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Characterizing Midlife-Onset Alcohol Dependence: Implications for Etiology, Prevention, and Healthy Aging

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Abstract

We evaluated the developmental epidemiology of midlife-onset alcohol dependence (AD) in the Dunedin Study (N = 1,037), a population-representative cohort followed across 5 decades. At ages 18, 21, 26, 32, 38, and 45, past-year AD prevalence was 11.0%, 18.4%, 13.6%, 8.1%, 9.6%, and 11.3%, respectively. As expected, relative to never-diagnosed individuals, individuals with early onset AD (first diagnosis at age 18 or age 21, prevalence = 22.9%) were distinguished by a range of early life and adult correlates. Individuals with midlife-onset AD (first diagnosis at age 38 or age 45, prevalence = 5.6%) were distinguished by fewer early life correlates, but exhibited a family history of AD and adolescent dysregulation and marijuana use. They were characterized by an array of adult correlates, including internalizing disorders, mental-health-treatment contact, criminal behavior, perceived stress, coping by drinking, lower likelihood of marriage and parenthood, and reduced preparedness for old age. They also experienced more adult alcohol-related impairment than the early onset group. Results can guide efforts to reduce midlife alcohol-related problems and support healthy aging.

Keywords

developmental psychopathology, epidemiology, prevention, public health, substance disorders

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Alcohol use disorders tend to increase in adolescence, peak in the early 20s, and decline thereafter (Dawson et al., 2006; Grant et al., 2004). However, not all individuals with alcohol use disorders follow this trajectory (Moss et al., 2007; Vergés et al., 2012). There is increasing recognition of the importance of examining heterogeneity in the course of alcohol-related problems across the life span (Chassin et al., 2013; National Institute on Alcohol Abuse and Alcoholism, 2021; Vergés et al., 2012). Here, we consider onset of alcohol dependence at midlife.

Midlife—generally considered to encompass ages 40 to 60, plus or minus 10 years (Infurna et al., 2020)—is a salient developmental stage to consider in alcohol research for at least three reasons. First, rates of risky alcohol consumption among adults in their 30s and 40s are elevated in some countries (e.g., the UK, Daly & Robinson, 2021; de Vocht et al., 2016; New Zealand, Ministry of Health, 2021; and Australia, Australian Bureau of Statistics, 2021) and increasing in others (e.g., the United States, Grant et al., 2017; Grucza et al., 2018). Second, midlife is characterized by unique role

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transitions, including preparations for financial, social, and health demands that accompany older age (Richmond-Rakerd et al., 2021). Third, risk for negative alcohol-related outcomes increases with advancing age (Van Montfoort-De Rave et al., 2016). Thus, identification and prevention of alcohol-related problems in midlife is an important component of efforts to support healthy aging.

Prior research has aimed to characterize new-onset alcohol use disorder in middle adulthood, focusing on the diagnostic designation of alcohol dependence and the early midlife period ranging from the mid-30s to early 40s (Jacob et al., 2005, 2009, 2010, 2012; Joos et al., 2012; Mattisson et al., 2010; Moss et al., 2007, 2010; Schuckit & Smith, 2011; Vergés et al., 2012). Existing studies suggest that between 3% and 6.7% of individuals first develop alcohol dependence at early midlife (Schuckit & Smith, 2011; Vergés et al., 2012). Previous work has found that relative to individuals who first develop dependence before midlife, individuals who do so in midlife tend to have a comparable or modestly elevated family history of alcohol dependence (Jacob et al., 2010; Moss et al., 2007); lower rates of psychiatric and substance-use comorbidities, with the exception of depression and frequent smoking (Jacob et al., 2010; Moss et al., 2007); lower impulsivity (Joos et al., 2012); greater treatment seeking; and lower probability of encountering legal problems (Moss et al., 2007); and they attribute their problem drinking to emotional, interpersonal, and work-related problems (Jacob et al., 2009). Findings concerning socioeconomic standing and marital status are mixed; some studies have suggested individuals with midlife-onset alcohol dependence have higher incomes and are more likely to be married than other alcohol-dependence groups (Moss et al., 2007, 2010), and others have reported that they have comparable incomes and lower marriage rates (Jacob et al., 2009).

Previous research has provided important information about the emergence of alcohol dependence in midlife. However, most work has relied on retrospective age-of-onset reports (e.g., Jacob et al., 2005, 2012), which entail sources of invalidity and can underestimate prevalence rates (Moffitt et al., 2010). Two studies used prospective data, but one considered only men (Schuckit & Smith, 2011) and the other comprised only two assessment waves (Vergés et al., 2012). Furthermore, studies have primarily employed selected samples, such as treatment samples (Joos et al., 2012) and male veterans (e.g., Jacob et al., 2005, 2012). Much research comes from U.S.-based, predominantly White samples (Jacob et al., 2005, 2009, 2010, 2012; Schuckit & Smith, 2011), with exceptions including studies in a Swedish sample (Mattisson et al., 2010) and a U.S. nationally representative sample (Moss et al., 2007, 2010; Vergés et al., 2012). In addition, studies of midlife-onset alcohol dependence have considered a limited range of diagnostic and psychosocial correlates (e.g., Joos et al., 2012; Moss et al., 2007), and early life predictors have not received systematic attention. Notably, factors relevant to the midlife transition period (e.g., midlife aging processes) have not been examined.

We addressed many of these gaps by conducting a comprehensive analysis of the developmental epidemiology of midlife-onset alcohol dependence using a population-based New Zealand (NZ) cohort followed from birth to age 45, with 94% retention. A prior report from this cohort (Meier et al., 2013) measured alcohol-dependence trajectories to age 32. Our study provides new information by extending to age 45 and considering alcohol-dependence onset at midlife. This study had two aims. First, we aimed to document the prevalence of midlife-onset alcohol dependence (onset at age 38 or 45 years) in an unselected, representative cohort, increasing the generalizability of our estimates. Furthermore, alcohol dependence was ascertained across repeated prospective assessments, reducing the potential for retrospective-reporting bias and misclassification of age of onset. Second, we aimed to identify prospective predictors and adult correlates that characterize individuals with midlife-onset alcohol dependence, and test whether these differ from the predictors and correlates of early onset alcohol dependence (onset at age 18 or 21 years). For this aim, using a multimethod approach, we ascertained measures identified in prior studies to characterize alcohol dependence in early life and/or adulthood, including middle adulthood: family psychiatric history, early life and adult mental health and substance use, personality, life functioning, stress and coping, and family characteristics (Meier et al., 2013; Moss et al., 2007; Sher & Gotham, 1999; Wertz et al., 2021; Zucker, 1986; Zucker et al., 1995). We also selected novel correlates pertaining to midlife aging processes (pace of aging and aging preparedness; Richmond-Rakerd et al., 2021).

