Chapter 2
Alcohol Use Disorders: Leveraging Informatics to Improve Patient Care

Calvin Hwang and Lyncan Williams

Abstract Alcohol use disorders (AUDs) is a worldwide public health problem. Incidence and severity may vary based on geography, culture, and individual genetics. Pharmacogenomics offers the potential for personalized medicine of patients with specific genetic profiles. Informatics may help clinicians better identify patients with have or are at-risk for AUD. It may also offer better, more standardized in-hospital and ambulatory treatments. Lastly, integrated informatics efforts may better inform decision makers of more effective public health approaches.

Keywords Alcohol use disorders · CIWA · SBI · Public health · EHR

2.1 Introduction

The use of electronic health records (EHRs) in clinical medicine has improved the detection, treatment, and prevention of alcohol use disorders in multiple settings. This chapter explores the various ways in which medical informatics has impacted laboratory research, clinical medicine, and finally, public health systems.

Worldwide, alcohol is the seventh leading risk factor for poor health. In 2016, it was estimated that alcohol was associated with three million deaths (5.3% of all deaths) and 132.6 million disability-adjusted life years (5.1% of all DALYs) (Fig. 2.1). Harmful alcohol use contributed to more than 200 diseases and injury-related health conditions, most notably DSM-IV alcohol dependence, liver cirrhosis, cancers, and injuries (WHO Alcohol Fact Sheet 2021).

According to the WHO, the European region continues to have the heaviest alcohol consumption in the world. It is estimated that of the 70% of Europeans

C. Hwang (✉)
Department of Medicine, New York Presbyterian/Queens Hospital, Queens, NY, USA

Clinical Medicine, Weill Cornell Medical College, New York, NY, USA
e-mail: cah9096@med.cornell.edu

L. Williams
Department of Medicine, New York Presbyterian/Queens Hospital, Queens, NY, USA

H. Shen et al. (eds.), *Regionalized Management of Medicine*, Translational Bioinformatics 17, https://doi.org/10.1007/978-981-16-7893-6_2

Fig. 2.1 Total alcohol per capita consumption (APC) (15+ years; in liters of pure alcohol), 2016 Source: WHO. Global status report on alcohol and health 2018

who drink, 31.5% of men and 12.6% of women report heavy episodic drinking. On average, Europeans consume 10.7 L of pure alcohol each year. Average consumption of alcoholic beverages varies widely between WHO European Region member countries, from an average of 3.9% in the Southeast European subregion (Anon n.d.-a) to as high as 14.4% in the Eastern European subregion (Anon n.d.-b; WHO Regional Office for Europe, Alcohol Use 2021).

Use of alcohol in the USA mirrors that of Europe, with 55.3% reporting use in the past month and 26.5% reporting heavy episodic drinking (Substance Abuse and Mental Health Services Administration (SAMSA) 2021). In 2010, alcohol misuse cost the USA $249 billion with three-quarters of the total cost related to heavy episodic drinking (Sacks et al. 2015).

Though the prevalence of alcohol consumption in China is lower than most Western populations, it has increased more than 50-fold from 0.4 L in 1952 to 4.9 L in 2009 of pure alcohol (Cochrane et al. 2003). The China Kadoorie Biobank cohort found that 33% of Chinese men drink regularly (compared to 2% of women) with an increase in the proportion engaging in heavy episodic drinking increasing from 30 to 35% between 2004 and 2008 (Im et al. 2019). Left unchecked, this will have profound systemic health impacts in the future.

Much of the variation in alcohol use behavior may be due to cultural norms. Unlike many diseases, AUDs are often described in qualitative terms. For instance, in the ICD-10 diagnosis of alcohol dependence, one criterion includes "difficulties in controlling substance-taking behaviors in terms of its onset, termination, or levels of use." But loss of control may depend on normalization of culturally acceptable behavior (Marques et al. 2019). Without absolute benchmarks, it may be difficult to compare national perceptions of alcohol use (Rehm and Room 2017).

Some have recommended using Europeans as the standard or benchmark for alcohol consumption. Yet even in Europe, acceptable behavior may be contextual (e.g., permissible during festivals or weekends) or evolve over time (Rehm et al.

2005). Similar findings have been found worldwide in Switzerland (Haug and Schaub 2016), China (3), and Australian Aborigines (Haroon et al. 2018).

Furthermore, the quantity of alcohol consumed may not directly correlate with observed injuries or costs. Self-report population surveys may underdetect AUDs based on acceptable normalized behavior (Gmel et al. 2013; Probst and Rehm 2018). Populations which consider loss-of-control behavior unacceptable may have less tolerance for aggressive behavior, translating into lower rates of injury and death (Norström 2001).

The overwhelming fact is that excessive consumption of alcohol affects the economy of all countries or regions due to potentially preventable harm, lost revenues and productivity. Informatics may help in the early identification of at-risk individuals, provide cost-effective preventative strategies to mitigate use, provide targeted treatment for AUD, and support public health initiatives.

2.2 Use of Informatics in Laboratory Research

Alcohol use disorders (AUDs) arise from a combination of chronic response to alcohol exposure, individual genetic makeup, and environmental disturbances over time. In many people, alcohol use disorder behavior patterns are established during adolescence, which are modulated by genetically influenced individual risk profiles (Blomeyer et al. 2013). Known as candidate gene and environment interaction studies (cGxE), these studies have identified potential candidate genes that influence the development of alcohol addiction and maladaptive behavior. These candidate genes typically influence reward seeking, inhibition, systemic stress response, or alcohol metabolism (Kim and Park 2018).

Current research has shown that the genetic component of vulnerability to alcohol addiction is complex, does not follow clear Mendelian inheritance, and is not linked to a single gene. Widespread availability of genomic mapping and analysis now allows genome-wide association studies (GWASs) to identify candidate genes for multiple diseases, including alcoholism. GWASs of European populations identified alcohol dehydrogenase cluster variants associated with alcohol use disorders (Treutlein et al. 2009; Schumann et al. 2011; Stacey et al. 2012; Frank et al. 2012; Biernacka et al. 2013; Kapoor et al. 2013).

Advances in pharmacogenomics have also identified potential epigenetic mechanisms influencing the onset of addictive behavior. Genomic DNA methylation mapping (Zhang et al. 2014) and hypermethylation (Taqi et al. 2011) of alcohol-dependent patients support the theory that such changes arise as a consequence of, rather than a cause of, the disorder (Nieratschker et al. 2014). Reversal of such methylation may be examples for potential future pharmacologic treatment of alcohol use disorders.

Pharmacogenomics can be used to predict treatment response. Some studies have suggested that functional single nucleotide polymorphism (SNP) in the μ-opioid receptor gene may predict clinical response to naltrexone (Oslin et al. 2003; Anton

et al. 2008; Kranzler et al. 2013; Chamorro et al. 2012). Similarly, genetic variations in GAT-binding protein 4 may influence treatment response to acamprosate (Kiefer et al. 2011; Mann et al. 2013). Other potential treatment candidates identified using genomic analysis of SNPs include topiramate and ondansetron, as well as sensitivity to benzodiazepines (Zastrozhin et al. 2019). Pharmacogenomics offers the potential for personalized treatment of AUDs.

2.3 Use of Informatics in Clinical Medicine

During the past decade, informatics has begun to positively impact the treatment and prevention of AUDs in several clinical settings: emergency departments, hospitalized inpatients, ambulatory practice, and adolescent medicine.

2.3.1 Emergency Medicine

In 2018, US motor vehicle drivers with blood alcohol concentrations (BAC) above 0.08 accounted for nearly one-third of all traffic-related deaths, or 10,511 (Thomas et al. 2019). This resulted in an estimated economic cost in 2010 (the most recent year that cost data is available) of $44 billion including direct and indirect costs. The impact of elevated BAC on driving has been well described. Effects include impaired coordination, judgment, self-control, loss of balance, concentration, and situational awareness (Anon 2020).

Among 25 European Union members, the number of traffic fatalities officially attributed to alcohol declined by nearly 50% between 2006 and 2016 from 4950 to 2630 (Fig. 2.2) (European Transport Safety Council 12th Annual Road Safety Performance Index (PIN) Report 2020). But there is widespread consensus that the real number of alcohol-related deaths may be as high as twice the reported rate due to several factors. These include inconsistent national definitions of deaths attributed to drunk driving, lack of systematic testing of all drivers involved in collisions, and use of police records as the sole data source (World Health Organization (WHO) 2012). Thus, international comparisons of the impact of drunk driving may not be possible.

Studies have not conclusively found direct associations between elevated BAC and clinical outcomes such as injury severity scores, in-hospital mortality, or discharge disposition in survivors (Ahmed and Greenberg 2019; Demetriades et al. 2004; Stübig et al. 2012; Lowenfels and Miller 1984; Maier 2001). Thus, the benefit of alcohol screening in trauma patients may be more impactful with the potential reduction of future harm rather than at the time of the incident.

