Fig. 12

8. Predictors of remission in alcoholism over 9 years

In evaluating stability and change in diagnosis over time in the initially alcoholic men in the study, approximately half (46%) did not meet a diagnosis at the 9 year follow-up. Numerous earlier studies have focused on the predictors of recovery in persons with an AUD. Most have been retrospective and have only measured predictors of short term recovery after the completion of treatment. McAweeney et al (2005) were able to evaluate the role of psychological and social (partner) factors in predicting recovery over the 9-year interval. Predictors of recovery were number of experiences with treatment, level of education, number of years of intervening recovery over the follow-up period, partner baseline AUD status, and extensiveness of partners social support network. Alcoholic's initial severity of drinking did not predict long-term outcome. Furthermore, **recovered men's partners' decreased their AUD in the interim while nonremitters' partners increased** (Fig 13). Findings highlight the transitions in and out of AUD with 62% of the men having stable drinking patterns of either remission or unremitting AUD diagnosis over the entire followup period, and 38% with considerable variability (Fig 14). Findings also indicate the importance of interpersonal factors in either maintaining AUD or in promoting recovery.

9. Contributors to cognitive dysfunction in adulthood: the contribution of cigarette smoking as well as alcohol involvement

Impaired problem solving, visual-spatial processing, memory, and cognitive proficiency are consequences of severe alcoholism. Smoking is much more prevalent among alcoholics than the general population, yet the possible neurocognitive effects of cigarette smoking in alcoholism have not previously been studied, despite evidence that long-term smoking is also associated with neurocognitive deficits. To determine whether smoking also contributed to neurocognitive function we examined these relationships among the MLS men using lifetime measures of alcohol and cigarette use as predictors of neurocognitive impairment. Neurocognitive function was measured with IQ (short version of WAIS-R), and cognitive proficiency (fast, accurate performance on the MICROCOG). Both alcoholism and smoking were negatively correlated with neurocognitive function. However, when alcoholism and smoking were included in regression models, smoking remained a significant predictor for both measures, but alcoholism remained significant only for IQ (Fig 15) Thus it appears that smoking may explain some of the relationship between alcoholism and neurocognitive function, perhaps especially for measures that focus on proficiency. Future studies are necessary to more fully understand these effects and their mechanisms of transmission.

Fig 15 Multiple Regression Results for Alcoholism and Smoking predicting Global Neurocognitive Function

	IQ	Outcome Variables Cognitive Proficiency
Standardized Regression Coefficients:		
LAPS	-.229**	-.127
Pack-years	-.230**	-.168*
Other drug use	-.058	.073
Depression		-.195**
R-Squared (Model):	.052	.097

Note: * = p < .05, ** = p < .01, LAPS=Lifetime Alcohol Problems Score, Depression=Hamilton Current Depression Score.

Conclusions

The evidence we have assembled so far, from a number of substudies involving multiple predictors of risk, is that a number of independent predictors of problem alcohol use and AUD exist. They appear to operate independently of family history risk (both alcoholic FH and parental ASB), and taken together they are suggestive of a multidomain, multivariate, nondrug specific matrix of risk and risk development that works to create the problem phenotype as well as the diagnostic outcome. The fact that the risk phenotypes (externalizing, internalizing, behavioral undercontrol, response inhibition, and the putative dysregulatory mechanism indexed by the sleep problem indicator) are separately known to predict a broad range of endpoints beyond alcohol involvement suggests that these are behavioral phenotypes of broad explanatory value, that index processes which mediate a number of different kinds of psychopathology. Most of them are in place long before the first alcohol use takes place. The critical next step work is to isolate the specific environments which moderate their intensity, specify the mediational mechanisms by which they work, attempt to establish a hierarchy of causes within this matrix, and establish the degree to which alcohol use itself is a mediator of their later development.

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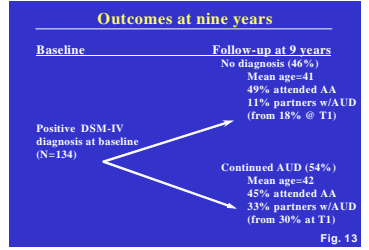


Fig. 13

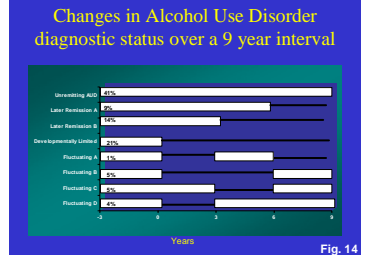


Fig. 14

Enlarged figures for: Identifying and Tracking Alcoholism Over the Life Course: 20 Years of Evidence

Percentage of Ss having Childhood Sleep Problems as Related to Onset of Adolescent Alcohol and Other Drug Use