Transparency and Openness

The analysis plan was preregistered (2021; https://sites.duke.edu/moffittcaspiprojects/). The Supplemental Material available online includes additional supporting information about the study. We report how we determined our sample size, all data exclusions, and all study measures. Because this study involves analysis of preexisting data, no experimental manipulations were introduced. Written informed consent was obtained from participants. Study protocols were approved by the institutional ethical review boards of the participating universities.

Method

Participants

Participants were members of the Dunedin Multidisciplinary Health and Development Study, a longitudinal investigation of health and behavior in a complete birth cohort. Dunedin participants (N = 1,037, 91% of eligible births, 52% male) were all individuals born between April 1972 and March 1973 in Dunedin, NZ, who were eligible based on residence in the province at age 3 years and who participated in the first assessment at age 3 years (Poulton et al., 2015, 2023). The cohort represents the full range of socioeconomic status (SES) in the general population of NZ's South Island. On adult health, the cohort matches the NZ National Health and Nutrition Survey on key health indicators (e.g., body mass index, smoking, visits to a physician) and matches the NZ census of people the same age on educational attainment (Richmond-Rakerd et al., 2020). The cohort is primarily White (≈93%), matching South Island demographics.

Assessments were carried out at birth and ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, 38, and most recently, 45 years, when 938 of the 997 participants (94.1%) still alive participated. Individuals who took part at age 45 did not differ significantly from other living participants in childhood social class, childhood IQ, childhood self-control, adverse childhood events, psychopathology history, or a polygenic score for educational attainment (see the Supplemental Methods in the Supplemental Material).

Measures

Alcohol dependence. Past-year alcohol dependence was assessed using the Diagnostic Interview Schedule at ages 18 through 45 years (Robins et al., 1995, 1981). At ages 18 and 21, diagnoses were made according to the third revised edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-III-R*; American Psychiatric Association [APA], 1987). At subsequent ages, diagnoses were made according to the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV*; APA, 1994). Although the age-45 assessment occurred after introduction of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*; APA, 2013), alcohol and other substance use disorders were diagnosed using *DSM-IV* because *DSM-5* removed the dependence and abuse distinction.

Following prior reports (Meier et al., 2013), we rescored alcohol-dependence criteria to be consistent across assessment waves and conform to *DSM-IV* (APA, 1994) criteria. Only one criterion at the age-18 and age-21 assessments differed from *DSM-IV* (APA, 1994) criteria: The withdrawal criterion required only one sign of withdrawal, or clinically significant distress or impairment caused by withdrawal, and did not include using a "closely-related substance" to relieve or avoid withdrawal because these subcriteria were not part of *DSM-III-R* (APA, 1987). To maintain consistency across ages, we did not use these subcriteria in making *DSM-IV* (APA, 1994) alcohol-dependence diagnoses for ages 26, 32, 38, or 45.

Alcohol-dependence groups. Participants were categorized into four groups based on their age at first diagnosis of alcohol dependence: "early onset" (first diagnosed at age 18 or 21), "midlife onset" (first diagnosed at age 38 or 45), "never diagnosed" (no diagnosis between ages 18 and 45), and "other onset" (first diagnosed at age 26 or 32). To be categorized, individuals had to have alcohol-dependence data for at least three assessment waves and have alcohol-dependence data at age 18 or 21 (to avoid misclassifying individuals with early onset dependence). Nine hundred seventy study members met these criteria, of whom 836 (86.2%) had data for all six waves, 93 (9.6%) had data for five waves, 30 (3.1%) had data for four waves, and 11 (1.1%) had data for three waves. They were categorized as early onset (n = 222), midlife onset (n = 54), never diagnosed (n = 601), and other onset (n = 93). Primary analyses compared the early onset, midlife-onset, and never-diagnosed groups. Standardized scores and frequencies for the other-onset group are reported in the Supplemental Material.

Prospective predictors and adult correlates. We ascertained prespecified and theory-driven prospective predictors and adult correlates of alcohol dependence. Measures were assessed using self-reports, observer ratings, informant reports, biological and physiological assessments, and administrative records. Measures are described briefly below and in detail in Table S1 in the Supplemental Material.

Prospective predictors included family psychiatric history, early life mental health and substance use (low childhood self-control, any adolescent psychiatric disorder, early substance exposure, and adolescent marijuana and hard-drug use), and personality traits. Secondary analyses considered childhood SES, childhood IQ, and specific adolescent psychiatric diagnoses.

Adult correlates included sex, adult mental health and substance use (depression, anxiety, suicide attempt, drug and nicotine dependence, self-reported alcohol impairment, informant-rated alcohol problems, and mental-health-treatment contact), life functioning (adult convictions, unemployment duration, social-welfare-benefit use, and adult SES), stress and coping (stressful life events, perceived stress, and coping by drinking),

family characteristics (parental status, marital status, and changes in intergenerational household structure), and midlife aging (pace of aging, perceived facial age, and aging preparedness). Adult SES, perceived stress, coping by drinking, parental status, and marital status were added after study preregistration in response to internal and peer review.

Statistical analyses

We estimated effect sizes and significance of differences between alcohol-dependence groups using logistic regression. Multinomial models compared the early onset and midlife-onset groups with the never-diagnosed group. Binomial models compared the midlife-onset group with the early onset group. Variables were treated as independent. Continuous predictors were standardized on the analytic cohort (M = 0, SD = 1). Models controlled for sex.

No adjustment to the alpha level was made for analyses of measures added before study preregistration because we tested prespecified hypotheses, analyzed variables that were intercorrelated (e.g., multiple indicators of aging), reported results for all tests, and did not test a universal null hypothesis. For measures added after preregistration, we also report results with Bonferroni-corrected confidence limits that account for multiple testing.

Statistical code is available at https://sites.lsa.umich.edu/richmond-rakerd-lab/statistical-code/. Analyses were checked for reproducibility by an independent data analyst who recreated the code by working from the manuscript and applied it to a fresh copy of the data set.

Results

Prevalence of alcohol dependence across age

Figure 1 shows the prevalence of past-year *DSM-IV* (APA, 1994) alcohol dependence in the full Dunedin cohort, from ages 18 to 45 years. At ages 18, 21, 26, and 32, alcohol-dependence rates were 11.0%, 18.4%, 13.6%, and 8.1%, respectively, peaking in emerging adulthood and subsequently declining across early adulthood. Alcohol-dependence rates increased again as cohort members entered midlife (9.6% at age 38 and 11.3% at age 45).