In the USA, alcohol screening in emergency departments is performed by hospitals voluntarily participating in the National Trauma Data Bank. Similar collaboratives exist elsewhere, such as in Germany (German In-Depth Accident Study) and Canada (British Columbia Trauma Registry).

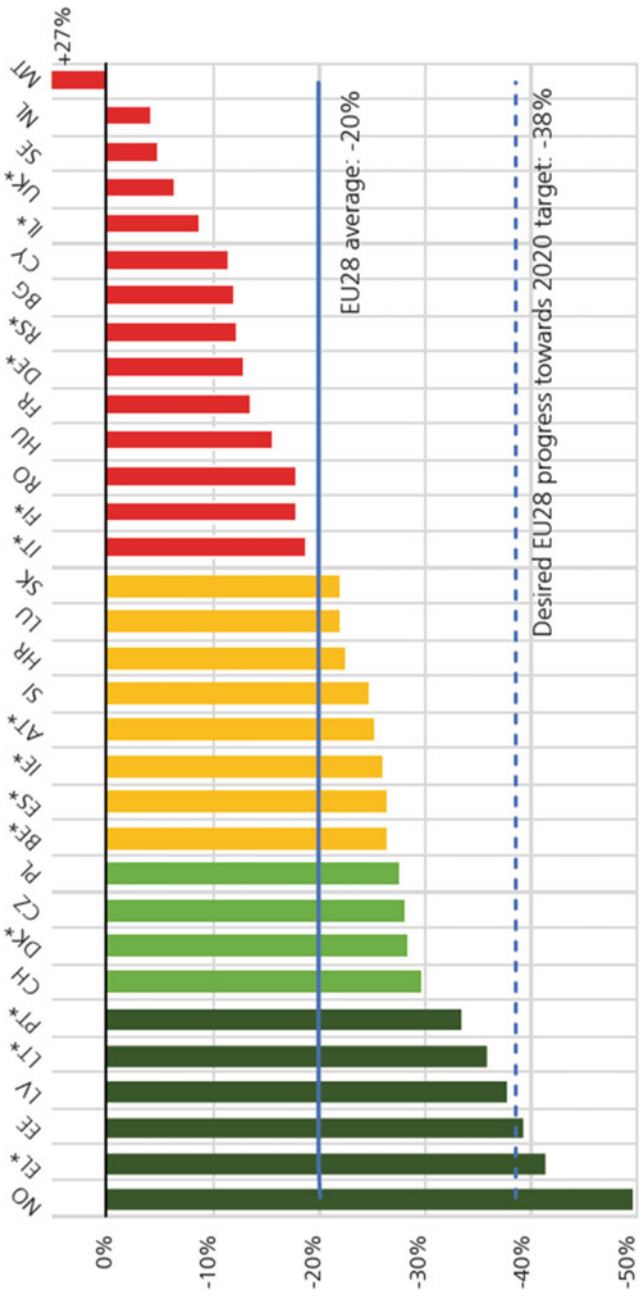

Fig. 2.2 Relative change (%) in European traffic fatalities between 2010 and 2017
Source: European Transport Safety Council 12th Annual Road Safety Performance Index (PIN) Report, accessed Aug 4, 2020

The American College of Surgeons Committee on Trauma (ACS/COT) began focusing on alcohol screening and brief intervention in 2006. Participating level 1 and level 2 trauma hospitals were required to develop protocols for alcohol screening and brief intervention (SBI). This mandate, however, did not specify which patients to screen, leading many centers to screen a limited subset of patients (Schermer 2005; Cunningham et al. 2010; Schermer et al. 2003; Terrell et al. 2008).

Some studies found that having an elevated BAC was the best blood test for detecting hazardous alcohol use (Savola et al. 2004). Not surprisingly, 71% of trauma centers used BAC as their sole method for alcohol screening (Schermer 2005). However, as much as 40% of trauma patients with hazardous alcohol behavior may be undetected based on BAC alone (Ewing et al. 2012).

A few studies of ED-based SBI programs have found positive results. One meta-analysis demonstrated that ED-based SBIs were correlated with fewer alcohol-related injuries at 6 or 12 months without an impact on ED visits or admissions (Landy et al. 2016).

A Scottish government medical informatics project linking anonymized personal healthcare records with core datasets found slightly different results. These datasets included medical outpatient attendance, inpatient admission, psychiatric inpatient admissions, emergency department visits, and pharmacy dispensing records. Targeted SBI of emergency department patients was associated with a reduction of emergency department visits for 2 years, while outpatient and inpatient usage returned to baseline by the end of the study period (Baldacchino et al. 2018).

Despite encouraging evidence of the effectiveness of ED-based SBIs, significant barriers exist. Factors include EHR system heterogeneity, lack of IT support and resources, funding, and resistance among clinical staff (Van Eaton et al. 2014). Studies examining the potential financial benefits of a coordinated SBI on a community-wide or national scale have yet to be published.

2.3.2 Adult Inpatient Medicine

The use of medical informatics in the inpatient hospital setting has focused primarily on treatments of alcohol withdrawal syndrome (AWS). Shaw first described the use of an objective alcohol withdrawal symptom scale, known as the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-A), in 38 chronic alcoholics admitted for AWS (Shaw et al. 1981). Foy et al. used the CIWA-A scale to guide treatment for AWS and found that higher scores were correlated with higher risk of severe withdrawal (Foy et al. 1988). Sullivan et al. later demonstrated that a pure symptom-based CIWA scale (CIWA-Ar) without the use of traditional clinical vital signs – such as tachycardia or elevated blood pressure – resulted in similar reliability as the original scale (Sullivan et al. 1989). The CIWA scale and its variants have been validated in several countries outside of the USA including Australia (51), Germany (Stuppaeck et al. 1994), and India (Sachdeva et al. 2014) (Fig. 2.3).

PHARMACOLOGICAL TREATMENT AND REASSESSMENT PARAMETERS

CIWA-Ar Score	Orders		
≤7	No treatment necessary. Reassess CIWA score every four (4) hours. If score remains ≤7 for 24 hours, contact provider to discontinue the protocol.		
8-10	Chlordiazepoxide 50mg PO every one (1) hour PRN. Reassess CIWA score every hour and re-dose as needed to achieve CIWA < 8.		
11-12	Diazepam 5 mg IV every ten (10) minutes PRN for CIWA score of 11-12. Reassess CIWA score every ten (10) minutes and re-dose as needed to achieve CIWA <11.	OR	LORazepam 1 mg IV every twenty (20) minutes PRN for CIWA score of 11-12. Reassess CIWA score every 20 minutes and re-dose as needed to achieve CIWA <11.
13-15	Diazepam 10 mg IV every ten (10) minutes PRN for CIWA score of 13-15. Reassess CIWA score every ten (10) minutes and re-dose as needed to achieve CIWA <13.	OR	LORazepam 2 mg IV every twenty (20) minutes PRN for CIWA score of 13-15. Reassess CIWA score every twenty (20) minutes and re-dose as needed to achieve CIWA <13.
≥16	Diazepam 10 mg IV every ten (10) minutes PRN for **Obtain ICU consult. Reassess CIWA score every ten (10) minutes and re-dose as needed to achieve CIWA <16.	OR	LORazepam 2 mg IV every twenty (20) minutes **Obtain ICU consult. Reassess CIWA score every twenty (20) minutes and re-dose as needed to achieve CIWA <16.

Fig. 2.3 Example of CIWA-Ar protocol used for EHR implementation
Source: Melkonian et al. (2019)

Since then, CIWA-Ar-based protocols have been incorporated into the EHRs of many individual hospitals. Most use benzodiazepines as the main treatment medication. Results have demonstrated significant clinical and operational improvements. Use of a symptom-triggered approach to AWS treatment has resulted in significant reductions in average medication dosage (Foy et al. 1988; Saitz et al. 1994; Reoux and Miller 2000; Eberly et al. 2016; Melkonian et al. 2019), duration of treatment in inpatient detox units (Shaw et al. 1981; Foy et al. 1988), inpatient length of stay (LOS) (Foy et al. 1988; Saitz et al. 1994), delirium tremens (Jaeger et al. 2001), and incidence of mechanical ventilation (Saitz et al. 1994; Sen et al. 2017). One study found no difference in outcomes including harm but was limited by a high exclusion rate and significant variation in protocol adherence (Waye et al. 2015).

Pope demonstrated that by linking nutritional supplements to the CIWA-Ar order set, more patients received appropriate doses of multivitamins, thiamine, and folate (Pope et al. 2016).

Other medications have been used as well with CIWA-Ar-based protocols. These include barbiturates (Askgaard et al. 2016; Tidwell et al. 2018), baclofen (Girish et al. 2016), and dexmedetomidine (Woods et al. 2015) but with mixed results.