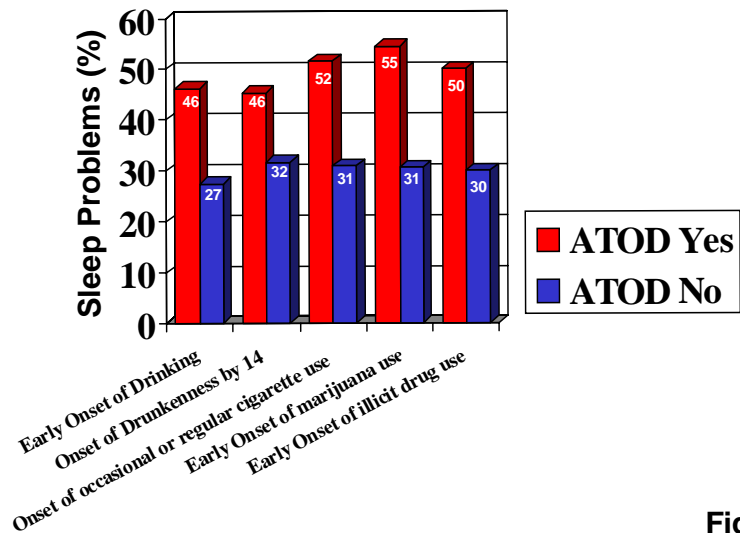


Fig. 8

Outcomes at nine years

Baseline

Follow-up at 9 years

Positive DSM-IV diagnosis at baseline (N=134)

No diagnosis (46%)
 Mean age=41
 49% attended AA
 11% partners w/AUD (from 18% @ T1)

Continued AUD (54%)
 Mean age=42
 45% attended AA
 33% partners w/AUD (from 30% at T1)

Fig. 13

Mean Levels of Hostile Behaviors by Couple Type

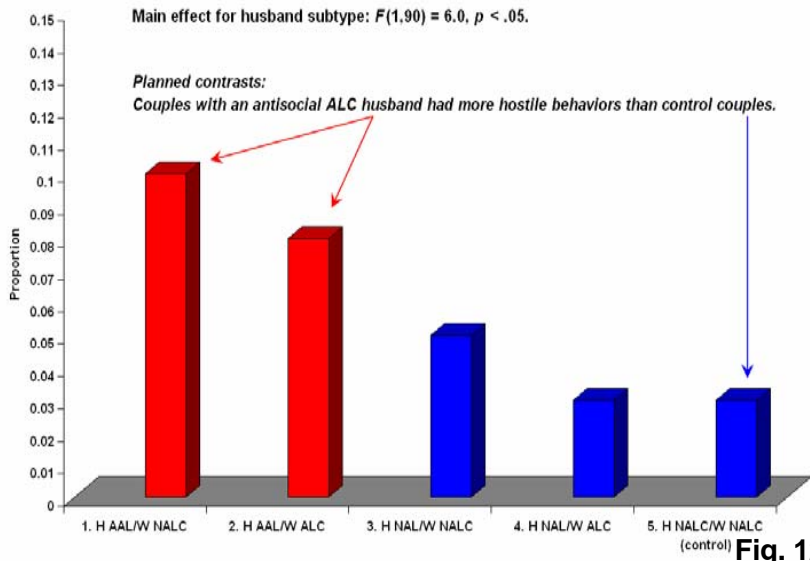


Fig. 12

Changes in Alcohol Use Disorder diagnostic status over a 9 year interval

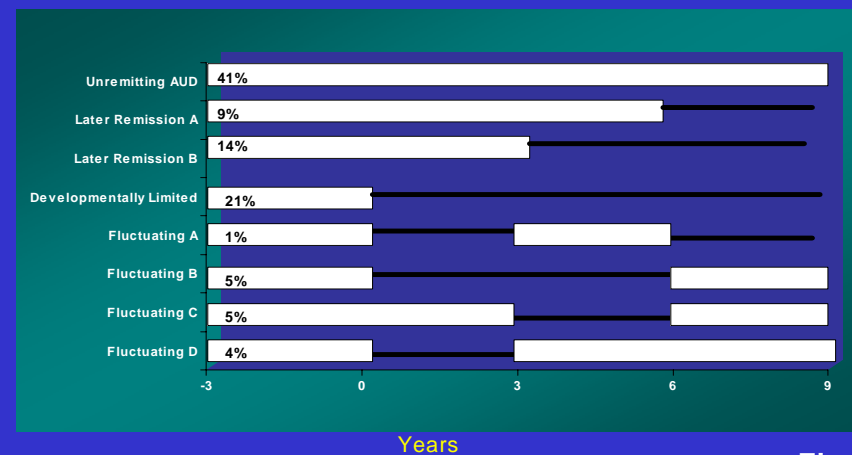


Fig. 14