Prevalence of early onset and midlife-onset alcohol dependence

Of the 970 study members who met inclusion criteria, 22.9% had early onset alcohol dependence and 5.6% had midlife-onset alcohol dependence. The early onset and midlife-onset groups comprised 60.2% and 14.6%, respectively, of individuals diagnosed with alcohol dependence between ages 18 and 45 (n = 369). Of individuals diagnosed with alcohol dependence at age 38 or 45 (n = 150), 36.0% were midlife-onset cases.

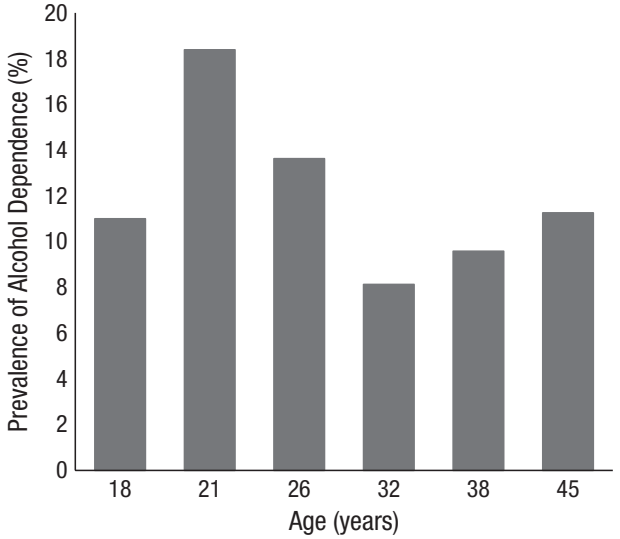

Fig. 1. Prevalence of past-year alcohol dependence at each assessment wave (using the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders*; American Psychiatric Association, 1994). Note: Prevalence estimates at each wave were calculated within the full cohort of individuals with available data for that wave (age 18: n = 936; age 21: n = 957; age 26: n = 976; age 32: n = 959; age 38: n = 950; age 45: n = 924).

Alcohol-dependence-criteria profiles

The early onset and midlife-onset groups had similar *DSM-IV* (APA, 1994) alcohol-dependence-criteria profiles. However, individuals with midlife-onset dependence were more likely to report inability to reduce drinking, and individuals with early onset dependence were more likely to report tolerance (Fig. 2).

Prospective predictors differentiating the alcohol-dependence groups

Standardized mean scores and frequencies on prospective predictors as a function of alcohol-dependence group membership are presented in Table 1 and Table S2 in the Supplemental Material.

Relative to individuals never diagnosed with alcohol dependence, individuals with early onset dependence were distinguished by a family history of psychiatric disorders, including alcohol dependence, drug abuse, anxiety, and depression; adolescent psychiatric disorders (including adolescent depression and conduct disorder); early substance exposure; adolescent marijuana