Some critics of CIWA-Ar-based protocols argue that these protocols are often implemented after symptom onset, thus missing an opportunity for AWS prophylaxis. The Alcohol Use Disorders Identification Test (AUDIT) has been studied as a predictive tool for the development of AWS (Bohn et al. 1995; Dolman and Hawkes 2005). Another tool is the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) (Maldonado et al. 2015). Further research is required to determine if use of a predictive AWS tool prior to implementation of an AWS treatment protocol (such as CIWA-Ar) improves clinical outcomes.

SBIs have also been attempted in the hospitalized medical inpatient setting. A Cochrane review showed that SBI may result in a non-sustainable decrease in alcohol intake (6–9 months) and a significant reduction in death at 6 months and 1 year (McQueen et al. 2011). However, the quality of included studies was mixed.

2.3.3 Adult Ambulatory Medicine

In the outpatient setting, much of the focus has been primarily on implementation and effectiveness of SBI (Fig. 2.4). Theoretically, the intimacy of the patient-provider relationship should facilitate screening and interventions. One study found that an overwhelming majority of surveyed patients agreed that doctors should screen for alcohol use (92%) and that the overwhelming majority (93%) would want their doctor to perform an SBI if indicated (Miller et al. 2006). They also expressed a willingness (89%) to undergo blood testing for harmful alcohol use if one was available.

However, in the USA, few patients with AUD received SBIs. According to the 2013 US National Survey on Drug Use and Health (NSDUH), though over 80% of subjects who reported heavy episodic drinking, alcohol abuse, or alcohol dependence were screened for potentially harmful alcohol use, less than one-fourth recalled receiving some form of SBI with 15.5% seeking alcohol treatment services (Anon n.d.-d). Among those with alcohol abuse, only 10.2% received some sort of SBI (Glass et al. 2016). A similar effect was observed among US veterans (Bachrach et al. 2018).

QUESTIONS	0	1	2	3	4	5	6	Score
1. How often do you have a drink containing alcohol?	Never	Less than Monthly	Monthly	Weekly	2–3 times a week	4–6 times a week	Daily	
2. How many drinks containing alcohol do you have on a typical day you are drinking?	1 drink	2 drinks	3 drinks	4 drinks	5–6 drinks	7–9 drinks	10 or more drinks	
3. How often do you have X (5 for men; 4 for women & men over age 65) or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	2–3 times a week	4–6 times a week	Daily	
							Total	

Fig. 2.4 The AUDIT 1–3 (US) example of a brief alcohol use screening tool. Drink sizes were modified for the US standard drink (14 g vs. 10 g in the international version). A score of 7 or more for women and men over age 65, or 8 or more for younger men is positive
Source: CDC. https://www.cdc.gov/ncbddd/fasd/documents/AlcoholSBIImplementationGuide-P.pdf, accessed January 29, 2021

A Cochrane review found that SBIs performed in the primary care setting by general practitioners (GPs) or nurses may have a small reduction in the frequency of binges per week, quantity consumed, and days drinking per week. However, extended interventions were not shown to be superior to SBIs (Kaner et al. 2018). Additionally, SBIs have not been shown to increase treatment or decrease in alcohol intake among adults with alcohol dependence (Saitz 2010; Hepner et al. 2018).

Similar findings have been found in Europe and non-European countries. One meta-analysis found a statistically significant decrease in weekly alcohol consumption after SBI (Elzerbi et al. 2015). While there was a study of population heterogeneity, subgroup analysis of alcohol consumption did not show significant effect variation between Europe and the rest of the world. Geographic bias may exist, however. The majority of studies involving SBI and primary care were conducted in English and Nordic speaking countries in high-income regions. The impact of structural, political, and cultural differences on SBI effectiveness in developing and transitional countries remains unclear (O'Donnell et al. 2014).

Electronic SBIs (e-SBIs) may be an alternative solution to in-person SBIs in selected populations, particularly in resource-limited settings (McCambridge and Cunningham 2014). A computerized SBI with computer-generated feedback letters and integrated therapeutic electronic information provided to patients with at-risk alcohol use but not more severe disorders produced a similar sustained reduction in alcohol intake for up to 24 months as in-person counseling (Freyer-Adam et al. 2018).

A meta-analysis independently assessing adult and college student alcohol misuse found a modest reduction of alcohol consumption at 6 months but not at 1 year (Dedert et al. 2015). Dedert et al. found that the most common e-SBI approach was the use of personalized normative feedback. Personalized normative feedback aims to correct participant misperceptions by showing that their behavior is atypical from the norm.

An alternative solution may be Internet-based SBI (i-SBI). A review of 17 randomized controlled trials with a high proportion of at-risk, heavy, or binge drinkers found a small but significant reduction in alcohol use (White et al. 2010). While another one-stage individual patient data meta-analysis (IPDMA) pooling 19 randomized control trials with 14,198 adult participants found that in-person SBIs were superior to fully automated i-SBI, it found that when compared to controls, i-SBI resulted in a significant reduction in total alcohol consumed and increased treatment response regardless of drinking profile (Riper et al. 2018). The study also found that participants treated with e-SBI using personal normative feedback were significantly less likely to sustain improvements compared to those treated with integrated therapeutic principles.

2.3.4 Pediatrics and Adolescent Medicine

There is a growing interest in the potential use and impact of SBI targeted at the adolescent population. US surveys found that between 28 and 60% of high school students reported binge drinking in the past (Committee on Substance Use and Prevention 2016). Underage drinking was estimated to be responsible for $361 million in total economic costs in the USA in 2006 (Sacks et al. 2013).

In Europe, serial surveys of 15–16-year-old adolescents between 1995 and 2015 found a high rate of alcohol use. Among the over 96,000 students surveyed in 35 European countries, 47% reported alcohol use within the past 30 days. More worrisomely, 35% of adolescents reported recent heavy alcohol use as well (The European School Survey Project on Alcohol and Other Drugs (ESPAD) 2020). The study noted significant differences in the adolescent intoxication rates among the various countries, ranging from as low as 1% up to 36%.

Mirroring ED SBI efforts in the adult trauma population, participating pediatric trauma EDs increased SBI screening from 11 to 73% of eligible patients (Yuma-Guerrero et al. 2012). SBIs at pediatric trauma EDs were easy to complete but subjects tended to question their credibility (Newton et al. 2017). Furthermore, successful completion of 1- and 3-month telephone follow-ups was generally moderate (40.9–53%) (Sacks et al. 2013; Linakis et al. 2013).

One study of e-SBI with normative feedback in adolescent volunteers demonstrated a 3-month reduction in alcohol ingestion (Spijkerman et al. 2010). Another meta-analysis found that three interventions targeted at adolescent health produced multiple positive effects: interpersonal skills training, emotional regulation, and alcohol and drug education (Skeen et al. 2019).

Though research on SBIs in this at-risk age group remains limited, the potential for future harm reduction is promising.

2.4 Use of Public Health Informatics for Alcohol Use Disorders

Modern healthcare has grown increasingly complex outside the traditional boundaries of disease diagnosis and treatment. As seen earlier, use of informatics is now being explored to identify and monitor at-risk individuals for AUD and prevent the development of long-term disease.

Due to the global impact of AUDs, the WHO and individual countries have implemented various responses to reduce alcohol consumption. Common policy responses include legal restrictions on the sale of alcoholic beverages including licensing or advertising, alcohol excise taxes, maximal permissible blood alcohol concentration (BAC) limits to prevent drunk driving, legal age limits for purchase, and disclosing alcohol content on labeling. Some countries have begun implementing national monitoring systems to collect data on alcohol consumption

and related health consequences. Fewer monitor social consequences and response to alcohol policies (WHO 2020). Informatics may play a key role in national monitoring systems.

2.4.1 US Public Health efforts

In the USA, various government agencies and private and public health facilities loosely collaborate in public health functioning. Quality standards established by public agencies such as the National Institutes of Health (NIH) and Agency for Healthcare Research and Quality (AHRQ) are used by public health insurers such as the Centers for Medicare & Medicaid Services (CMS) and Medicaid to establish financial incentives for providers.

But in much of the rest of the world, health systems remain fractured structurally (e.g., privately owned) or financially (e.g., large proportion of self-pay or private insurance). This presents challenges for the implementation of public health initiatives.

Public health relies heavily on information technology to gather and monitor data. Obstacles to overcome include availability of data (real time or delayed) and quality, depending on its source (community health centers, hospitals, clinics, urgent cares, and pharmacies) (Landais et al. 2014). In the USA, this is accomplished via a grid system that involves federal agencies, regional health information organizations (RHIO) or health information exchanges (HIE), state and local public health departments, and providers.

