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Phenotypic and genetic relationship between BMI and drinking in a sample of UK adults

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Abstract

The health impairments derived from both alcoholism and obesity are well known. However, reports that relate increased alcohol use with increased measures of obesity have been mixed in their findings, especially with respect to genetic factors that could potentially link these two behaviors. Here, using a large sample of adults from the UK ($n \approx 113,000$), we report both the observed and genetic correlations between BMI (kg/m^2) and two measures of alcohol use: reported quantity (drinks per week) and frequency of use (from never to daily). Overall, both observationally and genetically, alcohol intake is negatively correlated with BMI. Phenotypic correlations ranged from $-.01$ to $-.17$, and genetic correlations ranged from $-.1$ to $-.4$. Genetic correlations tended to be stronger than the phenotypic correlations, and these correlations were stronger in females and between BMI and, specifically, frequency of use. Though the mechanisms driving these relationships are yet to be identified, we can conclude that the genetic factors related to drinking both more and more often are shared with those responsible for lower BMI.

Keywords

alcohol use; bmi; obesity; SNP heritability; genetic correlation; UK Biobank

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Authors of the present analysis did not interact with participants. Details about UK Biobanks's procedures can be found at: <http://www.ukbiobank.ac.uk/wp-content/uploads/2011/05/EGF20082.pdf?phpMyAdmin=trmKQIYdjjnQIgJ%2CfAzikMhEnx6>

Informed consent: Informed consent was obtained from all individual participants included in the study. Authors of the present analysis did not interact with participants. Details about UK Biobanks's procedures can be found at: <http://www.ukbiobank.ac.uk/wp-content/uploads/2011/05/EGF20082.pdf?phpMyAdmin=trmKQIYdjjnQIgJ%2CfAzikMhEnx6>

Introduction

Both obesity and alcoholism are known public health concerns (World 2000, 2002). Given that both of these conditions result from the excessive consumption of either food or alcoholic beverages, researchers have questioned whether there may be an etiological link behind these two behaviors. Neurobiological evidence has hinted at a potential connection between drug (in this case, alcohol) and food addiction with the dopamine system serving as a prime contender for biologically linking these two conditions (Volkow & Wise, 2005; Volkow, Wang, Fowler, & Telang, 2008; Volkow, Wang, Fowler, Tomasi, & Baler, 2012).

Despite these potential links and the expectation that increase in alcohol consumption, and thus, caloric intake would necessarily increase the risk of obesity, the observed relationship between alcohol use and obesity has been mixed (Yeomans 2010). In a review of findings from both cross-sectional and longitudinal study designs, examinations of heavy and binge drinking tended to find positive associations between alcohol consumption and measures of obesity, while studies on light to moderate drinking were more likely to report either no or negative correlations (Sayon-Orea, Martinez-Gonzalez, & Bes-Rastrollo, 2011). Further, while drinking large quantities of alcohol may be associated with higher body mass, increased *frequency* of alcohol consumption may have a protective effect against obesity (Breslow & Smothers, 2005). Additionally, gender may have an impact on the magnitude and direction of these relationships (Breslow & Smothers, 2005; Colditz et al., 1991; Dallongeville et al., 1998). Thus, even though both alcohol and weight problems could stem from a similar predisposition to over consumption, their relationship is complex.

One thing that is known is that genetic factors play a role in both obesity and alcohol use behaviors. BMI is highly heritable with many genetic variance estimates reaching as high as around 80% (Bulik, Sullivan, & Kendler, 2003; Stunkard, Foch, & Hrubec, 1986). Heritability estimates for alcohol intake, including both measures of quantity and frequency, have ranged from 40 to 60 percent (Heath & Martin, 1994; Whitfield et al., 2004). Given the considerable role of genetic factors as well as neurobiological evidence for a shared etiology (Volkow & Wise, 2005; Volkow et al., 2008; Volkow et al., 2012), few studies have specifically examined the relationship between the contributing genetic factors for both BMI and alcohol use. Twin studies that have attempted to get a bivariate genetic correlation between BMI and measures of drinking have largely failed to find a solid link behind these two disorders (Eisen, Lyons, Goldberg, & True, 1993). Though one study did find a significant negative genetic correlation between weekly drinking and BMI in females, implying that genetic factors related to increased weekly drinking in young women are related to lower obesity (Duncan, Grant, Bucholz, Madden, & Heath, 2009). Studies that have examined the impact of familial risk for alcohol related problems on obesity have, however, suggested that there may be more to examine with respect to the potential for a genetic relationship between these conditions. Male adolescents with heightened familial risk for alcohol dependence had higher BMIs than low risk males (Lichenstein et al., 2014). Further the effect of family history of alcohol problems impacted frequency of alcohol consumption patterns particularly for non-obese individuals pointing to a theory in which alcohol and food may compete for similar neurobiological pathways related to addiction (Gearhardt & Corbin, 2009). Thus, the sum of existing literature remains largely

inconclusive with regard to the possibility of a shared genetic etiology between obesity and alcohol consumption.