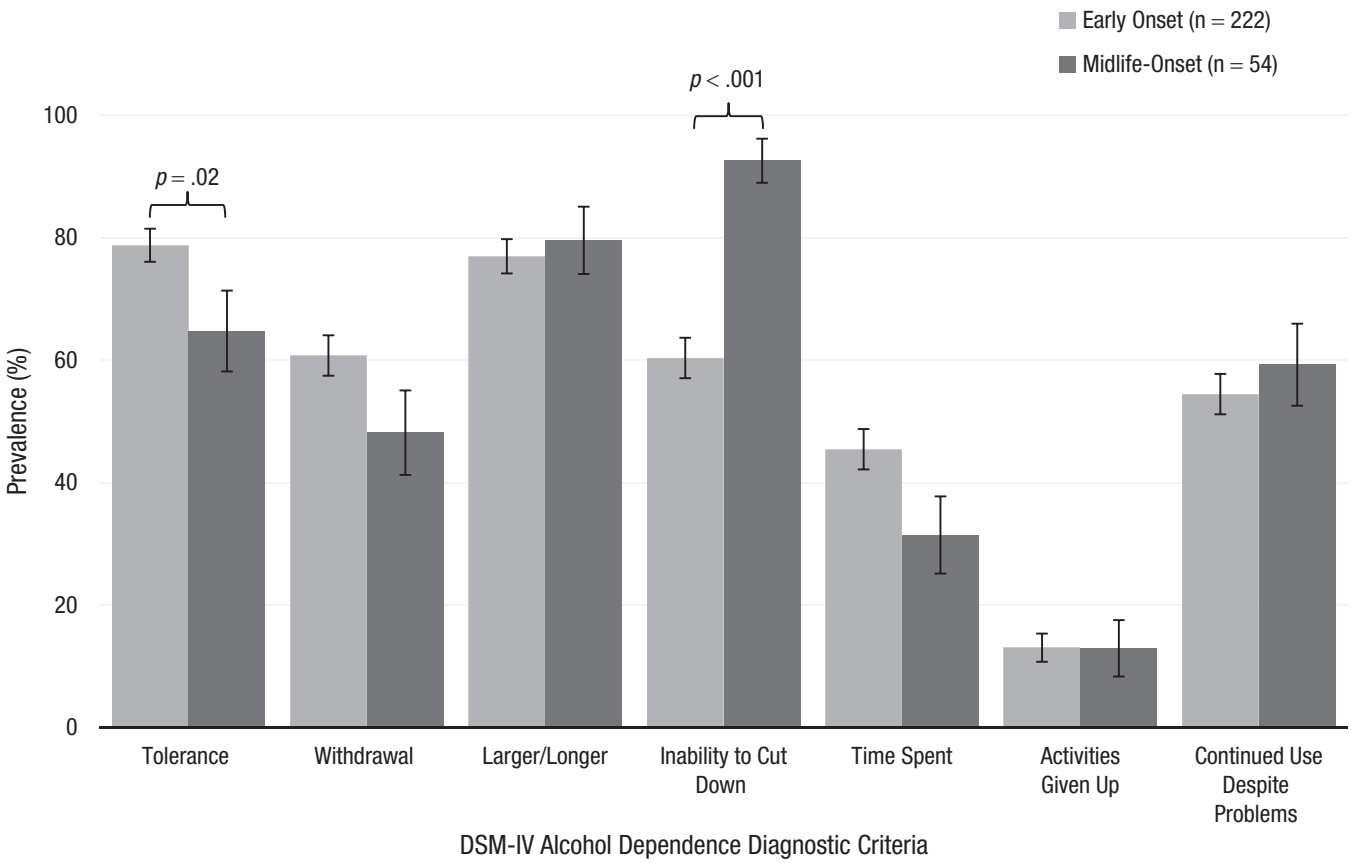

Fig. 2. Alcohol-dependence diagnostic-criteria profiles for the early onset and midlife-onset groups (using the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders*; American Psychiatric Association, 1994).
Note: Criterion-level prevalence rates were calculated using the criteria assessed at the age at which individuals first met diagnostic threshold for alcohol dependence. Percentages within each alcohol-dependence group sum to more than 100 because criteria are not independent (individuals could endorse multiple criteria). The early onset and midlife-onset groups did not significantly differ in their likelihood of experiencing the following: withdrawal; drinking in larger amounts or over a longer period than intended; spending a great deal of time obtaining, using, or recovering from the effects of drinking; giving up or reducing activities because of drinking; and continued drinking despite knowledge of problems relating to drinking (p values range: .08–.94). Statistical tests are sex-adjusted. Error bars are standard errors.

and hard-drug use; poorer impulse control (lower constraint); and greater distress (higher negative emotionality; Table 1).

Individuals with midlife-onset alcohol dependence were distinguished from never-diagnosed individuals by a family history of alcohol dependence, but they did not have an elevated family history of other psychiatric problems. They were characterized by higher rates of adolescent psychiatric disorders and adolescent marijuana use and lower constraint. The midlife-onset group did not differ from never-diagnosed individuals in their levels of childhood self-control, early substance exposure, hard-drug use, or negative and positive emotionality (Table 1).

Relative to individuals with early onset alcohol dependence, individuals with midlife-onset dependence had lower rates of adolescent marijuana use and lower negative emotionality (Table 1).

Analyses of secondary predictors indicated no differences among the alcohol-dependence groups with respect to childhood SES, childhood IQ, anxiety, or attention-deficit/hyperactive disorder. There were three differences among the groups: Relative to never-diagnosed individuals, individuals with early onset alcohol dependence were distinguished by higher rates of depression and conduct disorder, and individuals with midlife-onset dependence were distinguished by higher rates of conduct disorder (Table 1).

Adult correlates differentiating the alcohol-dependence groups

Standardized mean scores and frequencies on adult correlates as a function of alcohol-dependence group membership are presented in Table 2 and Table S2 in the Supplemental Material.

Table 1. Comparing Alcohol-Dependence Groups on Prospective Predictors

	Never-diagnosed (N = 601)	Early onset (N = 222)	Midlife-onset (N = 54)	Early onset vs. never-diagnosed	Midlife-onset vs. never-diagnosed	Midlife-onset vs. early onset
		M [*SD*] or *N* (%)		*OR* [95% CI]	*OR* [95% CI]	*OR* [95% CI]
Primary prospective predictors						
Family psychiatric history (32 years)						
FH + alcohol dependence	–0.14 [0.88]	0.22 [1.15]	0.16 [0.84]	**1.51 [1.28, 1.77]**	**1.41 [1.08, 1.85]**	0.93 [0.70, 1.24]
FH + drug abuse	–0.10 [0.85]	0.10 [1.05]	0.11 [1.13]	**1.30 [1.10, 1.53]**	1.29 [0.98, 1.68]	0.98 [0.74, 1.30]
FH + anxiety	–0.09 [0.97]	0.19 [0.98]	–0.01 [1.01]	**1.33 [1.14, 1.55]**	1.10 [0.82, 1.46]	0.79 [0.57, 1.10]
FH + depression	–0.09 [0.98]	0.15 [0.98]	0.06 [0.93]	**1.31 [1.12, 1.54]**	1.19 [0.90, 1.58]	0.88 [0.64, 1.21]
Early life mental health and substance use						
Low childhood self-control (3–11 years)	–0.09 [0.95]	0.18 [1.12]	–0.07 [0.97]	1.16 [1.00, 1.36]	0.96 [0.71, 1.29]	0.83 [0.60, 1.15]
Adolescent psychiatric disorder (11–15 years)	167 (28.8)	103 (47.9)	24 (45.3)	**2.25 [1.62, 3.13]**	**2.03 [1.15, 3.60]**	0.87 [0.48, 1.60]
Early substance exposure (13–15 years)	46 (8.0)	48 (22.5)	7 (13.2)	**3.46 [2.19, 5.44]**	1.77 [0.76, 4.16]	0.51 [0.22, 1.21]
Marijuana use (18 years)	–0.23 [0.84]	0.63 [1.16]	0.18 [1.01]	**1.55 [1.41, 1.69]**	**1.28 [1.10, 1.49]**	**0.82 [0.70, 0.96]**
Hard-drug use (18 years)	–0.11 [0.71]	0.35 [1.59]	–0.05 [0.68]	**1.68 [1.34, 2.10]**	1.14 [0.69, 1.89]	0.64 [0.38, 1.09]
MPQ personality traits (18 years)						
Constraint	0.22 [0.92]	–0.46 [1.01]	–0.27 [1.02]	**0.52 [0.44, 0.62]**	**0.61 [0.46, 0.82]**	1.17 [0.86, 1.59]
Negative emotionality	–0.24 [0.90]	0.55 [1.00]	–0.13 [0.86]	**2.26 [1.89, 2.70]**	1.12 [0.82, 1.53]	**0.47 [0.33, 0.67]**
Positive emotionality	0.04 [0.99]	–0.09 [0.96]	0.11 [1.07]	0.85 [0.73, 1.00]	1.05 [0.79, 1.40]	1.26 [0.92, 1.71]
Secondary prospective predictors						
Childhood SES (0–15 years)	0.05 [1.02]	–0.07 [0.96]	0.09 [0.98]	0.89 [0.76, 1.05]	1.04 [0.79, 1.37]	1.18 [0.86, 1.61]
Childhood IQ (7–11 years)	–0.01 [1.04]	0.00 [0.95]	0.13 [0.97]	0.97 [0.83, 1.14]	1.13 [0.85, 1.49]	1.15 [0.84, 1.57]
Depression (11–15 years)	32 (5.5)	21 (9.8)	4 (7.6)	**1.98 [1.10, 3.58]**	1.45 [0.49, 4.27]	0.72 [0.24, 2.21]
Anxiety (11–15 years)	109 (18.8)	49 (22.8)	12 (22.6)	1.42 [0.96, 2.10]	1.34 [0.68, 2.64]	0.91 [0.44, 1.89]
Conduct disorder (11–15 years)	60 (10.4)	65 (30.2)	15 (28.3)	**3.33 [2.22, 4.98]**	**3.22 [1.67, 6.24]**	0.96 [0.49, 1.88]
ADHD (11–15 years)	27 (4.7)	18 (8.4)	5 (9.4)	1.44 [0.76, 2.70]	1.86 [0.67, 5.12]	1.35 [0.46, 3.91]