Effective public health informatics must accomplish four pillars: first, utilization of information and technology to improve population health; second, focus on disease prevention over treatment; third, focus on preventative interventions in the steps prior to disease development or injuries; and lastly, work within the government and not the private sectors (O'Carroll et al. 2003). At the core, an informaticist must have consistent, reliable, meaningful data, an understanding of ethics, and knowledge of disease surveillance (Dixon et al. 2015).

Over time, informatics has evolved significantly to improve data collection especially in the inpatient and outpatient settings. With the invention and evolution of the computer, capturing data has rapidly improved. In the USA, collecting data is done via electronic health records (EHRs) which allows for easier aggregation of data from one or more sources. For the inpatient side, the EHR information is collected by providers interviewing and examining patients.

The US 2009 Health Information Technology for Economic and Clinical Health (HITECH) Act promoted the expansion and adoption of electronic health records (EHRs) by hospitals, clinics, and other healthcare-related entities, public and private. These EHRs are meant to serve as building blocks for data collection architecture. The infrastructure would also include event detection, laboratory results, management of contacts and threats, and automation of collecting and disseminating data and the most important provide security (Hanrahan et al. 2006).

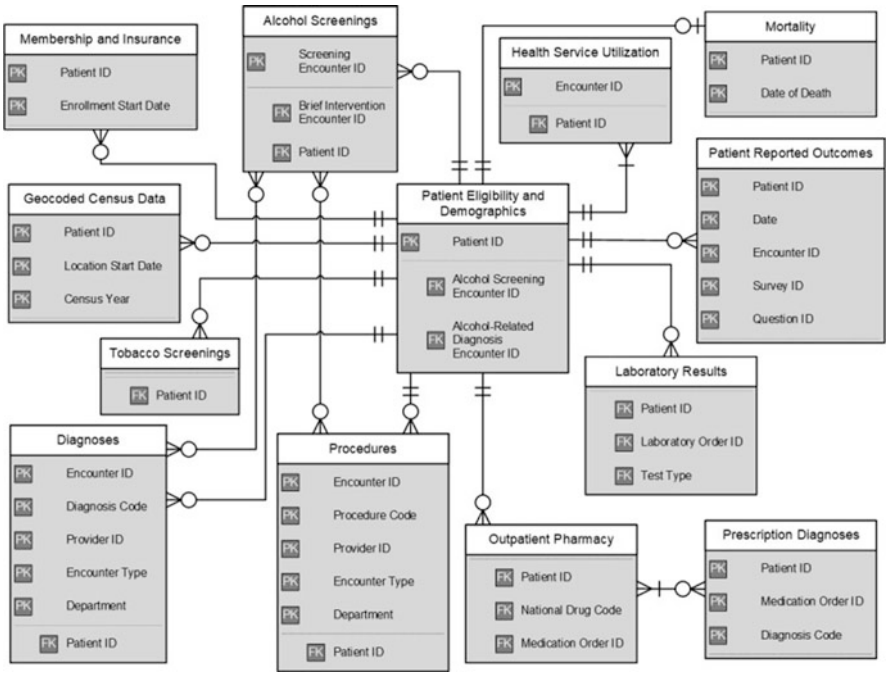

Fig. 2.5 Entity-relationship diagram representing the data structure of core files in the Kaiser Permanente Northern California Adult Alcohol Registry. PK, primary key; FK, foreign key
Source: Palzes et al. (2020a, b)

One example of the private sector creating its own regional health system is the Kaiser Permanente health system. A pioneer in the field of medical informatics, Kaiser Permanente Northern California (KPNC) implemented an alcohol registry within its closed network to monitor adult alcohol use disorders (Palzes et al. 2020a). Conventional national population-based surveys rely on primary data acquired at separate study visits. In contrast, the KPNC approach takes advantage of data collected at the time of healthcare delivery (secondary data) (Fig. 2.5). Similar to the US Veterans Health Administration (VA) alcohol screening protocol in 2004, the EHR approach better reflects the general population and may be a more cost-effective way to monitor population health (Bradley et al. 2006).

KPNC also found that certain conditions were more prevalent among patients reporting unhealthy drinking than those who were to drink within guidelines. These conditions included diabetes, atrial fibrillation, hypertension, COPD, and several others (Sterling et al. 2020). Informatics helped identify median time to remission from unhealthy drinking and potential factors (Palzes et al. 2020b). These findings may help health providers identify and target patients for earlier harmful alcohol use prevention and intervention. RHIOs may be a cost-effective model for countries with deregulated healthcare markets.

2.4.2 *European Public Health Efforts*

Countries such as Germany and France coordinate public health responses through nationwide collaborations within a highly regulated, universal health insurance system. National health systems such as in the UK implement public health initiatives through publicly owned and operated hospitals with salaried physicians. Single-payer national health insurance systems, as found in Canada, Denmark, Norway, Australia, and Sweden, allow public health policies to be enacted more directly (The Commonwealth Fund 2020).

Germany provides universal healthcare through a mandatory multi-payer system. Public health goals are achieved largely through regulation, legislation, and funding. Earlier informatics attempts relied on primary data: hospitalized patients discharged for AUD were asked to self-report. Not surprisingly, the main challenge was post-discharge treatment adherence due to self-reporting (Freund et al. 2013). In contrast, secondary data from addiction treatment centers fed into the national German Monitoring System allowed AUD screening, treatment, and patient monitoring with relative ease (Ritchie 2018).

Unlike the USA or Germany, Finland relies on decentralized but mainly public-funded universal healthcare system (National Health Insurance). The EHR was developed by the Finnish government and is used in both inpatient and outpatient settings, thus allowing it to be linked concurrently to a registry. Of interest, investigators found that alcohol-related visits to primary care providers were associated with higher mortality rates (Rautiainen et al. 2019), raising the question if Finnish primary care providers have adequate resources to address the care of patients with AUD.

2.5 Use of Personal Devices

Besides traditional population surveys or linking EHRs with RHIOs or national registries, other technology-based approaches on AUD informatics have been explored. These include text-based artificial intelligence-driven conversational agents (aka chatbots) (Crutzen et al. 2011), wearable fitness trackers (Abrantes et al. 2017), printable biosensors (Khan et al. 2019), and mobile phone apps (You et al. 2017; Gustafson et al. 2014; Bertholet et al. 2017). Other sources include alcohol ignition interlock devices (Marques et al. 2003) with geolocation tracking capabilities (Voas 2014).

2.6 Conclusion

Medical informatics now plays an increasing role for the prevention, diagnosis, and management of alcohol use disorders. While informatics offers the promise of personalized medicine, we believe that it is most impactful when used to implement hospital system-wide solutions, to manage patient populations, or to support public health efforts.

Some barriers to widespread adoption of informatics in AUDs include patient privacy concerns, proprietary EHR/databases/registries with limited external support, multiple regional private and public entities, regulatory agencies, and lack of familiarity among clinical providers. It remains to be seen how future leaders will navigate the tension between individual patient data privacy concerns and the public health needs of the community.

References

Abrantes AM, Blevins CE, Battle CL, Read JP, Gordon AL, Stein MD. Developing a Fitbit-supported lifestyle physical activity intervention for depressed alcohol dependent women. J Subst Abus Treat. 2017;80:88–97. https://doi.org/10.1016/j.jsat.2017.07.006.

Ahmed N, Greenberg P. Assessing the impact of blood alcohol concentration on the rate of in-hospital mortality following traumatic motor vehicle crash injury: a matched analysis of the National Trauma Data Bank. Injury. 2019;50(1):33–8. https://doi.org/10.1016/j.injury.2018.09.022.

Anon. https://www.cdc.gov/motorvehiclesafety/impaired_driving/impaired-drv_factsheet.html, accessed August 4, 2020.

Anon (n.d.-a) Southeast European subregion is defined as Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Tajikistan, Turkey, Turkmenistan and Uzbekistan.

Anon (n.d.-b) Eastern European subregion is defined as Russian Federation, Belarus, Republic of Moldova and Ukraine.

Anon (n.d.-d). https://www.samhsa.gov/data/sites/default/files/NSDUHresultsPDFWHTML2013/Web/NSDUHresults2013.pdf, accessed September 4, 2020.

Anton RF, Oroszi G, O'Malley S, Couper D, Swift R, Pettinati H, Goldman D. An evaluation of mu-opioid receptor (OPRM1) as a predictor of naltrexone response in the treatment of alcohol dependence: results from the Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence (COMBINE) study. Arch Gen Psychiatry. 2008;65(2):135–44. https://doi.org/10.1001/archpsyc.65.2.135.

Askgaard G, Hallas J, Fink-Jensen A, Molander AC, Madsen KG, Pottegård A. Phenobarbital compared to benzodiazepines in alcohol withdrawal treatment: a register-based cohort study of subsequent benzodiazepine use, alcohol recidivism and mortality. Drug Alcohol Depend. 2016;161:258–64. https://doi.org/10.1016/j.drugalcdep.2016.02.016.