Recent methods and an influx of phenotypic and molecular genetic data on a large numbers of individuals have made the need for family data (and the assumptions of twin and family studies – especially those dealing with potential confounds of the shared environment) to understand the genetic components of these traits unnecessary (Turkheimer 2011). Instead, we used a linear mixed model approach, which utilizes the conglomerate of all common genotyped variants, or single nucleotide polymorphisms (SNPs), to get both a heritability estimate from these SNPs (SNP h^2) and the genetic correlation due to SNPs (rg-sNP) between two traits. Briefly, this approach estimates distal genetic relatedness between ‘unrelated’ individuals to create a genetic relatedness matrix (GRM) and assesses the degree to which this genetic similarity corresponds to phenotypic similarity, or in the case of getting the genetic correlation, a phenotypic covariance matrix between the two traits (Lee, Yang, Goddard, Visscher, & Wray, 2012; Yang et al., 2011). This method has been primarily implemented using a program called Genome-wide Complex Trait Analysis (GCTA) to get SNP-based heritability for a number of traits (Yang et al., 2010, 2011). Most relevant in terms of the present study, SNP based heritability estimates for BMI have ranged from .14 to .42 (Vattikuti, Guo, & Chow, 2012; Zaitlen et al., 2013) and estimates for alcohol consumption have ranged from .14 to .16 (McGue et al., 2013; Vrieze, McGue, Miller, Hicks, & Iacono, 2013). These estimates are expectedly lower than those from family studies of heritability due to the exclusion of rare or other variants that are poorly tagged by DNA arrays as well as the potential for non-additive genetic effects (Yang et al., 2010). A further limitation of this approach is the large sample size needed to achieve adequate statistical power to estimate the genetic variance explained by SNPs, especially when attempting to attain the genetic correlation between two traits (Visscher et al., 2014). As a result, well established heritabilities and genetic correlations could fail to reach statistical significance in SNP-based estimations. Here, we circumvented this limitation with use of genetic data from the UK Biobank, a large population based sample of adults in the United Kingdom.

In summary, research has demonstrated that there may be a common etiology behind obesity and alcohol use. However, given the seemingly contradictory observational reports relating alcohol use and obesity as well as the recent interest in how these substances might, even competitively, hijack neurobiological systems related to addiction in general (Gearhardt & Corbin, 2009; Kleiner et al., 2004), it is surprising to find little work on the shared genetic etiology of these traits. Additionally, few studies have jointly examined the effect of ‘how much’ versus ‘how often’ one drinks in relation to alcohol’s effect on obesity. Thus, using recent methods that incorporate the conglomerate of genome-wide SNPs and a large sample of adults in the UK, we assessed to what degree the genetic factors that contribute to adult obesity, defined as BMI, also contributed to adult alcohol use. Due to competing findings regarding the relationship between obesity and quantity consumed versus the frequency of consumption, we analyzed these two dimensions of alcohol use separately. Additionally, gender may impact these relationships, and thus we conducted both combined and gender stratified analyses.

Methods

Data: UK Biobank

The UK Biobank includes 500,000 adult volunteers (aged 40–69 years) recruited from the United Kingdom (UK Biobank 2016). Details regarding recruitment and participant follow up can be found elsewhere (Allen et al., 2012; Sudlow et al., 2015). We used a subset of this larger sample, the first released batch of genetic data, that included ~50,000 individuals genotyped on the UK BiLEVE array and another ~100,000 participants that were genotyped on the UK Axiom array (UK Biobank 2016).

Quality Control—Genetic quality control on the data released to us was carried out by the Wellcome Trust Centre for Human Genetics. Details of their quality control procedures can be found at http://www.ukbiobank.ac.uk/wp-content/uploads/2014/04/UKBiobank_genotyping_QC_documentation-web.pdf. Briefly, these steps included excluding individuals that had conflicts between reported and genotypic sex ($n = 191$) or had poor quality samples as defined by low call rate or extreme heterozygosity ($n = 1548$). Problematic SNP positions that exhibited batch effects, deviated from Hardy-Weinberg equilibrium, or had different frequencies on the two arrays were also excluded.