Note: Ages indicate ages at assessment. Mean scores are standardized. Estimates are derived using the number of participants in each group with available data for the measure (never-diagnosed: *n*s = 572–601; early onset: *n*s = 213–222; midlife-onset: *n*s = 53–54). Models controlled for sex. Bold estimates indicate significant differences between groups; *OR* = odds ratio; CI = confidence interval. FH = family history; MPQ = multidimensional personality questionnaire; SES = socioeconomic status; ADHD = attention-deficit/hyperactivity disorder.

Table 2. Comparing Alcohol-Dependence Groups on Adult Correlates

Adult correlates	Never-diagnosed (*N* = 601)	Early onset (*N* = 222)	Midlife-onset (*N* = 54)	Early onset vs. never-diagnosed	Midlife-onset vs. never-diagnosed	Midlife-onset vs. early onset
	M [*SD*] or *N* (%)			*OR* [95% CI]	*OR* [95% CI]	*OR* [95% CI]
Male sex	256 (42.6)	145 (65.3)	30 (55.6)	**2.54 [1.84, 3.50]**	1.69 [0.96, 2.95]	0.66 [0.36, 1.21]
Adult mental health and substance use						
Depression (45 years)	68 (11.9)	45 (22.4)	16 (30.2)	**2.41 [1.57, 3.70]**	**3.47 [1.82, 6.62]**	1.44 [0.73, 2.84]
Generalized anxiety disorder (45 years)	31 (5.4)	13 (6.5)	7 (13.2)	1.42 [0.72, 2.81]	**2.94 [1.22, 7.12]**	2.11 [0.80, 5.62]
Suicide attempt (18–45 years)	52 (8.7)	47 (21.2)	7 (13.0)	**3.25 [2.08, 5.07]**	1.69 [0.72, 3.96]	0.52 [0.22, 1.22]
Drug dependence (45 years)	7 (1.2)	17 (8.5)	2 (3.8)	**7.99 [3.21, 19.93]**	3.30 [0.67, 16.37]	0.40 [0.09, 1.79]
Nicotine dependence (45 years)	41 (7.2)	43 (21.3)	7 (13.2)	**3.74 [2.32, 6.01]**	2.05 [0.87, 4.83]	0.57 [0.24, 1.35]
Self-reported alcohol impairment (45 years)	–0.28 [0.71]	0.40 [1.25]	1.04 [1.29]	**2.34 [1.88, 2.91]**	**3.48 [2.62, 4.61]**	**1.47 [1.17, 1.84]**
Informant-rated alcohol problems (45 years)	–0.26 [0.61]	0.34 [1.26]	1.03 [1.63]	**2.05 [1.68, 2.50]**	**2.85 [2.22, 3.66]**	**1.40 [1.13, 1.74]**
Mental-health-treatment contact (21–45 years)	299 (50.5)	124 (57.9)	34 (63.0)	**1.70 [1.22, 2.38]**	**1.95 [1.08, 3.53]**	1.15 [0.61, 2.16]
Life functioning						
Court conviction (18–45 years)	112 (18.8)	102 (46.6)	21 (39.6)	**3.09 [2.18, 4.39]**	**2.62 [1.41, 4.86]**	0.84 [0.44, 1.60]
Unemployment duration (32–45 years)	–0.04 [0.98]	0.14 [1.23]	0.03 [0.79]	**1.16 [1.01, 1.34]**	1.07 [0.82, 1.40]	0.90 [0.66, 1.23]
Social-welfare-benefit receipt (21–45 years)	–0.09 [0.91]	0.26 [1.21]	–0.11 [0.74]	**1.43 [1.23, 1.66]**	1.00 [0.71, 1.40]	**0.66 [0.45, 0.97]**
Adult SES (45 years)[a]	0.10 [0.98]	–0.26 [1.03]	–0.003 [0.94]	**0.72 [0.61, 0.85]**	0.92 [0.69, 1.22]	1.26 [0.93, 1.72]
Stress and coping						
Stressful life events (45 years)	–0.10 [0.87]	0.25 [1.23]	0.003 [0.86]	**1.49 [1.26, 1.75]**	1.17 [0.87, 1.58]	0.79 [0.58, 1.07]
Perceived stress (45 years)[a]	–0.11 [0.95]	0.16 [1.10]	0.33 [0.96]	**1.38 [1.17, 1.63]**	**1.57 [1.20, 2.05]**	1.15 [0.86, 1.53]
Coping by drinking (45 years)[a]	–0.20 [0.88]	0.21 [1.08]	0.82 [1.13]	**1.57 [1.33, 1.86]**	**2.48 [1.91, 3.22]**	**1.62 [1.22, 2.14]**
Family characteristics						
Parent (21–45 years)[a]	472 (82.1)	161 (79.7)	35 (66.0)	0.87 [0.58, 1.31]	**0.43 [0.23, 0.79]**	**0.50 [0.26, 0.98]**
Married (45 years)[a]	358 (62.3)	85 (43.2)	20 (38.5)	**0.44 [0.32, 0.62]**	**0.37 [0.21, 0.66]**	0.85 [0.45, 1.58]
Change in intergenerational household structure (38–45 years)	293 (51.2)	99 (49.5)	24 (45.3)	0.96 [0.70, 1.34]	0.80 [0.46, 1.42]	0.82 [0.45, 1.52]
Midlife aging						
Pace of aging (26–45 years)	–0.05 [0.98]	0.16 [1.04]	–0.21 [1.04]	**1.24 [1.06, 1.45]**	0.83 [0.60, 1.13]	**0.68 [0.49, 0.95]**
Facial age (45 years)	–0.05 [0.99]	0.23 [0.99]	–0.38 [0.99]	**1.34 [1.13, 1.59]**	**0.70 [0.52, 0.94]**	**0.54 [0.39, 0.76]**
Low financial preparedness (45 years)[b]	–0.12 [0.95]	0.30 [1.10]	0.17 [0.95]	**1.52 [1.29, 1.78]**	**1.36 [1.04, 1.78]**	0.89 [0.66, 1.19]
Low social preparedness (45 years)[b]	–0.14 [0.93]	0.27 [1.09]	0.32 [0.84]	**1.50 [1.27, 1.77]**	**1.57 [1.21, 2.03]**	1.04 [0.78, 1.39]
Low health preparedness (45 years)[b]	–0.14 [0.92]	0.27 [1.11]	0.11 [1.02]	**1.45 [1.23, 1.72]**	1.26 [0.95, 1.68]	0.87 [0.65, 1.17]

Note: Ages indicate ages at assessment. Mean scores are standardized. Estimates are derived using the number of participants in each group with available data for the measure (never-diagnosed: *n*s = 554–601; early onset: *n*s = 183–222; midlife-onset: *n*s = 49–54). Models controlled for sex. Bold estimates indicate significant differences between groups. *OR* = odds ratio; CI = confidence interval; SES = socioeconomic status.

