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Measuring spatial and temporal trends of nicotine and alcohol consumption in Australia using wastewater-based epidemiology

Foon Yin Lai^{a,b,*}, Coral Gartner^c, Wayne Hall^d, Steve Carter^e, Jake O'Brien^a, Benjamin J. Tscharke^a, Frederic Been^b, Cobus Gerber^f, Jason White^f, Phong Thai^g, Raimondo Bruno^h, Jeremy Prichardⁱ, K. Paul Kirkbride^j, Jochen F. Mueller^a

- a. The University of Queensland, Queensland Alliance for Environmental Health Sciences (QAEHS), formerly National Research Centre for Environmental Toxicology (Entox), 39 Kessels Road, Coopers Plains, QLD 4108, Australia.
- b. Toxicological Centre, Department of Pharmaceutical Sciences, University of Antwerp, 2610
 Wilirjk, Antwerp, Belgium.
- c. The University of Queensland, School of Public Health, Herston Road, Herston, QLD 4006, Australia.
- d. The University of Queensland, Centre for Clinical Research, Brisbane, QLD 4000, Australia
- e. Queensland Health Forensic Scientific Services (QHFSS), Queensland Government, 39 Kessels Road, Coopers Plains, QLD 4108, Australia.
- f. School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, SA 5000, Australia.
- g. School of Chemistry, Physics and Mechanical Engineering, Queensland University of Technology, Brisbane, QLD 4001, Australia.
- h. School of Psychology, University of Tasmania, Hobart, TAS 7001, Australia.
- i. Faculty of Law, University of Tasmania, Hobart, TAS 7001, Australia.
- j. School of Chemical and Physical Sciences, Flinders University, Adelaide, SA 5001, Australia.

*Corresponding author: Dr. Foon Yin Lai (<u>foonyin.lai@uantwerpen.be; foon.lai@uqconnect.edu.au</u>), Toxicological Centre, Department of Pharmaceutical Sciences, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium. Telephone no.: +32-3-265 2498. Fax no.: +32-3-265 2722.

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Abstract

Background and aims: Tobacco and alcohol consumption remain priority public health issues worldwide. As participation in population-based surveys has fallen, it is increasingly challenging to estimate accurately the prevalence of alcohol and tobacco use. Wastewater-based epidemiology (WBE) is an alternative approach for estimating substance use at the population level that does not rely on survey participation. This study examined spatio-temporal patterns in nicotine (a proxy for tobacco) and alcohol consumption in the Australian population via WBE.

Methods: Daily wastewater samples (n=164) were collected at 18 selected wastewater treatment plants across Australia, covering approximately 45% of the total population. Nicotine and alcohol metabolites in the samples were measured using liquid chromatography-tandem mass spectrometry. Daily consumption of nicotine and alcohol and its associated uncertainty were computed using Monte Carlo simulations. Nationwide daily average and weekly consumption of these two substances were extrapolated using ordinary least squares and mixed effect models.

Findings: Nicotine and alcohol consumption was observed in all communities. Consumption of these substances in rural towns was three-to-four times higher than in urban communities. The spatial consumption pattern of these substances was consistent across the monitoring periods in 2014-2015. Nicotine metabolites significantly reduced by 14-25% (p=0.001-0.008) (2014-2015) in some catchments. Alcohol consumption remained constant over the studied periods. Strong weekly consumption patterns were observed for alcohol but not nicotine. Nationwide, the daily average consumption per person (aged 15-79 years) was estimated at about 2.5 cigarettes and 1.3-2.0 standard drinks (weekday-weekend) of alcohol. These estimates were close to the sale figure and apparent consumption respectively.

Conclusions: Wastewater-based epidemiology is a feasible method for objectively evaluating the geographic, temporal and weekly profiles of nicotine and alcohol consumption in different communities nationally.

Keywords: Tobacco, alcohol, cigarettes, ethyl sulfate, cotinine, hydroxycotinine, LC-MS/MS

INTRODUCTION

Globally, tobacco and alcohol use are major public health issues; consumption of both is associated with substantial social, health and economic burden [1, 2]. In 2004-05, tobacco smoking and alcohol drinking were estimated to cost \$46.8 billion in Australia in treatment of tobacco and alcohol-related diseases, lost workforce productivity, alcohol-related road collisions and alcohol-related crime (e.g. violence) [3, 4]. This was about six times higher than the estimated costs due to illicit drug use [3, 4].