We only used individuals of Caucasian descent. This included individuals that self reported as “British” and whose genetic principal components grouped with CEU populations on the HapMap3 reference panel. Additionally, individuals that self-identified as “Irish” or having “Any other white background” were also included if their first 4 PC scores fell within the range of the UK Biobank’s identified Caucasians. To further control for ethnic stratification we adjusted for UK Biobank’s 15 genetic principal components (*Data Field 22009*).

In addition to the quality control procedures carried out by UK Biobank, we also excluded SNPs with minor allele frequencies less than 1%, per SNP genotyping call rates less than 95%, and deviations from Hardy-Weinburg equilibrium ($p < 0.00001$). Further we removed multi-allelic SNPs or those with duplicate positions. Because closely related individuals may also share more similar environments, we also removed individuals with $\hat{\pi}$ (measure of pairwise genetic relatedness) values $> .05$. After all quality control procedures, we had a total of 120,890 individuals and 535,060 bi-allelic SNPs.

Measures

Individuals were assessed using a touchscreen device. All sample-wide distributions for each specific variable can be accessed through UK Biobank’s Data Showcase (<http://biobank.ctsu.ox.ac.uk/crystal/>) using the noted *Data Field*.

Drinks per week—We computed this measure by summing responses to the following UK Biobank questions:

1. “In an average WEEK, how many pints of beer or cider would you drink? (Include bitter, lager, stout, ale, Guinness)” (*Data Field 1588*),
2. “In an average WEEK, how many glasses of WHITE wine or champagne would you drink? (There are six glasses in an average bottle)” (*Data Field 1578*),

3. “In an average WEEK, how many glasses of RED wine would you drink? (There are six glasses in an average bottle)” (*Data Field 1568*),
4. “In an average WEEK, how many measures of spirits or liqueurs would you drink? (there are 25 standard measures in a normal sized bottle; spirits include drinks such as whisky, gin, rum, vodka, brandy)” (*Data Field 1598*),
5. “In an average WEEK, how many glasses of fortified wine would you drink? (There are 12 glasses in an average bottle) (Fortified wines include drinks such as sherry, port, vermouth)” (*Data Field 1608*),
6. “In an average WEEK, how many glasses of other alcoholic drinks (such as alcopops) would you drink?” (*Data Field 5364*).

The UK Biobank had individuals who reported more than 100 for each question confirm their response and excluded individuals who reported responses less than 0 or greater than 250.

Responses of “Do not know” or “Prefer not to answer” for each type of drink were not included in an individual’s summed response. We excluded individuals with summed responses greater than 100 ($n = 174$). Due to a positively skewed distribution, we added a constant of 1 (to keep individuals reporting 0 total drinks) and log transformed this variable.

Alcohol frequency (Data Field 1558)—Individuals were asked by the touchscreen questionnaire: “About how often do you drink alcohol?” and could respond with, “Never”, “Special occasions only”, “One to three times a month”, “Once or twice a week”, “Three to four times a week” or “Daily or almost daily”. If participants felt that this value varied, they were instructed to give an average over the last year.

We scored this item in terms of increasing frequency with individuals reporting never drinking getting a score of 0 and individuals reporting daily drinking getting a score of 5. Individuals that preferred not to answer this question were excluded from the analysis ($n = 605$). Due to restrictions of the software package used for our genetic analysis, this variable was treated as a quantitative, continuous measure instead of as an ordinal measure.

Obesity (BMI)—We used the UK Biobank’s electrical impedance measure of BMI (*Data Field 23104*) as a continuous measure to assess obesity.

All primary study variables were adjusted for gender (*Data Field 31*), genotype measurement batch (*Data Field 22000*), 15 UK Biobank genetic principal components (*Data Field 22009*), and socioeconomic deprivation (*Data Field 189*) by using the residuals from models that used these adjusted factors to predict the primary variables. Individuals missing genetic data, any of the adjusted factors, or phenotypes of interest were not included in the analysis.

Analyses

Due to the large cohort size, we used the BOLT-REML algorithm implemented in the BOLT-LMM software package to estimate SNP based heritabilities and correlations, because it has

been demonstrated to be more computationally efficient than other variance component methods using restricted maximum likelihood (e.g. GCTA) (Loh 2015). Details regarding this method and comparison to other REML algorithms used in genetic analysis are described elsewhere (Loh 2015). Analyses were first conducted in a combined sample that included both male and female participants and then conducted in subsamples that only included either males or females. In the gender specific analyses, gender was no longer adjusted for in the residualized phenotypes.

We estimated the SNP heritability for drinks per week, drinking frequency, and BMI using the variance component analysis implemented by BOLT-REML and then estimated the SNP correlations between: (1) drinks per week and BMI and (2) drinking frequency and BMI using BOLT-REML's option for multiple traits.