[a]Added after study preregistration in response to internal and peer review. For these five variables, we reran models with Bonferroni-corrected confidence limits. There was one change in statistical inference: The comparison of the midlife-onset versus early onset groups on parental status was no longer statistically significant (see Table S3 in the Supplemental Material available online).

[b]Higher scores indicate lower levels of preparedness (poorer preparedness).

Relative to individuals never diagnosed with alcohol dependence, individuals with early onset dependence were more likely to be male. They were also distinguished by mental-health and substance-use problems, including depression, suicide attempts, drug dependence, nicotine dependence, self- and informant-reported alcohol problems, and mental-health-treatment contact (Table 2). The early onset group evidenced more difficulties in life functioning, including an adult-conviction history, longer duration of unemployment, social-welfare-benefit receipt, and lower adult SES. Relative to the never-diagnosed group, the early onset group reported experiencing more stressful life events, perceived their lives as more stressful, and were more likely to drink to cope with stress. They were also less likely to be married. Individuals with early onset dependence showed evidence of poorer aging at midlife: They had a faster pace of biological aging, looked older in facial photographs shown to independent raters, and were less prepared for age-related financial, social, and heath demands (Table 2).

Relative to never-diagnosed individuals, individuals with midlife-onset alcohol dependence were distinguished by internalizing disorders, including depression and generalized anxiety disorder (Table 2). The midlife-onset group did not show elevated rates of suicide attempts, drug dependence, or nicotine dependence, but they had higher levels of self- and informant-reported alcohol impairment and problems. They were also more likely to report treatment for mental-health problems. They were more likely to have received a conviction, but they did not exhibit other difficulties in life functioning. Despite not reporting more stressful life events than the never-diagnosed group, the midlife-onset group perceived their lives as more stressful, and they were more likely to cope with stress by drinking. Regarding family characteristics, they were less likely to be married and parents. The midlife-onset group did not show an accelerated pace of biological aging, and somewhat surprisingly, they appeared younger than the never-diagnosed group in facial photographs. However, they evidenced poor preparedness for later-life financial and social demands (Table 2).

Relative to individuals with early onset alcohol dependence, individuals with midlife-onset dependence exhibited higher levels of self- and informant-reported alcohol impairment and problems. They had lower levels of social-welfare-benefit use, were more likely to report coping by drinking, and were less likely to be parents (but this difference did not remain after correction for multiple testing; see Table S3 in the Supplemental Material). The midlife-onset group was further distinguished from the early onset group by a slower pace of aging, and they appeared younger in facial photographs (Table 2).

Did the midlife-onset group show evidence of alcohol problems at earlier ages?

At ages 18 and 21, 15.7% and 24.1%, respectively, of the midlife-onset group fell just below the diagnostic threshold for alcohol dependence (reported two criteria). At both ages, individuals in the midlife-onset group had higher levels of informant-rated alcohol problems than individuals in the never-diagnosed group (age 18: odds ratio [*OR*] = 1.57, 95% confidence intervals [CI] = [1.21, 2.03]; age 21: *OR* = 1.60, 95% CI = [1.22, 2.11]). Their levels of informant-rated problems were lower than but did not significantly differ from those for the early onset group (age 18: *OR* = 0.90, 95% CI = [0.70, 1.17]; age 21: *OR* = 0.77, 95% CI = [0.59, 1.01]). At all assessments before midlife (ages 18–32), the largest proportion of the midlife-onset group comprised individuals who endorsed no alcohol-dependence criteria (see Table S4 in the Supplemental Material).

Were the early onset group's adult outcomes attributable to persistence in alcohol dependence?

In secondary analyses added in response to internal review, we tested whether the early onset group's challenges in adult functioning were attributable to persistence of alcohol dependence into midlife. Of the 222 individuals in the early onset group, 214 (96.4%) had alcohol-dependence data at age 38 or 45 and were included in this analysis. Individuals with dependence at midlife (diagnosed at age 38 or 45; early onset persistent, n = 65 [30.4%]) and individuals without (no diagnosis at age 38 or 45; early onset remitted, n = 149 [69.6%]) scored similarly on most adult correlates (see Fig. S1 in the Supplemental Material). Of the 20 adult correlates on which early onset cases scored more poorly than never-diagnosed individuals (excluding sex; Table 2), only six differed between the persistent and remitted subgroups, three of which reflected their difference in midlife alcohol-dependence status (higher self-reported alcohol-related impairment, informant-rated alcohol problems, and coping by drinking in the persistent group; see Fig. S1 note in the Supplemental Material).

Discussion

Much research has focused on the development of alcohol use disorder in late adolescence and early adulthood (Chassin et al., 2013), but onset of alcohol use disorder in middle adulthood remains understudied despite the period's developmental salience. In this 5-decade prospective study of a population-representative cohort, we contribute new knowledge about the

developmental epidemiology of a previously understudied group: individuals with midlife-onset alcohol dependence. We also generate novel information about a well-studied group—individuals with early onset alcohol dependence—by measuring their outcomes into middle adulthood. Results regarding these groups are summarized below.

Early onset alcohol dependence

Individuals with early onset alcohol dependence (first diagnosis at age 18 or 21 years) represented 22.9% of the cohort. Relative to never-diagnosed individuals, individuals with early onset dependence had dense family histories of internalizing and externalizing disorders. As adolescents, they had elevated scores on psychiatric disorders (particularly depression and conduct disorder), early substance exposure, and marijuana- and hard-drug-use frequency, and they exhibited poor impulse control and a tendency toward negative affect. As adults, they experienced mental-health and substance-use problems, including depression, drug and nicotine dependence, and alcohol-related impairment; elevated levels of mental-health-treatment contact; life-functioning difficulties, including a conviction history, unemployment, social-welfare-benefit receipt, and lower SES; stressful life events, perceived stress, and coping by drinking; and lower likelihood of marriage. Furthermore, at midlife, individuals with early onset dependence showed evidence of accelerated physiological aging and poor preparedness to manage later-life demands.