The prevalence of tobacco and alcohol use varies across demographic and socio-economic groups and geographically [5]. Spatial information on the use of these substances over time can help determine if all communities are responding similarly to whole-of-population interventions (e.g. taxation increases). It could also evaluate the effects of local interventions (e.g. state-based mass-media campaigns) by comparing trends between communities located inside and outside the geographic areas receiving interventions. Spatial and temporal monitoring data on tobacco and alcohol use at the population level are essential to evaluate the impact of public strategies to reduce the harms associated with both of these substances.

Current estimates of the prevalence of alcohol and tobacco use in communities mainly rely on selfreported data collected in household surveys. In Australia, for instance, the National Drug Strategy Household Survey (NDSHS) and the National Health Survey are the main sources of national statistics on tobacco and alcohol use [5]. These surveys are conducted every three years and their data are combined with other indicators, such as tobacco and alcohol excise data, to provide a picture of the overall level of use of these substances in the population. National survey data collection and processing is expensive, often takes several months to be completed and for these reasons surveys are only conducted every three years in Australia [5]. There is a time lag in reporting data from these surveys (e.g. of 12 months) and they provide low spatial and temporal resolution. This makes it difficult to perform a timely evaluation of changes in the usage patterns of these substances in the community and to examine differences in use between communities. Declining response rates in population surveys also make these estimates potentially less representative of the overall population if, as is likely, respondents differ from non-respondents in their patterns of use (e.g. if heavy drinkers or smokers are less likely to complete surveys than light drinkers or non-smokers) [5]. Smoking is also becoming increasingly concentrated in population groups that have low participation rates in general population surveys (e.g. people who are of lower socio-economic status, live in rural and remote areas, are homeless, have mental illnesses, and come from culturally and linguistically diverse populations) [6, 7]. Recall bias is also a limitation in surveys because respondents often underestimate their personal consumption of alcohol and tobacco [8].

Over the last decade, wastewater-based epidemiology (WBE) has become an established method to objectively estimate illicit drug use at the population level [9-11]. This approach has recently been extended to estimate population alcohol and tobacco consumption. Measures of the ethanol metabolite (ethyl sulfate) were used to estimate alcohol consumption for the first time in the Norwegian population [12] and a recent WBE study reported spatial patterns of alcohol consumption across 20 cities in 11 countries [13]. Other studies have been conducted in Belgium, Greece, Italy and Spain [14-19].

The feasibility of estimating tobacco consumption was first demonstrated in the Italian population [20] through an analysis of nicotine metabolites (cotinine and trans-3'-hydroxycotinine) in wastewater. Nicotine absorption was estimated and cigarette consumption calculated based on the average absorption of nicotine from tobacco cigarettes [20]. The approach has now been applied in Belgium, China, Czech and Slovak Republics, Portugal and Spain [21-25]. Publications to date have mainly concentrated on European communities. Given that both tobacco and alcohol are the most widely used psychoactive substances in many developed societies, and given their contribution to global disease burden [1, 2], simultaneous assessment of both substances will allow a better characterisation of population health.

The overall objective of our study was to investigate the spatio-temporal profile of tobacco and alcohol consumption in Australia by analysing metabolites of the two target substances (nicotine and ethanol) in raw wastewater samples obtained from 18 catchments in Australia. The total population size contributing to the wastewater samples is estimated to be 45% of the Australian population. Specifically, this study aimed to (a) evaluate the quantity of nicotine, its cigarette equivalent, and alcohol consumed per 1000 population; (b) examine the spatial and temporal patterns of use across different communities; (c) compare the WBE results with epidemiological data contained in the NDSHS

survey, sale data of tobacco and apparent alcohol consumption record; and (d) extrapolate the nationwide average daily consumption of these substances using linear regression models.