All analyses and quality control were conducted using PLINK v1.90b3.34 (Chang et al., 2015; Purcell & Chang, 2016), R version R 3.2.1 (R Core Team 2015), and BOLT-LMM v2.2 version 1.24.3 (Loh 2015).

Results

Table I lists means and standard deviations for raw scores of BMI, drinks per week, and drinking frequency for the entire sample and for each gender. Males had higher BMIs ($t(113860) = -27.109, p < .0001$), reported more drinks per week ($t(115780) = -94.098, p < .0001$), and drank more frequently than females ($t(115750) = -62.582, p < .0001$).

Table II lists the phenotypic correlations between adjusted variables. Drinking frequency was highly correlated with quantity of weekly drinking. In all analyses (combined, female, and male), higher BMIs were associated with less drinks consumed per week and a lower frequency of drinking. Yet, the phenotypic correlation between frequency of drinking and BMI is stronger than the correlation between drinks per week and BMI (combined male and female: $z = 12.05, p < .001$; females: $z = 7.09, p < .001$; males: $z = 9.09, p < .001$). The inverse relationship between drinking behavior and BMI was also stronger in females than in males for both drinks per week ($z = 20.32, p < .001$) and drinking frequency ($z = 17.18, p < .001$).

SNP heritability estimates for BMI, drinks per week, and drinking frequency are displayed in Figure 1. Gender did not have an impact on SNP heritability estimates for BMI ($t(112909) = .75, p = .46$) or drinks per week ($t(114808) = 1.4907, p = .14$), but females had a higher SNP heritability for frequency of alcohol consumption than males ($t(114788) = 2.98, p = .003$).

Figure 2 displays the inverse relationships between both BMI and number of drinks per week ($t(112603) = -33.73, p < .001$) and between BMI and frequency of drinking ($t(112839) = -117.43, p < .001$). In the combined analysis, the relationship between BMI and frequency of drinking is stronger than that between BMI and drinks per week ($z = 57.57, p < .001$). For both the relationship between BMI and drinks per week ($z = 40.86, p < .001$) and BMI and drinking frequency ($z = 27.29, p < .001$), females had stronger correlations than males.

Discussion

Here we reported on both the phenotypic and genetic relationship between BMI and two measures of alcohol consumption: quantity of drinks per week and frequency of drinking in a large sample of adults from the UK. In correspondence with much of the literature, within a normal range of drinking, the more one drinks (for both frequency and quantity), the lower the BMI (Colditz et al., 1991; Gruchow, Sobocinski, Barboriak, & Scheller, 1985; Hellerstedt, Jeffery, & Murray, 1990). Observed correlations between BMI and the drinking measures were generally low to modest, but stronger for drinking frequency than quantity. Further, when the sample was restricted to males, these correlations weakened. This suggests that the inverse relationship between drinking and BMI may be particularly salient for females.

SNP heritability estimates for BMI and drinking are in line with other reports (McGue et al., 2013; Vattikuti et al., 2012; Vrieze et al., 2013; Zaitlen et al., 2013). However, given the large sample size (and, thus, smaller standard errors), we are more confident in these estimates. Further, genetic correlations mirror on to phenotypic correlations, demonstrating that the genetic factors related to increased alcohol drinking habits are somewhat 'protective' against obesity. This is especially true for the relationship between BMI and drinking frequency, and again, these relationships were stronger for females than for males. At the most rudimentary level, these findings imply that there is some shared genetic etiology between these two behaviors in that the genetic factors or effects that contribute to increased BMI contribute to lower consumption of alcohol. When broken down by gender, we found that this relationship was particularly relevant for females for both drinking quantity and drinking frequency, but may only be relevant for drinking frequency in males. This finding of a stronger relationship between BMI and drinking in females is substantiated in the literature, but reasons for the gender discrepancy remain unclear (Breslow & Smothers, 2005; Colditz et al., 1991; Dallongeville et al., 1998).

However, the major limitation here is that the specific shared genetic factors between BMI and alcohol use are still unknown and, without designs that can experimentally investigate the relationship between these phenotypes, it is difficult to interpret this pattern of correlations. One possibility that could explain the negative phenotypic correlations between drinking behavior and BMI, is that alcohol has a direct effect on obesity such that higher consumption of alcohol induces less weight gain through certain metabolic mechanisms (Lands & Zakhari, 1991; Lieber 1991). Another possibility is that individuals with decreased BMI, for whatever reason including the scenario above, tend to drink more or more often, or vice versa. A third possibility is that there may be a common genetic liability to addiction or overconsumption in that an individual with this liability chooses to either partake in the overconsumption of food or alcohol since both food and alcohol compete for similar neurobiological pathways (Gearhardt & Corbin, 2009; Kleiner et al., 2004) such that choosing one substance reduces the consumption of the other. In all these cases, we would expect a negative phenotypic correlation, but given that this method does not give any insight into the actual genetic factors and biological pathways involved, we are unable to specifically endorse or deny any of these mechanisms based on our reported negative genetic correlations.