Bachrach RL, Blosnich JR, Williams EC. Alcohol screening and brief intervention in a representative sample of veterans receiving primary care services. J Subst Abus Treat. 2018;95:18–25. https://doi.org/10.1016/j.jsat.2018.09.003.

Baldacchino A, O'Rourke L, Humphris G. Investigating the effect of Alcohol Brief Interventions within accident and emergency departments using a data informatics methodology. Drug Alcohol Depend. 2018;188:47–52. https://doi.org/10.1016/j.drugalcdep.2018.03.035.

Bertholet N, Daeppen JB, McNeely J, Kushnir V, Cunningham JA. Smartphone application for unhealthy alcohol use: a pilot study. Subst Abus. 2017;38(3):285–91. https://doi.org/10.1080/08897077.2017.1281860.

Biernacka JM, Geske JR, Schneekloth TD, Frye MA, Cunningham JM, Choi DS, Tapp CL, Lewis BR, Drews MS,Pietrzak T, Colby CL, Hall-Flavin DK, Loukianova LL, Heit JA, Mrazek DA, Karpyak VM Replication of genome wide association studies of alcohol dependence: support for association with variation in ADH1C. PLoS One 2013;8(3):e58798. doi: https://doi.org/10.1371/journal.pone.0058798.

Blomeyer D, Buchmann AF, Lascorz J, Zimmermann US, Esser G, Desrivieres S, Schmidt MH, Banaschewski T, Schumann G, Laucht M. Association of PER2 genotype and stressful life events with alcohol drinking in young adults. PLoS One. 2013;8(3):e59136. https://doi.org/10.1371/journal.pone.0059136.

Bohn MJ, Babor TF, Kranzler HR. The Alcohol Use Disorders Identification Test (AUDIT): validation of a screening instrument for use in medical settings. J Stud Alcohol. 1995;56(4):423–32. https://doi.org/10.15288/jsa.1995.56.423.

Bradley KA, Williams EC, Achtmeyer CE, Volpp B, Collins BJ, Kivlahan DR. Implementation of evidence-based alcohol screening in the Veterans Health Administration. Am J Manag Care. 2006;12(10):597–606.

Chamorro AJ, Marcos M, Mirón-Canelo JA, Pastor I, González-Sarmiento R, Laso FJ. Association of μ-opioid receptor (OPRM1) gene polymorphism with response to naltrexone in alcohol dependence: a systematic review and meta-analysis. Addict Biol. 2012;17(3):505–12. https://doi.org/10.1111/j.1369-1600.2012.00442.x.

Cochrane J, Chen H, Conigrave KM, Hao W. Alcohol use in China. Alcohol Alcohol. 2003;38(6):537–42. https://doi.org/10.1093/alcalc/agg111.

Committee on Substance Use and Prevention. Substance use screening, brief intervention, and referral to treatment. Pediatrics. 2016;138(1):e20161210. https://doi.org/10.1542/peds.2016-1210.

Crutzen R, Peters GJ, Portugal SD, Fisser EM, Grolleman JJ. An artificially intelligent chat agent that answers adolescents' questions related to sex, drugs, and alcohol: an exploratory study. J Adolesc Health. 2011;48(5):514–9. https://doi.org/10.1016/j.jadohealth.2010.09.002.

Cunningham JA, Wild TC, Cordingley J, Van Mierlo T, Humphreys K. Twelve-month follow-up results from a randomized controlled trial of a brief personalized feedback intervention for problem drinkers. Alcohol Alcohol. 2010;45(3):258–62. https://doi.org/10.1093/alcalc/agq009.

Dedert EA, McDuffie JR, Stein R, McNiel JM, Kosinski AS, Freiermuth CE, Hemminger A, Williams JW Jr. Electronic interventions for alcohol misuse and alcohol use disorders: a systematic review. Ann Intern Med. 2015;163(3):205–14. https://doi.org/10.7326/M15-0285.

Demetriades D, Gkiokas G, Velmahos GC, Brown C, Murray J, Noguchi T. Alcohol and illicit drugs in traumatic deaths: prevalence and association with type and severity of injuries. J Am Coll Surg. 2004;199(5):687–92. https://doi.org/10.1016/j.jamcollsurg.2004.07.017.

Dixon BE, Kharrazi H, Lehmann HP. Public health and epidemiology informatics: recent research and trends in the United States. Yearb Med Inform. 2015;10(1):199–206. https://doi.org/10.15265/IY-2015-012.

Dolman JM, Hawkes ND. Combining the audit questionnaire and biochemical markers to assess alcohol use and risk of alcohol withdrawal in medical inpatients. Alcohol Alcohol. 2005;40(6):515–9. https://doi.org/10.1093/alcalc/agh189.

Eberly ME, Lockwood AG, Lockwood S, Davis KW. Outcomes after implementation of an alcohol withdrawal protocol at a single institution. Hosp Pharm. 2016;51(9):752–8. https://doi.org/10.1310/hpj5109-752.

Elzerbi C, Donoghue K, Drummond C. A comparison of the efficacy of brief interventions to reduce hazardous and harmful alcohol consumption between European and non-European countries: a systematic review and meta-analysis of randomized controlled trials. Addiction. 2015;110(7):1082–91. https://doi.org/10.1111/add.12960.

European Transport Safety Council 12th Annual Road Safety Performance Index (PIN) Report. https://etsc.eu/12th-annual-road-safety-performance-index-pin-report/, accessed August 4, 2020.

Ewing T, Barrios C, Lau C, Patel MS, Cui E, Garcia SD, Kong A, Lotfipour S, Lekawa M, Malinoski D. Predictors of hazardous drinking behavior in 1340 adult trauma patients: a computerized alcohol screening and intervention study. J Am Coll Surg. 2012;215(4):489–95. https://doi.org/10.1016/j.jamcollsurg.2012.05.010.

Foy A, March S, Drinkwater V. Use of an objective clinical scale in the assessment and management of alcohol withdrawal in a large general hospital. Alcohol Clin Exp Res. 1988;12(3): 360–4. https://doi.org/10.1111/j.1530-0277.1988.tb00208.x.

Frank J, Cichon S, Treutlein J, Ridinger M, Mattheisen M, Hoffmann P, Herms S, Wodarz N, Soyka M, Zill P, Maier W, Mössner R, Gaebel W, Dahmen N, Scherbaum N, Schmäl C, Steffens M, Lucae S, Ising M, Müller-Myhsok B, Nöthen MM, Mann K, Kiefer F, Rietschel M. Genome-wide significant association between alcohol dependence and a variant in the ADH gene cluster. Addict Biol. 2012;17(1):171–80. https://doi.org/10.1111/j.1369-1600.2011.00395.x.

Freund JE, Martin BA, Kieser MA, Williams SM, Sutter SL. Transitions in care: medication reconciliation in the community pharmacy setting after discharge. Inov Pharm. 2013;4(2): Article 117. http://pubs.lib.umn.edu/innovations/vol4/iss2/7

Freyer-Adam J, Baumann S, Haberecht K, Tobschall S, Bischof G, John U, Gaertner B. In-person alcohol counseling versus computer-generated feedback: Results from a randomized controlled trial. Health Psychol. 2018 Jan;37(1):70–80. https://doi.org/10.1037/hea0000556.

Girish K, Vikram Reddy K, Pandit LV, Pundarikaksha HP, Vijendra R, Vasundara K, Manjunatha R, Nagraj M, Shruthi R. A randomized, open-label, standard controlled, parallel group study of efficacy and safety of baclofen, and chlordiazepoxide in uncomplicated alcohol withdrawal syndrome. Biom J. 2016;39(1):72–80. https://doi.org/10.1016/j.bj.2015.09.002.

Glass JE, Bohnert KM, Brown RL. Alcohol screening and intervention among United States Adults who attend ambulatory healthcare. J Gen Intern Med. 2016 Jul;31(7):739–45. https://doi.org/10.1007/s11606-016-3614-5.

Gmel G, Shield KD, Kehoe-Chan TA, Rehm J. The effects of capping the alcohol consumption distribution and relative risk functions on the estimated number of deaths attributable to alcohol consumption in the European Union in 2004. BMC Med Res Methodol. 2013;13:24. https://doi.org/10.1186/1471-2288-13-24.

Gustafson DH, McTavish FM, Chih MY, Atwood AK, Johnson RA, Boyle MG, Levy MS, Driscoll H, Chisholm SM, Dillenburg L, Isham A, Shah D. A smartphone application to support recovery from alcoholism: a randomized clinical trial. JAMA Psychiatry. 2014;71(5):566–72. https://doi.org/10.1001/jamapsychiatry.2013.4642.

Hanrahan LP, Foldy S, Barthell EN, Wood S. Medical informatics in population health: building Wisconsin's strategic framework for health information technology. WMJ. 2006;105(1):16–20.