METHODS

Wastewater collection

This study included 18 wastewater treatment plants (WWTPs) across two territories and five states in Australia: Queensland (QLD), New South Wales (NSW), the Australian Capital Territory (ACT), Victoria (VIC), South Australia (SA), Western Australia (WA), and the Northern Territory (NT) (see details in the Supporting Information). Sixteen WWTPs were linked to major cities [26]; seven of these serviced >500,000 inhabitants, five serviced 150,000-500,000 inhabitants, and four serviced <150,000 inhabitants. Three WWTPs were in regional and rural towns [26] which serviced <150,000 inhabitants. The sum of the estimated catchment populations equated to approximately 45% of the Australian population (24 million).

The sampling program was conducted over a week in March-April 2014 at six WWTPs and March-May in 2015 at 18 WWTPs. Over the sampling week, no special large events (e.g. holidays or festivals) were scheduled in the sampled catchments, with the exception of one weekend event in NSW-A. We provided a sampling protocol to the WWTP staff to collect twenty-four hour composite samples that were frozen until analysis.

The sampling schemes (see details in Supporting Information) were appraised in our study for monitoring Australia-wide illicit drug consumption to have a modest sampling uncertainty of 5-20% [27]. Substances with high prevalence of consumption in the general population (e.g. tobacco and alcohol use) lead to higher concentrations and less short-term variations in the concentration of its biomarker(s) in wastewater. Thus, lower sampling errors are expected compared to substances with low prevalence substances [28, 29]. Thus, the applied sampling schemes were deemed adequate for a representative assessment of tobacco and alcohol consumption in the communities under study.

Chemical analysis

The analytical method used to measure the excreted metabolites of nicotine (i.e., cotinine and trans-3'-hydroxycotinine) and ethanol (i.e., ethyl sulfate) were adopted from the validated methods in the literature [12, 20] and previously applied [13]. Direct injection method (i.e. no sample extractions) was applied for all the samples, except for those from SA. Briefly, prior to instrumental analysis, samples were filtered and spiked with the related deuterated mass-labelled internal standards (IS, cotinine-D3 and ethyl sulfate-D5) which compensate for potential instrumental variations and matrix effects during analysis. Together with the calibration solutions at different concentrations (0.5-50 μ g/L; IS 10 μ g/L), the target analytes in the samples were identified and quantified using liquid-chromatography coupled with tandem-mass-spectrometry. For the SA samples, solid-phase extraction was used to enrich the concentrations of the target analyte (only cotinine) followed by instrumental analysis. Details of the analytical methods are reported in Supporting Information and Table S1.

Estimation of daily consumption

The estimation and the associated uncertainty were computed using Monte Carlo simulations with different parameters (Table S2) similar to the practice in other related studies [13, 22, 30] based on the established equation: (concentrations × wastewater volumes) × excretion rates ÷ catchment populations. Two major steps of the back-estimation were included: (a) obtaining the average daily mass load (mg/day) of the metabolite by multiplying its measured concentration with the daily total wastewater volume; and (b) extrapolating to population-normalised consumption (mg/day/1000 people) based on the mass load, average excretion rate (Table S2) and molecular weight ratio of the parent substance to its metabolite [12, 20]. Catchment populations and daily wastewater volume were provided by WWTP personnel. Alcohol consumption was estimated from ethyl sulfate [12]. Both cotinine and trans-3'-hydroxycotinine were used to estimate nicotine consumption. The resulting estimate was used to estimate the equivalent number of cigarettes smoked based on an average of 0.9±0.15 mg of nicotine per cigarette [20, 22] (Table S2). Daily consumption figures were estimated from log-transformed data to account for skewness. Given our undertaking to preserve anonymity of the four individual SA WWTPs, data were reported as the population weighted average for SA.

Extrapolation to nationwide estimates

Nationwide figures of nicotine-equivalent cigarette consumption were estimated using ordinary least square models because no week day effects were expected. Nationwide alcohol consumption was estimated using mixed effect models to account for higher figures during weekends compared to weekdays. Various functions were tested including linear, square root, quadratic, cubic, fractional polynomials and cubic splines (Table S3). Data were log-transformed to correct for heteroscedasticity. The estimated amount of substance consumed on each day was used as the response variable, whilst population size was used as the predictor. For mixed effects models, the day of the week (Monday-Friday) was included as an additional random predictor variable, following an approach previously used to estimate nationwide illicit drug consumption in Switzerland and Germany [30]. Model performances were assessed using the root-mean-square error (RMSE) and the adjusted coefficient of determination (R²) (Table S3). Leave-one-out cross-validation was used to assess the performances of the tested models, which were selected based on root-mean-square error (RMSE) and the adjusted coefficient of determination (R2) (Table S3). The best model, showing the smallest RMSE and largest R^2 , was then used to extrapolate nationwide estimates. The populations of other Australian catchments [31] which were not included in this study were fed into the model to compute daily consumption estimates. These estimates (from about 55% of the Australian population) were then summed with those results obtained from this study (from about 45% of the Australian population) for the final national level. The statistical tests, ordinary least squares and mixed effect models were performed using R software.