Further, the two measures of alcohol use habits we studied, drinking quantity and drinking frequency, are necessarily correlated, though each does capture a unique aspect of alcohol consumption. The drinking quantity measure, which allows assessment of heavier drinking, may capture more problem or addictive dimensions of drinking behavior. In contrast, the drinking frequency measure, in which the maximum level of endorsement is “Daily or almost daily”, may better capture levels of normative or moderate levels of drinking. While we did not observe differences in the heritability of these measures, drinking frequency measures were more strongly correlated with BMI than measures of drinking quantity. There are several reports that tout the health benefits of moderate drinking, and since the drinking frequency measure seems to more adequately capture this dimension of drinking habits, it could be one reason why we see this variable relate more strongly to lowered BMI (Baum-Baicker 1985; German & Walzem, 2000; Nova, Baccan, Veses, Zapatera, & Marcos, 2012) . Further the literature supports the finding that the relationship between quantity of alcohol consumed and BMI may not be linear, such that low to moderate levels of drinking may be related to lower levels of adiposity, while excessive levels of drinking are related to higher levels of adiposity (Lukasiewicz et al., 2005; Sayon-Orea et al., 2011; Wannamethee, Shaper, & Whincup, 2005). Since we did not have any metrics related to problem or very heavy drinking, we focused on a moderate range of drinking behaviors by excluding those reporting very high numbers for drinks per week. Thus, disentangling the complexity of this specific relationship, by dividing our sample into ‘heavy’ versus ‘light’ drinkers or fitting non-linear relationships, was beyond the scope of the present analysis, but is an important consideration when interpreting these results.

Other factors to consider include the fact that BMI and alcohol use could be related to each other in other ways that impact the observed correlations. For example, individuals with higher BMIs would need greater quantities of alcohol to reach equivalent levels of blood alcohol concentration (Gearhardt & Corbin, 2009). Thus, negative phenotypic correlations induced by the scenarios above would be attenuated by relationships such as this. This point may be particularly relevant in the male sample where the phenotypic correlations are particularly low. Additionally, we did not consider the specific type of drink consumed, because subsequent reductions in our sample size would jeopardize our power to get reliable genetic correlations between BMI and alcohol use. However, other reports have demonstrated that the type of alcohol consumed may impact the relationship between alcohol use and adiposity measures (Lukasiewicz et al., 2005; Wannamethee et al., 2005).

Also, BMI may also not be the ideal measure for assessing the relationship between excessive eating and alcohol consumption; other studies have examined the relationship between drinking and, in addition to BMI, waist-hip ratio, waist girth, etc., and have sometimes found contradictory results to those for BMI (Dallongeville et al., 1998). In addition to BMI, we also had data on body fat percentage (*Data Field 23099*). This measure could prove interesting in light of our finding that the correlations between BMI and alcohol use are stronger in females, because women have higher body fat percentages than men. However, our results using this alternative measure of obesity illustrated a similar pattern to that of BMI.

Further, our choice of variables here was based on the convenience of already being collected in a large sample. Measures of alcohol problem use and addiction as well as better indices of food consumption that may better capture addictive or problematic habits would better answer the question of whether there is a common underlying tendency to over consume food and alcohol. For example, a number of studies have both phenotypically and genetically linked certain eating disorders with alcohol dependence or problem use (Krug et al., 2009; Munn-Chernoff et al., 2013; Slane, Burt, & Klump, 2012).

Many of these remaining questions and limitations could be addressed in future analyses that (1) implement longitudinal designs or implicate specific biological pathways to get a better idea of the contributing mechanisms behind our observed and genetic correlations, (2) have even greater sample sizes to reduce the reduction in power as a result of further splitting samples based on type of drink consumed and individual drinking patterns (e.g. 'heavy' versus 'light'), (3) implement methods that can detect the potential for non-linear relationships between drinking and BMI and (4) are phenotyped more specifically, especially in relation to problem alcohol use and food consumption.