Haroon S, Wooldridge D, Hoogewerf J, Nirantharakumar K, Williams J, Martino L, Bhala N. Information standards for recording alcohol use in electronic health records: findings from a national consultation. BMC Med Inform Decis Mak. 2018;18(1):36. https://doi.org/10.1186/s12911-018-0612-z.

Haug S, Schaub MP. Treatment outcome, treatment retention, and their predictors among clients of five outpatient alcohol treatment centres in Switzerland. BMC Public Health. 2016;16:581. https://doi.org/10.1186/s12889-016-3294-4.

Hepner KA, Hoggatt KJ, Bogart A, Paddock S. Does documented brief intervention predict decreases in alcohol use in primary care? Subst Use Misuse. 2018;53(10):1633–7. https://doi.org/10.1080/10826084.2017.1421225.

Im PK, Millwood IY, Guo Y, et al. Patterns and trends of alcohol consumption in rural and urban areas of China: findings from the China Kadoorie Biobank. BMC Public Health. 2019;19:217. https://doi.org/10.1186/s12889-019-6502-1.

Jaeger TM, Lohr RH, Pankratz VS. Symptom-triggered therapy for alcohol withdrawal syndrome in medical inpatients. Mayo Clin Proc. 2001;76(7):695–701. https://doi.org/10.4065/76.7.695.

Kaner EF, Beyer FR, Muirhead C, Campbell F, Pienaar ED, Bertholet N, Daeppen JB, Saunders JB, Burnand B. Effectiveness of brief alcohol interventions in primary care populations. Cochrane Database Syst Rev. 2018;2(2):CD004148. https://doi.org/10.1002/14651858.CD004148.pub4.

Kapoor M, Wang JC, Wetherill L, Le N, Bertelsen S, Hinrichs AL, Budde J, Agrawal A, Bucholz K, Dick D, Harari O, Hesselbrock V, Kramer J, Nurnberger JI Jr, Rice J, Saccone N, Schuckit M, Tischfield J, Porjesz B, Edenberg HJ, Bierut L, Foroud T, Goate A. A meta-analysis of two genome-wide association studies to identify novel loci for maximum number of alcoholic drinks. Hum Genet. 2013;132(10):1141–51. https://doi.org/10.1007/s00439-013-1318-z.

Khan S, Ali S, Bermak A. Recent developments in printing flexible and wearable sensing electronics for healthcare applications. Sensors (Basel). 2019;19(5):1230. https://doi.org/10.3390/s19051230.

Kiefer F, Witt SH, Frank J, Richter A, Treutlein J, Lemenager T, Nöthen MM, Cichon S, Batra A, Berner M, Wodarz N, Zimmermann US, Spanagel R, Wiedemann K, Smolka MN, Heinz A, Rietschel M, Mann K. Involvement of the atrial natriuretic peptide transcription factor GATA4 in alcohol dependence, relapse risk and treatment response to acamprosate. Pharmacogenomics J. 2011;11(5):368–74. https://doi.org/10.1038/tpj.2010.51.

Kim J, Park A. A systematic review: candidate gene and environment interaction on alcohol use and misuse among adolescents and young adults. Am J Addict. 2018; https://doi.org/10.1111/ajad.12755.

Kranzler HR, Armeli S, Covault J, Tennen H. Variation in OPRM1 moderates the effect of desire to drink on subsequent drinking and its attenuation by naltrexone treatment. Addict Biol. 2013;18(1):193–201. https://doi.org/10.1111/j.1369-1600.2012.00471.x.

Landais P, Boudemaghe T, Suehs C, Dedet G, Lebihan-Benjamin C. Computerized medico-economic decision making: an international comparison. In: Venot A, Burgun A, Quantin C, editors. Medical informatics, e-Health. Health informatics. Paris: Springer; 2014. https://doi.org/10.1007/978-2-8178-0478-1_9.

Landy MS, Davey CJ, Quintero D, Pecora A, McShane KE. A systematic review on the effectiveness of brief interventions for alcohol misuse among adults in emergency departments. J Subst Abus Treat. 2016;61:1–12. https://doi.org/10.1016/j.jsat.2015.08.004.

Linakis JG, Bromberg J, Baird J, Nirenberg TD, Chun TH, Mello MJ, Jackson KM, Spirito A. Feasibility and acceptability of a pediatric emergency department alcohol prevention intervention for young adolescents. Pediatr Emerg Care. 2013;29(11):1180–8. https://doi.org/10.1097/PEC.0b013e3182a9f7da.

Lowenfels AB, Miller TT. Alcohol and trauma. Ann Emerg Med. 1984;13(11):1056–60. https://doi.org/10.1016/s0196-0644(84)80070-0.

Maier RV. Ethanol abuse and the trauma patient. Surg Infect. 2001;2(2):133–41. https://doi.org/10.1089/109629601750469456.

Maldonado JR, Sher Y, Das S, Hills-Evans K, Frenklach A, Lolak S, Talley R, Neri E. Prospective Validation Study of the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) in medically ill inpatients: a new scale for the prediction of complicated alcohol withdrawal syndrome. Alcohol Alcohol. 2015;50(5):509–18. https://doi.org/10.1093/alcalc/agv043.

Mann K, Lemenager T, Hoffmann S, Reinhard I, Hermann D, Batra A, Berner M, Wodarz N, Heinz A, Smolka MN, Zimmermann US, Wellek S, Kiefer F, Anton RF. PREDICT Study Team. Results of a double-blind, placebo-controlled pharmacotherapy trial in alcoholism conducted in Germany and comparison with the US COMBINE study. Addict Biol. 2013;18(6):937–46. https://doi.org/10.1111/adb.12012.

Marques PR, Voas RB, Tippetts AS. Behavioral measures of drinking: patterns from the alcohol interlock record. Addiction. 2003;98(Suppl. 2):13–9. https://doi.org/10.1046/j.1359-6357.2003.00584.x.

Marques A, Peralta M, Martins J, Loureiro V, Almanzar PC, de Matos MG. Few European adults are living a healthy lifestyle. Am J Health Promot. 2019;33(3):391–8. https://doi.org/10.1177/0890117118787078.

McCambridge J, Cunningham JA. The early history of ideas on brief interventions for alcohol. Addiction. 2014;109(4):538–46. https://doi.org/10.1111/add.12458.

McQueen J, Howe TE, Allan L, Mains D, Hardy V. Brief interventions for heavy alcohol users admitted to general hospital wards. Cochrane Database Syst Rev. 2011;(8):CD005191. https://doi.org/10.1002/14651858.CD005191.pub3.

Melkonian A, Patel R, Magh A, Ferm S, Hwang C. Assessment of a hospital-wide CIWA-Ar protocol for management of alcohol withdrawal syndrome. Mayo Clin Proc Innov Qual Outcomes. 2019;3(3):344–9. https://doi.org/10.1016/j.mayocpiqo.2019.06.005.

Miller WR, Baca C, Compton WM, Ernst D, Manuel JK, Pringle B, Schermer CR, Weiss RD, Willenbring ML, Zweben A. Addressing substance abuse in health care settings. Alcohol Clin Exp Res. 2006;30(2):292–302. https://doi.org/10.1111/j.1530-0277.2006.00027.x.

Newton AS, Dow N, Dong K, Fitzpatrick E, Cameron Wild T, Johnson DW, Ali S, Colman I, Rosychuk RJ, Pediatric Emergency Research Canada. A randomised controlled pilot trial evaluating feasibility and acceptability of a computer-based tool to identify and reduce harmful and hazardous drinking among adolescents with alcohol-related presentations in Canadian pediatric emergency departments. BMJ Open. 2017;7(8):e015423. https://doi.org/10.1136/bmjopen-2016-015423.

Nieratschker V, Grosshans M, Frank J, Strohmaier J, von der Goltz C, El-Maarri O, Witt SH, Cichon S, Nöthen MM, Kiefer F, Rietschel M. Epigenetic alteration of the dopamine transporter gene in alcohol-dependent patients is associated with age. Addict Biol. 2014;19(2):305–11. https://doi.org/10.1111/j.1369-1600.2012.00459.x.

Norström T. Per capita alcohol consumption and all-cause mortality in 14 European countries. Addiction. 2001;96(Suppl. 1):S113–28. https://doi.org/10.1080/09652140020021215.

O'Carroll PW, Yasnoff WA, Ward ME, Ripp LH, Martin EL, editors. Public health informatics and information systems. Paris: Springer; 2003.

O'Donnell A, Anderson P, Newbury-Birch D, Schulte B, Schmidt C, Reimer J, Kaner E. The impact of brief alcohol interventions in primary healthcare: a systematic review of reviews. Alcohol Alcohol. 2014;49(1):66–78. https://doi.org/10.1093/alcalc/agt170.