Our findings align with prior research elucidating the role of family histories of alcohol dependence and other psychiatric problems in the development of early onset alcohol dependence (Dawson, 2000; Meier et al., 2013) and the externalizing risk profile experienced by the early onset group across the life span (Le Strat et al., 2010; McGue et al., 2001; White et al., 2001).

Individuals with early onset dependence also exhibited an internalizing risk profile from adolescence to middle adulthood, consistent with studies linking negative affect (Chassin et al., 2004; Elkins et al., 2006) and depression (Hussong et al., 2001; Kushner & Sher, 1993) with early onset alcohol problems. The presence of both externalizing and internalizing profiles—along with life-functioning challenges—supports the hypothesis that individuals with early emerging drinking problems experience global impairment (King et al., 2004).

At midlife, individuals with early onset alcohol dependence were aging more quickly biologically than their chronologically same-aged peers. Previous research has linked heavy alcohol consumption to epigenetic age acceleration (Fiorito et al., 2019; Kresovich et al., 2021; Luo et al., 2020; Rosen et al., 2018) and substance use disorders to altered aging-related biomarkers (Reece, 2007). To our knowledge, this study is the first to show that individuals with early onset dependence exhibit an accelerated pace of physiological aging, across multiple organ systems, and poor preparedness to manage age-related financial, social, and health demands.

Approximately one-third of individuals with early onset alcohol dependence continued to experience dependence at midlife. Somewhat surprisingly, there were relatively few differences in midlife outcomes between the early onset persistent and remitted groups. This suggests that early onset dependence is a marker of dysregulation into midlife even if problem drinking does not persist. Heavy alcohol use in late adolescence and early adulthood might also confer persistent harmful effects even if dependence desists.

Midlife-onset alcohol dependence

The midlife-onset alcohol-dependence group (first diagnosis at age 38 or 45 years) comprised only 5.6% of the cohort but accounted for 36.0% of all midlife alcohol-dependence cases. Relative to never-diagnosed individuals, individuals with midlife-onset dependence had an elevated family history of alcohol dependence but not other psychiatric disorders. They did not differ in childhood self-control problems, but as they entered adolescence, they experienced more impulse-control difficulties, including elevated rates of psychiatric diagnoses (particularly conduct disorder), low constraint, and marijuana use. Relative to the early onset group, individuals with midlife-onset alcohol dependence had lower rates of adolescent marijuana use and negative emotionality.

In adulthood, relative to never-diagnosed individuals, individuals with midlife-onset alcohol dependence exhibited a broader range of problems, including alcohol-related impairment, higher rates of depression and anxiety, and greater need for mental-health support. Adults with midlife-onset dependence continued to evidence lower impulse control in some domains but not others (higher rates of adult convictions but not other substance use disorders). Despite not reporting more stressful life events, they perceived their lives as more stressful and reported drinking to cope with stress more frequently than individuals never diagnosed with alcohol dependence. They were also less likely than never-diagnosed individuals to be married and parents. Although individuals with midlife-onset dependence did not exhibit accelerated biological aging, they were less prepared to manage later-life financial and social demands.

Relative to individuals with early onset alcohol dependence, individuals with midlife-onset dependence experienced more self-reported alcohol impairment and informant-reported alcohol problems, had less social-welfare use, and were more likely to report coping by drinking. They were aging more slowly physiologically than the early onset group but experienced similar levels of difficulty in managing age-related demands.

Evaluating our findings regarding the midlife-onset alcohol-dependence group relative to prior research is somewhat difficult because of variability in study designs and comparison groups. However, we can draw comparisons across several dimensions. First, like previous work, we observed an association of alcohol-dependence family history with midlife-onset dependence (Moss et al., 2007). Second, the developmental profile we identified—in which the midlife-onset group had fewer early life risk factors than the early onset group—aligns with the conceptualization of "Type-1 alcoholics" (defined as individuals who first experience alcohol dependence at age 30, on average; Babor et al., 1992). However, the presence of a family history of alcohol dependence and adolescent impulse-control difficulties in the midlife-onset group also suggests early life roots, indicating potential prevention opportunities.

Third, existing theories suggest that later-onset alcohol problems lack an externalizing profile (Cloninger et al., 1996). Contrary to this, relative to never-diagnosed individuals, we observed elevated rates of adolescent conduct disorder, adolescent marijuana use, and adult convictions among the midlife-onset group (although their marijuana-use levels were lower than the early onset group's). This suggests externalizing tendencies across their life span, although less pronounced than for early onset cases.

Fourth, in early life, individuals with midlife-onset alcohol dependence did not show internalizing vulnerabilities, such as a family history of internalizing disorders, depression, or negative emotionality. However, as adults, they experienced problems with depression and anxiety, perceived high stress, and used alcohol to cope with stress. Negative affect may act as a trigger for the onset of alcohol dependence in adulthood (Zucker, 1986), or adult drinking may lead to internalizing problems (Hasin & Grant, 2002). Greater temporal resolution is needed to resolve these processes. Our findings suggest that this group has an alcohol-specific vulnerability (family history of alcohol dependence) that is "activated" in midlife, potentially from events conferring negative affect and stress, which aligns with the notion of drinking for "tension-reduction" (Cooper et al., 1995; Jacob et al., 2005). We note that compared with never-diagnosed individuals, individuals with midlife-onset dependence did not show significant elevations in stressful life events. However, they perceived their lives to be more stressful and struggled with preparing to manage later-life financial and social demands. They also were less likely than never-diagnosed individuals to be married and have children. These factors may decrease social support and partly account for the midlife-onset group's lower levels of social preparedness. Future research should evaluate the extent to which stress related to the midlife transition period—including subjective feelings of low preparedness for aging—may underlie problematic alcohol consumption in this group.

Strengths, limitations, and future directions

Our analysis has several strengths. First, we employed a multimethod approach for assessment of correlates. Second, we ascertained an array of measures to comprehensively distinguish between alcohol-dependence groups, including factors relevant to the midlife transition period. Third, early life predictors were prospectively measured. Fourth, we assessed alcohol dependence repeatedly from ages 18 to 45, minimizing misclassification errors. Fifth, we employed a population-representative cohort, increasing generalizability. Finally, the Dunedin cohort's high retention rate (94%) reduced the potential for attrition bias.