In conclusion, from a statistical perspective, alcohol intake quantity and frequency is inversely related to BMI in sample of adults in the UK. Thus, within a normative range of drinking, our results supported previous findings that increased alcohol intake is not related to increased obesity (Colditz et al., 1991b; Gruchow, Sobocinski, Barboriak, & Scheller, 1985; Hellerstedt, Jeffery, & Murray, 1990). However, this relationship is most notably observed in females and for the frequency dimension of alcohol use. Because we had access to a large sample, we were able to further investigate this relationship with the genetic correlation between BMI and alcohol use. Overall, the genetic correlations corroborated our phenotypic findings, demonstrating that some degree of the genetic predisposition to increased alcohol use, especially frequency of use, is related to a genetic predisposition to lower BMI. Though we are unclear of the mechanism(s) at work, being able to confidently establish the relationship between BMI and alcohol use provides a sound framework upon which additional work may elucidate how these two health maladies of consumption may work in concert.

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References

- Allen N, Sudlow C, Downey P, Peakman T, Danesh J, Elliott P, Pell J. UK biobank: Current status and what it means for epidemiology. *Health Policy and Technology*. 2012; 1(3):123–126.
- Baum-Baicker C. The health benefits of moderate alcohol consumption: A review of the literature. *Drug and Alcohol Dependence*. 1985; 15(3):207–227. DOI: 10.1016/0376-8716(85)90001-8 [PubMed: 4028954]

- Breslow RA, Smothers BA. Drinking patterns and body mass index in never smokers: National health interview survey, 1997–2001. *American Journal of Epidemiology*. 2005; 161(4):368–76. DOI: 10.1093/aje/kwi061 [PubMed: 15692081]
- Bulik CM, Sullivan PF, Kendler KS. Genetic and environmental contributions to obesity and binge eating. *Int J Eat Disord*. 2003; 33(3):293–298. DOI: 10.1002/eat.10140 [PubMed: 12655626]
- Chang CC, Chow CC, Tellier LC, Vattikuti S, Purcell SM, Lee JJ. Second-generation PLINK: Rising to the challenge of larger and richer datasets. *Gigascience*. 2015; 4(7)
- Colditz GA, Giovannucci E, Rimm EB, Stampfer MJ, Rosner B, Speizer FE, Willett WC. Alcohol intake in relation to diet and obesity in women and men. *The American Journal of Clinical Nutrition*. 1991; 54(1):49–55. [PubMed: 2058587]
- Dallongeville J, Marecaux N, Ducimetiere P, Ferrieres J, Arveiler D, Bingham A, Amouyel P. Influence of alcohol consumption and various beverages on waist girth and waist-to-hip ratio in a sample of french men and women. *International Journal of Obesity & Related Metabolic Disorders*. 1998; 22(12)
- Duncan AE, Grant JD, Bucholz KK, Madden PA, Heath AC. Relationship between body mass index, alcohol use, and alcohol misuse in a young adult female twin sample. *Journal of Studies on Alcohol and Drugs*. 2009; 70(3):458. [PubMed: 19371498]
- Eisen SA, Lyons MJ, Goldberg J, True WR. The impact of cigarette and alcohol consumption on weight and obesity. An analysis of 1911 monozygotic male twin pairs. *Arch Intern Med*. 1993; 153(21):2457–63. [PubMed: 8215750]
- Gearhardt AN, Corbin WR. Body mass index and alcohol consumption: Family history of alcoholism as a moderator. *Psychology of Addictive Behaviors*. 2009; 23(2):216.doi: 10.1037/a0015011 [PubMed: 19586138]
- German JB, Walzem RL. The health benefits of wine. *Annual Review of Nutrition*. 2000; 20(1):561–593.
- Gruchow HW, Sobocinski KA, Barboriak JJ, Scheller JG. Alcohol consumption, nutrient intake and relative body weight among US adults. *The American Journal of Clinical Nutrition*. 1985; 42(2): 289–295. [PubMed: 4025199]
- Heath AC, Martin NG. Genetic influences on alcohol consumption patterns and problem drinking: Results from the australian NH&MRC twin panel follow-up survey. *Ann N Y Acad Sci*. 1994; 708:72–85. [PubMed: 8154691]
- Hellerstedt WL, Jeffery RW, Murray DM. The association between alcohol intake and adiposity in the general population. *American Journal of Epidemiology*. 1990; 132(4):594–611. [PubMed: 2206044]
- Kleiner KD, Gold MS, Frostpineda K, Lenzbrunsmann B, Perri MG, Jacobs WS. Body mass index and alcohol use. *Journal of Addictive Diseases*. 2004; 23(3):105–118. [PubMed: 15256347]
- Krug I, Pinheiro AP, Bulik C, Jiménez-Murcia S, Granero R, Penelo E, Fernández-Aranda F. Lifetime substance abuse, family history of alcohol abuse/dependence and novelty seeking in eating disorders: Comparison study of eating disorder subgroups. *Psychiatry and Clinical Neurosciences*. 2009; 63(1):82–87. DOI: 10.1111/j.1440-1819.2008.01908.x [PubMed: 19154214]
- Lands WE, Zakhari S. The case of the missing calories. *The American Journal of Clinical Nutrition*. 1991; 54(1):47–48. [PubMed: 2058586]
- Lee SH, Yang J, Goddard ME, Visscher PM, Wray NR. Estimation of pleiotropy between complex diseases using single-nucleotide polymorphism-derived genomic relationships and restricted maximum likelihood. *Bioinformatics*. 2012; 28(19):2540–2. DOI: 10.1093/bioinformatics/bts474 [PubMed: 22843982]
- Lichenstein SD, Jones BL, O'Brien JW, Zezza N, Stiffler S, Holmes B, Hill SY. Familial risk for alcohol dependence and developmental changes in BMI: The moderating influence of addiction and obesity genes. *Pharmacogenomics*. 2014; 15(10):1311–21. DOI: 10.2217/pgs.14.86 [PubMed: 25155933]
- Lieber CS. Perspectives: Do alcohol calories count? *The American Journal of Clinical Nutrition*. 1991; 54(6):976–82. [PubMed: 1957830]