RESULTS

Spatial examination. In 2015, the average estimated daily quantity of nicotine consumed across the 15 Australian communities ranged from 750 to 3020 mg which was equivalent to 850-3400 cigarettes per 1000 people (Table 1). Two (NT-A and QLD-D) out of three rural towns had the highest estimated consumption of cigarettes (3400 and 3020/day/1000 people, respectively) (Table 1 and Fig. 1A). In contrast, the three large cities (NSW-B, C and D) in NSW showed the lowest nicotine consumption, equivalent to cigarettes of 1360, 850 and 890/day/1000 people respectively (Table 1 and Fig. 1A). Nicotine consumption in rural towns was up to four times that observed in the urban communities. The

average amount of nicotine consumed in the cities of WA, SA and VIC-A was around the median among all the communities.

The average estimated daily consumption of alcohol across the communities in 2015 ranged from approximately 7 to 24 L per 1000 people (Table 1). The two studied communities in NT had the highest estimated alcohol consumption (Table 1; Fig. 1B). Also, the usage in most of the monitoring days (26-37 (NT-A) and 29-43 (NT-B) mL/day/person) exceeded the guideline threshold (regular basis) of alcohol drinking recommended by the World Health Organisation (WHO) (30 mL/day/person) [2] and the National Health and Medical Research Council (NHMRC) in Australia (25 mL/day/person, i.e., 2 standard drinks) [32]. The lowest estimated alcohol consumption was observed in the large cities in WA and NSW (< 10 L/day/1000 people). The difference (median) among the studied geographical areas was about 3.8 times (the highest of 25 L/day/1000 people in NT-A vs. the lowest of 7 L/day/1000 people in NSW-A). The extent of the spatial variation in alcohol consumption was up to about three-fold between rural towns and urban communities in Australia. The urban communities, VIC-B and ACT, were ranked around the median alcohol consumption among all these sites.

Temporal assessment. The six selected sites in 2014 revealed a very similar ranking of nicotine consumption compared to 2015, but varied in the amount of usage between the two years (Figs. 1C & 1D). Four urban communities (QLD-A, VIC-B, SA, ACT) showed significant (p=0.001-0.008) reductions in nicotine/cigarette consumption in 2015 by 14%, 19%, 12% and 25%, respectively (Fig. 1C). This was also observed for the rural site (QLD-C) but the reduction (11%) did not meet criteria for statistical significance. There was a small increase (p=0.035) of 7% in nicotine/cigarette consumption in one urban community (VIC-A) in 2015. These five communities showed similar patterns and levels of alcohol consumption between the two years (Fig. 1D).

Weekly patterns. There was no distinct weekly pattern in nicotine consumption across the Australian communities studied (Fig. 2A). The daily consumption of nicotine in all studied communities was approximately 15% (median) of the weekly total (Fig. 2A). By contrast, all studied communities showed a higher consumption of alcohol on weekends than weekdays (Table S4). The increase in estimated

alcohol consumption was up to twice as high during weekends, particularly in the urban communities of QLD-B, NSW-A, NT-B and VIC-B (Table S4). Overall, the consumption of alcohol between Tuesdays and Thursdays (the trough of the week) accounted for about 11% (median) of the weekly consumption (Fig. 2B). Consumption of alcohol began to increase from Friday which accounted for an estimated 13% of the weekly use. It rose on Saturday to an estimated 18% of weekly consumption and peaked on Sundays which represented about 20% of weekly consumption, twice the midweek trough (Fig. 2B).