Oslin DW, Berrettini W, Kranzler HR, Pettinati H, Gelernter J, Volpicelli JR, O'Brien CP. A functional polymorphism of the mu-opioid receptor gene is associated with naltrexone response in alcohol-dependent patients. Neuropsychopharmacology. 2003;28(8):1546–52. https://doi.org/10.1038/sj.npp.1300219.

Palzes VA, Weisner C, Chi FW, Kline-Simon AH, Satre DD, Hirschtritt ME, Ghadiali M, Sterling S. The Kaiser permanente Northern California adult alcohol registry, an electronic health records-based registry of patients with alcohol problems: development and implementation. JMIR Med Inform. 2020a;8(7):e19081. https://doi.org/10.2196/19081.

Palzes VA, Kline-Simon AH, Satre DD, Sterling S, Weisner C, Chi FW. Remission from unhealthy drinking among patients with an alcohol use disorder: a longitudinal study using systematic, primary care-based alcohol screening data. J Stud Alcohol Drugs. 2020b;81(4):436–45. https://doi.org/10.15288/jsad.2020.81.436.

Pope S, Gustaw-Rothenberg K, Delos RC. Linking orders in electronic medical records can improve the frequency with which recommended treatments are ordered as illustrated in the treatment of alcohol withdrawal. J Psychiatr Pract. 2016;22(1):64–7. https://doi.org/10.1097/PRA.0000000000000127.

Probst C, Rehm J. Alcohol use, opioid overdose and socioeconomic status in Canada: a threat to life expectancy? CMAJ. 2018;190(44):E1294–5. https://doi.org/10.1503/cmaj.180806.

Rautiainen E, Ryynänen OP, Reissell E, Kauhanen J, Laatikainen T. Alcohol-related social and health service use patterns as predictors of death and remission in patients with AUD, J Subst Abuse Treat. 2019;96:65–74. https://doi.org/10.1016/j.jsat.2018.10.013. Erratum in: J Subst Abuse Treat. 2019;98:89

Rehm J, Room R. The cultural aspect: How to measure and interpret epidemiological data on alcohol-use disorders across cultures. Nordisk Alkohol Nark. 2017;34(4):330–41. https://doi.org/10.1177/1455072517704795.

Rehm J, Room R, van den Brink W, Jacobi F. Alcohol use disorders in EU countries and Norway: an overview of the epidemiology. Eur Neuropsychopharmacol. 2005;15(4):377–88. https://doi.org/10.1016/j.euroneuro.2005.04.005.

Reoux JP, Miller K. Routine hospital alcohol detoxification practice compared to symptom triggered management with an Objective Withdrawal Scale (CIWA-Ar). Am J Addict. 2000;9(2):135–44. https://doi.org/10.1080/10550490050173208.

Riper H, Hoogendoorn A, Cuijpers P, Karyotaki E, Boumparis N, Mira A, Andersson G, Berman AH, Bertholet N, Bischof G, Blankers M, Boon B, Boß L, Brendryen H, Cunningham J, Ebert D, Hansen A, Hester R, Khadjesari Z, Kramer J, Murray E, Postel M, Schulz D, Sinadinovic K, Suffoletto B, Sundström C, de Vries H, Wallace P, Wiers RW, Smit JH. Effectiveness and treatment moderators of internet interventions for adult problem drinking: an individual patient data meta-analysis of 19 randomised controlled trials. PLoS Med. 2018;15(12):e1002714. https://doi.org/10.1371/journal.pmed.1002714.

Hannah Ritchie (2018) "Alcohol Consumption". Published online at OurWorldInData.org. Retrieved from: https://ourworldindata.org/alcohol-consumption [Online Resource].

Sachdeva A, Chandra M, Deshpande SN. A comparative study of fixed tapering dose regimen versus symptom-triggered regimen of lorazepam for alcohol detoxification. Alcohol Alcohol. 2014;49(3):287–91. https://doi.org/10.1093/alcalc/agt181.

Sacks JJ, Roeber J, Bouchery EE, Gonzales K, Chaloupka FJ, Brewer RD. State costs of excessive alcohol consumption, 2006. Am J Prev Med. 2013;45(4):474–85. https://doi.org/10.1016/j.amepre.2013.06.004.

Sacks JJ, Gonzales KR, Bouchery EE, Tomedi LE, Brewer RD. 2010 National and State Costs of Excessive Alcohol Consumption. Am J Prev Med. 2015;49(5):e73–9. https://doi.org/10.1016/j.amepre.2015.05.031.

Saitz R. Alcohol screening and brief intervention in primary care: absence of evidence for efficacy in people with dependence or very heavy drinking. Drug Alcohol Rev. 2010;29(6):631–40. https://doi.org/10.1111/j.1465-3362.2010.00217.x.

Saitz R, Mayo-Smith MF, Roberts MS, Redmond HA, Bernard DR, Calkins DR. Individualized treatment for alcohol withdrawal. A randomized double-blind controlled trial. JAMA. 1994;272(7):519–23.

Savola O, Niemelä O, Hillbom M. Blood alcohol is the best indicator of hazardous alcohol drinking in young adults and working-age patients with trauma. Alcohol Alcohol. 2004;39(4):340–5. https://doi.org/10.1093/alcalc/agh064.

Schermer CR. Feasibility of alcohol screening and brief intervention. J Trauma. 2005;59(Suppl. 3):S119–23. https://doi.org/10.1097/01.ta.0000174679.12567.7c.

Schermer CR, Gentilello LM, Hoyt DB, Moore EE, Moore JB, Rozycki GS, Feliciano DV. National survey of trauma surgeons' use of alcohol screening and brief intervention. J Trauma. 2003;55(5):849–56. https://doi.org/10.1097/01.TA.0000091110.83692.38.

Schumann G, Coin LJ, Lourdusamy A, Charoen P, Berger KH, Stacey D, Desrivières S, Aliev FA, Khan AA, Amin N, Aulchenko YS, Bakalkin G, Bakker SJ, Balkau B, Beulens JW, Bilbao A, de Boer RA, Beury D, Bots ML, Breetvelt EJ, Cauchi S, Cavalcanti-Proença C, Chambers JC, Clarke TK, Dahmen N, de Geus EJ, Dick D, Ducci F, Easton A, Edenberg HJ, Esko T, Fernández-Medarde A, Foroud T, Freimer NB, Girault JA, Grobbee DE, Guarrera S, Gudbjartsson DF, Hartikainen AL, Heath AC, Hesselbrock V, Hofman A, Hottenga JJ, Isohanni MK, Kaprio J, Khaw KT, Kuehnel B, Laitinen J, Lobbens S, Luan J, Mangino M, Maroteaux M, Matullo G, McCarthy MI, Mueller C, Navis G, Numans ME, Núñez A, Nyholt DR, Onland-Moret CN, Oostra BA, O'Reilly PF, Palkovits M, Penninx BW, Polidoro S, Pouta A, Prokopenko I, Ricceri F, Santos E, Smit JH, Soranzo N, Song K, Sovio U, Stumvoll M, Surakk I, Thorgeirsson TE, Thorsteinsdottir U, Troakes C, Tyrfingsson T, Tönjes A, Uiterwaal CS, Uitterlinden AG, van der Harst P, van der Schouw YT, Staehlin O, Vogelzangs N,

Vollenweider P, Waeber G, Wareham NJ, Waterworth DM, Whitfield JB, Wichmann EH, Willemsen G, Witteman JC, Yuan X, Zhai G, Zhao JH, Zhang W, Martin NG, Metspalu A, Doering A, Scott J, Spector TD, Loos RJ, Boomsma DI, Mooser V, Peltonen L, Stefansson K, van Duijn CM, Vineis P, Sommer WH, Kooner JS, Spanagel R, Heberlein UA, Jarvelin MR, Elliott P. Genome-wide association and genetic functional studies identify autism susceptibility candidate 2 gene (AUTS2) in the regulation of alcohol consumption. Proc Natl Acad Sci U S A. 2011;108(17):7119–24. https://doi.org/10.1073/pnas.1017288108. Epub 2011 Apr 6. Erratum in: Proc Natl Acad Sci U S A. 2011 May 31;108(22):9316. Esk, Tõnu [corrected to Esko, Tõnu]

Sen S, Grgurich P, Tulolo A, Smith-Freedman A, Lei Y, Gray A, Dargin J. A symptom-triggered benzodiazepine protocol utilizing SAS and CIWA-Ar scoring for the treatment of alcohol withdrawal syndrome in the critically ill. Ann Pharmacother. 2017;51(2):101–10. https://doi.org/10.1177/1060028016672036.

Shaw JM, Kolesar GS, Sellers EM, Kaplan HL, Sandor P. Development of optimal treatment tactics for alcohol withdrawal. I. Assessment and effectiveness of supportive care. J Clin Psychopharmacol. 1981;1(6):382–9. https://doi.org/10.1097/00004714-198111000-00006.