- Loh P-R, Bhatia G, Gusev A, Finucane HK, Bulik-Sullivan BK, Pollack SJ, Kendler KS. Contrasting regional architectures of schizophrenia and other complex diseases using fast variance components analysis. *BioRxiv*. 2015; 016527
- Lukasiewicz E, Mennen LI, Bertrais S, Arnault N, Preziosi P, Galan P, Hercberg S. Alcohol intake in relation to body mass index and waist-to-hip ratio: The importance of type of alcoholic beverage. *Public Health Nutrition*. 2005; 8(03):315–320. [PubMed: 15918929]
- McGue M, Zhang Y, Miller MB, Basu S, Vrieze S, Hicks B, Iacono WG. A genome-wide association study of behavioral disinhibition. *Behavior Genetics*. 2013; 43(5):363–373. [PubMed: 23942779]
- Munn-Chernoff MA, Duncan AE, Grant JD, Wade TD, Agrawal A, Bucholz KK, Heath AC. A twin study of alcohol dependence, binge eating, and compensatory behaviors. *Journal of Studies on Alcohol and Drugs*. 2013; 74(5):664–73. [PubMed: 23948525]
- Nova E, Baccan GC, Veses A, Zapatera B, Marcos A. Potential health benefits of moderate alcohol consumption: Current perspectives in research. *Proceedings of the Nutrition Society*. 2012; 71(02): 307–315. [PubMed: 22391060]
- Purcell & Chang. PLINK v1.90b3.34. 2016. *PLINK v1.90b3.34* [Computer Software]. Retrieved from <https://www.cog-genomics.org/plink2>
- R Core Team. R: A language and environment for statistical computing [Computer Software]. Vienna, Austria: R Foundation for Statistical Computing; 2015. Retrieved from <http://www.R-project.org/>
- Sayon-Orea C, Martinez-Gonzalez MA, Bes-Rastrollo M. Alcohol consumption and body weight: A systematic review. *Nutr Rev*. 2011; 69(8):419–31. DOI: 10.1111/j.1753-4887.2011.00403.x [PubMed: 21790610]
- Slane JD, Burt SA, Klump KL. Bulimic behaviors and alcohol use: Shared genetic influences. *Behavior Genetics*. 2012; 42(4):603–613. [PubMed: 22302528]
- Stunkard AJ, Foch TT, Hrubec Z. A twin study of human obesity. *JAMA*. 1986; 256(1):51–54. DOI: 10.1001/jama.1986.03380010055024 [PubMed: 3712713]
- Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, Landray M. UK biobank: An open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med*. 2015; 12(3):e1001779. [PubMed: 25826379]
- Turkheimer E. Still missing. *Research in Human Development*. 2011; 8(3–4):227–241. DOI: 10.1080/15427609.2011.625321
- UK Biobank. 2016. [Web page]. Retrieved from <http://www.ukbiobank.ac.uk/>
- Vattikuti S, Guo J, Chow CC. Heritability and genetic correlations explained by common snps for metabolic syndrome traits. *PLoS Genet*. 2012; 8(3):e1002637. [PubMed: 22479213]
- Visscher PM, Hemani G, Vinkhuyzen AAE, Chen G-B, Lee SH, Wray NR, Yang J. Statistical power to detect genetic (co)variance of complex traits using SNP data in unrelated samples. *PLOS Genet*. 2014; 10(4):e1004269.doi: 10.1371/journal.pgen.1004269 [PubMed: 24721987]
- Volkow ND, Wise RA. How can drug addiction help us understand obesity? *Nat Neurosci*. 2005; 8(5): 555–60. DOI: 10.1038/nn1452 [PubMed: 15856062]
- Volkow ND, Wang GJ, Fowler JS, Telang F. Overlapping neuronal circuits in addiction and obesity: Evidence of systems pathology. *Philos Trans R Soc Lond B Biol Sci*. 2008; 363(1507):3191–200. DOI: 10.1098/rstb.2008.0107 [PubMed: 18640912]
- Volkow ND, Wang GJ, Fowler JS, Tomasi D, Baler R. Food and drug reward: Overlapping circuits in human obesity and addiction. *Curr Top Behav Neurosci*. 2012; 11:1–24. DOI: 10.1007/7854_2011_169 [PubMed: 22016109]
- Vrieze SI, McGue M, Miller MB, Hicks BM, Iacono WG. Three mutually informative ways to understand the genetic relationships among behavioral disinhibition, alcohol use, drug use, nicotine use/dependence, and their co-occurrence: Twin biometry, GCTA, and genome-wide scoring. *Behavior Genetics*. 2013; 43(2):97–107. [PubMed: 23362009]
- Wannamethee SG, Shaper AG, Whincup PH. Alcohol and adiposity: Effects of quantity and type of drink and time relation with meals. *Int J Obes Relat Metab Disord*. 2005; 29(12):1436–1444. DOI: 10.1038/sj.ijo.0803034
- Whitfield JB, Zhu G, Madden PA, Neale MC, Heath AC, Martin NG. The genetics of alcohol intake and of alcohol dependence. *Alcoholism: Clinical & Experimental Research*. 2004; 28(8):1153–1160. DOI: 10.1097/01.ALC.0000134221.32773.69