We also acknowledge limitations. First, although using *DSM-IV* (APA, 1994) alcohol-dependence diagnostic cutoffs ensured consistency across waves, some members of the midlife-onset group exhibited early life alcohol-related problems that fell below the diagnostic threshold. Future research should evaluate how the current findings extend to the dimensional *DSM-5* (APA, 2013) operationalization of alcohol use disorder. Second, although we used alcohol-dependence data from multiple assessment waves, some individuals could have met dependence criteria between waves. However, the nine Dunedin Study diagnostic interviews between ages 11 and 45 captured all but 17 participants who reported treatment for mental-health or substance-use problems in the 4 decades (Caspi et al., 2020). Third, our data are right censored at age 45. Future research should evaluate longer-term outcomes for the midlife-onset group, including how they are aging into older adulthood and whether they develop persistent or time-limited alcohol problems. Fourth, the midlife-onset group's somewhat modest size limited statistical power to test group differences for rare outcomes (e.g., drug dependence).

Finally, our findings are based on a primarily White NZ cohort born in the 1970s. Research indicates that Māori individuals in NZ and Native American, Hispanic,

and Black populations in the United States experience elevated alcohol-related harms and treatment-access barriers (Chartier & Caetano, 2010; Statis NZ, 2018; Zemore et al., 2018), and some data suggest that Black individuals have elevated rates of midlife alcohol dependence (Moss et al., 2010). More work is needed testing potential variation in predictors and correlates of midlife-onset alcohol-related problems across race and ethnicity.

Research on midlife-onset alcohol use disorder has concerned samples from Western and industrialized countries; to our knowledge, no studies have yet been conducted in low- and middle-income countries (LMICs). Data indicate lower overall levels of alcohol use disorder but a rise in the prevalence of midlife alcohol use disorder in LMICs (Global Burden of Disease Collaborative Network, 2021). In addition, the association of individual SES with heavy drinking may vary by country income such that higher individual SES may be a protective factor in upper-middle-income countries, a risk factor in low-income countries, and have no association in lower-middle-income countries (Xu et al., 2022). Furthermore, individuals in LMICs may experience age-related health deterioration earlier than individuals in high-income countries (Tan, 2022). Future research should evaluate whether the age-related health burden associated with midlife-onset alcohol use disorder differs by country income level given that data suggest the burden may be greater among LMICs.

Concerning the generalizability of our findings to later-born cohorts, the onset and peak of alcohol consumption in some industrialized countries have been shifting to later ages, and the prevalence of heavy drinking among middle-age adults has increased in more recently born individuals, with some data suggesting the increase is concentrated among higher-SES women (Keyes, 2022). If these trends continue, midlife alcohol-related problems may continue to increase among more recently born cohorts, particularly higher-SES women.

Implications

Our findings have implications for the assessment, etiology, prevention, and treatment of alcohol use disorder at midlife. Concerning assessment, our findings reinforce the benefits of long-term prospective measurement of alcohol problems. This enabled us to uncover a group of individuals who should represent a high-priority focus for follow-up studies concerning drinking patterns, health, and processes of aging. In the context of an aging global population and evidence for elevated and increasing rates of midlife drinking in some countries, such follow-ups are becoming increasingly important.

Regarding etiology and prevention, we identified a constellation of early life risk factors for the development of midlife alcohol-related problems. These include a family history of alcohol dependence and adolescent conduct disorder, marijuana use, and low constraint. We also identified divergent risk factors for the midlife-onset and early onset alcohol-dependence groups. Although both groups evidenced a family history of alcohol dependence and problems with adolescent impulse control, individuals with midlife-onset dependence had fewer early life internalizing problems (e.g., lower rates of negative emotionality). Our findings suggest that in adolescence, individuals with midlife-onset alcohol dependence do not tend to show global mental-health impairment but rather, exhibit an "externalizing-specific" profile. These factors may be particularly predictive of risk for individuals who already exhibit signs of alcohol-related problems in early life (individuals who we identified as experiencing some alcohol-dependence criteria at ages 18 and 21). Preventing midlife-onset alcohol-related problems may involve targeting externalizing vulnerabilities and problems in adolescence through self-regulation-focused interventions.

Concerning treatment, our findings suggest that individuals with midlife-onset alcohol dependence may benefit from adult interventions targeting depressed mood and anxious feelings because their alcohol use might serve as a tension-reduction strategy (Jacob et al., 2005). In addition, these individuals show poor preparedness to manage later-life financial and social demands. Age-related diseases typically do not onset until the 60s in industrialized nations (Crimmins, 2004), meaning that midlife may offer an important prevention window to disrupt problematic alcohol-use patterns that can contribute to unhealthy aging. Practitioners working with middle-aged individuals with alcohol use disorder should evaluate how well they are managing the midlife transition period. Alcohol treatment among individuals experiencing poor preparedness for aging could involve not only cognitive and behavioral approaches to reduce alcohol problems but also strategies targeting financial and social well-being, such as retirement planning and fostering social connections. Strengthening social ties may be particularly important given that we found that individuals with midlife-onset alcohol dependence were less likely to be married and to be parents.

Relative to individuals with early onset alcohol dependence, individuals with midlife-onset dependence were more likely to report frequent efforts to quit or cut down on their drinking, which suggests motivation to change that could be channeled in treatment. They were also less likely to endorse tolerance to alcohol, suggesting they are less affected by physiological dependence. Treatments among individuals

with midlife-onset alcohol dependence could focus on behavioral manifestations of alcohol-related problems (e.g., loss of control over drinking) while monitoring accumulation of psychological dependence as a secondary target (Heilig & Egli, 2006).

Conclusion

This study contributes to a limited but growing body of literature highlighting the developmental salience of midlife for understanding the emergence of alcohol use disorder across the life span. The current findings (a) identify prevention and intervention targets that may help to reduce the onset of alcohol-related problems in middle adulthood, (b) indicate opportunities for future research to characterize later-life trajectories and outcomes among individuals with midlife alcohol-related problems, and (c) highlight midlife as a potential window of opportunity to support healthy aging, including through prevention of alcohol use disorder.

Transparency

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Declaration of Conflicting Interests

The author(s) declared that there were no conflicts of interest with respect to the authorship or the publication of this article.

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Supplemental Material

Additional supporting information can be found at http://journals.sagepub.com/doi/suppl/10.1177/21677026241260249

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