Elevated consumption of nicotine and alcohol in NSW-A observed on the weekend (Sunday) coincided with a large public event in the catchment. Alcohol consumption (36 mL pure ethanol/day/person; Fig. 1B) on that day was greater than the WHO and NHMRC recommended guidelines for a regular basis but remained below the NHMRC threshold for a single occasion of drinking (50 mL pure ethanol/day/person, i.e., four standard drinks) [32].

Nationwide estimates. Ordinary least squares regression using a square root function was the best fitting model for the estimation of nationwide nicotine consumption (Fig. 3A; Table S3). Based on the model, the average nationwide daily consumption of nicotine was estimated to be 38-41 kg which corresponds to approximately 43-46 million cigarettes (Table 2). This suggested the consumption of about 2.10-2.23 mg of nicotine (2.37-2.52 cigarettes) per day per capita among persons aged 15-79 years (Table 2).

A mixed effect model with a square root function was the best fitting model for estimating nationwide alcohol consumption based on catchment size and each week day (Fig. 3B; Table S3). This model took differences in consumption between weekdays and weekends into account and nationwide average daily consumption was estimated to be 280,000-442,000 L of pure ethanol depending on the week day (Table 2), and the total weekly consumption was estimated at 2.42 ML pure ethanol. This represents about 16-25 mL of pure ethanol (1.3-2.0 standard drinks; one standard drink of 12.5 mL) consumed per day per capita among persons aged 15-79 years (Table 2).

Discussion

In this study, we launched a national monitoring campaign to explore nicotine and alcohol consumption by measuring their excreted metabolites in wastewater samples from communities covering approximately 45% of the Australian population. Our results revealed a clear spatial and temporal pattern of these two substances across the country.

The patterns observed in this WBE study overall (higher levels of cigarette smoking and alcohol consumption in rural areas than urban communities) were very similar to those reported from the NDSHS [32] with the important difference that we observed a greater difference in consumption between rural and urban communities: approximately two-fold in the NDSHS compared to three-fold in WBE estimates for nicotine/cigarette consumption, and two-fold in the NDSHS and four-fold in the WBE for alcohol consumption. The potential reasons for these differences could be that the studied sites may not be representative of all rural areas or the < 50% response rate may mean that the NDSHS data are not be fully representative of the population.

The data showed that the two NT communities were among the highest estimated nicotine consumption of all locations tested, with a daily average equivalent of about three cigarettes per capita. This is also consistent with the NDSHS report [5] that found the NT had the highest proportion of daily smokers in Australia in 2010 and 2013. The lowest daily smoking prevalence estimated by the NDSHS was in the ACT [5]. This agrees with our WBE finding of about one cigarette per capita. Furthermore, both the NDSHS and WBE revealed that among the jurisdictions in Australia, the NT's communities had the greatest alcohol consumption whereas the communities in NSW and VIC had the lowest alcohol consumption. The results demonstrate broad consistency between the two methods for assessing the spatial pattern of cigarette and alcohol consumption.

As expected, the weekly pattern of consumption differed between nicotine and alcohol. Nicotine was relatively stable throughout the week while alcohol consumption was higher on weekends than weekdays. Most cigarette users are nicotine addicted and therefore smoke daily to avoid withdrawal symptoms, whereas the proportion of alcohol drinkers who are dependent on alcohol is much lower. Both substances showed elevated consumption in NSW-A during an event on the weekend, suggesting

the recreational consumption of these substances. This finding highlights the high-resolution of WBE data, which can potentially identify daily consumption changes within a community.

In 2010, the Australian Government introduced annual increases in the tobacco excise tax. A further series of four annual tobacco tax increases was announced in November 2013 [33]. The first of these in December 2013 increased the tobacco tax by 12.5%; and the remaining increases applied in September each year since. Our WBE data revealed that nicotine consumption in 2015 was significantly less than in 2014 in five out of six communities (Fig. 1C), including four urban communities and one rural town. This result confirms that tobacco use was declining across Australia in different settings, consistent with the expected impact of increased tobacco taxation during this time period. These findings demonstrate the utility of WBE in detecting changes in the consumption of nicotine in response to public health strategies, something that is more difficult to do using three-yearly household survey data. The increase in nicotine consumption in the urban community VIC-A observed (Fig. 1C) against the prevailing downward trend may be worth further study.