Skeen S, Laurenzi CA, Gordon SL, du Toit S, Tomlinson M, Dua T, Fleischmann A, Kohl K, Ross D, Servili C, Brand AS, Dowdall N, Lund C, van der Westhuizen C, Carvajal-Aguirre L, Eriksson de Carvalho C, Melendez-Torres GJ. Adolescent mental health program components and behavior risk reduction: a meta-analysis. Pediatrics. 2019;144(2):e20183488. https://doi.org/10.1542/peds.2018-3488.

Spijkerman R, Roek MA, Vermulst A, Lemmers L, Huiberts A, Engels RC. Effectiveness of a web-based brief alcohol intervention and added value of normative feedback in reducing underage drinking: a randomized controlled trial. J Med Internet Res. 2010;12(5):e65. https://doi.org/10.2196/jmir.1465.

Stacey D, Bilbao A, Maroteaux M, Jia T, Easton AC, Longueville S, Nymberg C, Banaschewski T, Barker GJ, Büchel C, Carvalho F, Conrod PJ, Desrivières S, Fauth-Bühler M, Fernandez-Medarde A, Flor H, Gallinat J, Garavan H, Bokde AL, Heinz A, Ittermann B, Lathrop M, Lawrence C, Loth E, Lourdusamy A, Mann KF, Martinot JL, Nees F, Palkovits M, Paus T, Pausova Z, Rietschel M, Ruggeri B, Santos E, Smolka MN, Staehlin O, Jarvelin MR, Elliott P, Sommer WH, Mameli M, Müller CP, Spanagel R, Girault JA, Schumann G, IMAGEN Consortium. RASGRF2 regulates alcohol-induced reinforcement by influencing mesolimbic dopamine neuron activity and dopamine release. Proc Natl Acad Sci U S A. 2012;109(51):21128–33. https://doi.org/10.1073/pnas.1211844110.

Sterling SA, Palzes VA, Lu Y, Kline-Simon AH, Parthasarathy S, Ross T, Elson J, Weisner C, Maxim C, Chi FW. Associations between medical conditions and alcohol consumption levels in an adult primary care population. JAMA Netw Open. 2020;3(5):e204687. https://doi.org/10.1001/jamanetworkopen.2020.4687.

Stübig T, Petri M, Zeckey C, Brand S, Müller C, Otte D, Krettek C, Haasper C. Alcohol intoxication in road traffic accidents leads to higher impact speed difference, higher ISS and MAIS, and higher preclinical mortality. Alcohol. 2012;46(7):681–6. https://doi.org/10.1016/j.alcohol.2012.07.002.

Stuppaeck CH, Barnas C, Falk M, Guenther V, Hummer M, Oberbauer H, Pycha R, Whitworth AB, Fleischhacker WW. Assessment of the alcohol withdrawal syndrome--validity and reliability of the translated and modified Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-A). Addiction. 1994;89(10):1287–92. https://doi.org/10.1111/j.1360-0443.1994.tb03307.x.

Substance Abuse and Mental Health Services Administration (SAMSA). https://www.samhsa.gov/data/release/2019-national-survey-drug-use-and-health-nsduh-releases, accessed January 26, 2021.

Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). Br J Addict. 1989;84(11):1353–7. https://doi.org/10.1111/j.1360-0443.1989.tb00737.x.

Taqi MM, Bazov I, Watanabe H, Sheedy D, Harper C, Alkass K, Druid H, Wentzel P, Nyberg F, Yakovleva T, Bakalkin G. Prodynorphin CpG-SNPs associated with alcohol dependence: elevated methylation in the brain of human alcoholics. Addict Biol. 2011;16(3):499–509. https://doi.org/10.1111/j.1369-1600.2011.00323.x.

Terrell F, Zatzick DF, Jurkovich GJ, Rivara FP, Donovan DM, Dunn CW, Schermer C, Meredith JW, Gentilello LM. Nationwide survey of alcohol screening and brief intervention practices at US Level I trauma centers. J Am Coll Surg. 2008;207(5):630–8. https://doi.org/10.1016/j.jamcollsurg.2008.05.021.

The Commonwealth Fund. Considering "Single Payer" Proposals in the U.S.: Lessons from Abroad. https://www.commonwealthfund.org/publications/2019/apr/considering-single-payer-proposals-lessons-from-abroad, accessed September 15, 2020.

The European School Survey Project on Alcohol and Other Drugs (ESPAD). http://www.espad.org/news/2016/new-espad-results, accessed September 15, 2020.

Thomas M, Riemann B, Jones J. Epidemiology of alcohol and drug screening among pedestrian fatalities in the United States, 2014-2016. Traffic Inj Prev. 2019;20(6):557–62. https://doi.org/10.1080/15389588.2019.1622006.

Tidwell WP, Thomas TL, Pouliot JD, Canonico AE, Webber AJ. Treatment of alcohol withdrawal syndrome: phenobarbital vs CIWA-Ar protocol. Am J Crit Care. 2018;27(6):454–60. https://doi.org/10.4037/ajcc2018745.

Treutlein J, Cichon S, Ridinger M, Wodarz N, Soyka M, Zill P, Maier W, Moessner R, Gaebel W, Dahmen N, Fehr C, Scherbaum N, Steffens M, Ludwig KU, Frank J, Wichmann HE, Schreiber S, Dragano N, Sommer WH, Leonardi-Essmann F, Lourdusamy A, Gebicke-Haerter-P, Wienker TF, Sullivan PF, Nöthen MM, Kiefer F, Spanagel R, Mann K, Rietschel M. Genome-wide association study of alcohol dependence. Arch Gen Psychiatry. 2009;66(7):773–84. https://doi.org/10.1001/archgenpsychiatry.2009.83.

Van Eaton EG, Zatzick DF, Gallagher TH, Tarczy-Hornoch P, Rivara FP, Flum DR, Peterson R, Maier RV. A nationwide survey of trauma center information technology leverage capacity for mental health comorbidity screening. J Am Coll Surg. 2014;219(3):505–10..e1. https://doi.org/10.1016/j.jamcollsurg.2014.02.032.

Voas RB. Enhancing the use of vehicle alcohol interlocks with emerging technology. Alcohol Res. 2014;36(1):81–9.

Waye C, Wong M, Lee S. Implementation of a CIWA-Ar alcohol withdrawal protocol in a veterans hospital. South Med J. 2015;108(1):23–8. https://doi.org/10.14423/SMJ.0000000000000216.

White A, Kavanagh D, Stallman H, Klein B, Kay-Lambkin F, Proudfoot J, Drennan J, Connor J, Baker A, Hines E, Young R. Online alcohol interventions: a systematic review. J Med Internet Res. 2010;12(5):e62. https://doi.org/10.2196/jmir.1479.

WHO. Global status report on alcohol and health 2018. https://www.who.int/publications/i/item/9789241565639 downloaded July 26, 2020.

WHO Alcohol Fact Sheet. https://www.who.int/news-room/fact-sheets/detail/alcohol, accessed January 27, 2021.

WHO Regional Office for Europe, Alcohol Use. https://www.euro.who.int/en/health-topics/disease-prevention/alcohol-use, accessed January 28, 2021.

Woods AD, Giometti R, Weeks SM. The use of dexmedetomidine as an adjuvant to benzodiazepine-based therapy to decrease the severity of delirium in alcohol withdrawal in adult intensive care unit patients: a systematic review. JBI Database System Rev Implement Rep. 2015;13(1):224–52. https://doi.org/10.11124/jbisrir-2015-1602.

World Health Organization (WHO). Alcohol in the European Union: Consumption, harm and policy approaches. 2012. https://www.euro.who.int/__data/assets/pdf_file/0003/160680/e96457.pdf, accessed August 7, 2020.

You CW, Chen YC, Chen CH, Lee CH, Kuo PH, Huang MC, Chu HH. Smartphone-based support system (SoberDiary) coupled with a Bluetooth breathalyser for treatment-seeking alcohol-dependent patients. Addict Behav. 2017;65:174–8. https://doi.org/10.1016/j.addbeh.2016.10.017.

Yuma-Guerrero PJ, Lawson KA, Velasquez MM, von Sternberg K, Maxson T, Garcia N. Screening, brief intervention, and referral for alcohol use in adolescents: a systematic review. Pediatrics. 2012;130(1):115–22. https://doi.org/10.1542/peds.2011-1589.

Zastrozhin MS, Skryabin VY, Miroshkin SS, Bryun EA, Sychev DA. Pharmacogenetics of alcohol addiction: current perspectives. Appl Clin Genet. 2019;12:131–40. https://doi.org/10.2147/TACG.S206745.

Zhang H, Wang F, Xu H, Liu Y, Liu J, Zhao H, Gelernter J. Differentially co-expressed genes in postmortem prefrontal cortex of individuals with alcohol use disorders: influence on alcohol metabolism-related pathways. Hum Genet. 2014;133(11):1383–94. https://doi.org/10.1007/s00439-014-1473-x.