- World, HH. Obesity: Preventing and managing the global epidemic. Geneva: World Health Organization; 2000.
- World, HH. The world health report 2002: Reducing risks, promoting healthy life. Geneva: World Health Organization; 2002.
- Yang J, Benyamin B, McEvoy BP, Gordon S, Henders AK, Nyholt DR, Visscher PM. Common snps explain a large proportion of the heritability for human height. *Nat Genet.* 2010; 42(7):565–9. DOI: 10.1038/ng.608 [PubMed: 20562875]
- Yang J, Manolio TA, Pasquale LR, Boerwinkle E, Caporaso N, Cunningham JM, Visscher PM. Genome partitioning of genetic variation for complex traits using common snps. *Nat Genet.* 2011; 43(6):519–25. DOI: 10.1038/ng.823 [PubMed: 21552263]
- Yeomans MR. Alcohol, appetite and energy balance: Is alcohol intake a risk factor for obesity? *Physiology & Behavior.* 2010; 100(1):82–89. DOI: 10.1016/j.physbeh.2010.01.012 [PubMed: 20096714]
- Zaitlen N, Kraft P, Patterson N, Pasaniuc B, Bhatia G, Pollack S, Price AL. Using extended genealogy to estimate components of heritability for 23 quantitative and dichotomous traits. *PLoS Genet.* 2013; 9(5):e1003520. [PubMed: 23737753]

Figure 1. SNP heritability (SNP h^2) estimates for BMI, drinks per week, and drinking frequency for the combined sample, females, and males.

Figure 2. Correlations due to SNPs (r_{g-SNP}) between BMI and drinks per week and BMI and drinking frequency. Correlations are displayed in the combined sample, females, and males.

Table 1

Descriptive statistics for raw scores of BMI, drinks per week, and drinking frequency

	Combined		Females		Males	
	n	M (SD)	n	M (SD)	n	M (SD)
BMI	113,864	27.52 (4.80)	60,070	27.16 (5.19)	53,794	27.93 (4.29)
Drinks per week	115,777	8.50 (10.14)	61,026	5.94 (7.62)	54,751	11.35 (11.72)
Drinking frequency	115,756	3.13 (1.50)	60,991	2.87 (1.53)	54,765	3.41 (1.41)

Table II

Phenotypic correlations (*r*) between BMI and drinking measures

	Combined		Females		Males		
	n	r	p	n	r	p	p
BMI – Drinks per week	113,668	-.08	< .001	59,995	-.13	< .001	.02
BMI – Drinking frequency	113,650	-.13	< .001	59,962	-.17	< .001	< .001
Drinks per week – Drinking frequency	115,555	.88	< .001	60,914	.88	< .001	< .001