In contrast to nicotine consumption, the six selected communities showed similar pattern and level of alcohol consumption between the two years (Fig. 1D). Unlike tobacco, there was no specific national alcohol-related policies (such as changes in taxation) implemented between the two years.

In 2015, an estimated 16.2 billion cigarettes were sold in Australia [34], which was equivalent to 2.5 cigarettes sold each day per capita aged 15-79 years. This amount is similar to the study estimate of nationwide daily average consumption of cigarettes (Table 2), suggesting that the legal supply of cigarette is very similar to the cigarette demand estimated using WBE.

In 2015, 183 ML of pure ethanol was recorded as the apparent yearly consumption of alcohol in Australia [35]. This corresponds to a daily use of about 26 mL pure ethanol per capita aged +15 years. Our estimates, especially the weekend, were similar to the 2015 ABS-reported level of alcohol consumption (Table 2). The apparent consumption record is based on the amount of alcohol available for consumption, excise, import and sales [35]. Thus, the difference between the recorded apparent consumption and the estimated daily average consumption in this study likely reflects the fact that some alcohol is stored, disposed of or used in cooking.

Interpretation of our results should be mindful of some minor uncertainties. First, the small average excretion of ethyl sulfate induces a large correction factor for estimation of alcohol use [12]. This uncertainty could be, however, reduced by high prevalence of alcohol use in the studied populations that will lead to smaller deviations from the mean excretion [36, 37]. There is a need for human pharmacokinetic studies of alcohol excretion because only one article provided these data [38]. Nevertheless, the observed profiles in this study and another international comparison study [13] imply that the average excretion fraction of alcohol used for WBE approach remains valid in catchment areas with large populations. Second, there could be an uncertainty related to the stability of the target metabolites in wastewater. They have shown stable in wastewater, i.e. over sample collections and storages but in-sewer field experiments may help to understand the stability of these metabolites and provide better estimates in future studies. Third, our wastewater samples did not come from a random sample of all communities in Australia. Our model was constructed with more samples from urban areas where the usage was lower than rural sites so we could have under-estimated national consumption. The inclusion of more rural communities in future studies may improve estimation. Nevertheless, the WWTPs included have a good balance between large/small and urban/rural catchments across the whole of Australia for this study. This provided the basis for extrapolation to nationwide figures about nicotine and alcohol use. Lastly, our results based on the monitoring across a week may not be representative of consumption over the year during which usage may vary seasonally as it does with illicit drugs [39]. Nevertheless, the uncertainties remain minor since the obtained national figures in this study were consistent with survey and sale data. Our data are deemed to provide a reasonable estimate of average consumption and patterns of nicotine and alcohol use across the country.

Conclusions

The results of the WBE on 45% of Australians demonstrated the feasibility of using wastewater analysis to estimate alcohol and tobacco consumption in the national population. It also provides support for the validity of these data in showing variations in space and time in the consumption of both substances that is broadly consistent with patterns in three yearly household surveys. The observed high consumption of these substances in particular communities may suggest a need of public health responses to promote healthier lifestyles in these populations. The decline in nicotine metabolites shows the potential use of WBE in measuring the impact of taxation strategies on tobacco use. This suggests that WBE can assist governments to evaluate policies to reduce the consumption of alcohol and tobacco and their related public health harms.

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References

- 1. World Health Organization, World Health Organization Global Report: Mortality Attributable To Tobacco. 2012.
- 2. World Health Organization, Global status report on alcohol and health. 2014.
- 3. Collins, D.J. and Lapsley, H.M., The costs of tobacco, alcohol and illicit drug abuse to Australian society in 2004/05. National Drug Strategy, 2008. Australian Government.
- 4. Reitsma, M.B., Fullman, N., Ng, M., Salama, J.S., Abajobir, A., Abate, K.H., *et al.*, Smoking prevalence and attributable disease burden in 195 countries and territories, 1990-2015: a systematic analysis from the Global Burden of Disease Study 2015. The Lancet. 389(10082): p. 1885-1906.
- 5. AIHW, Australian Institute of Health and Welfare (AIHW) 2016. Canberra: AIHW., 2016. http://www.aihw.gov.au/alcohol-and-other-drugs/data-sources/ndshs-2016/key-findings/.
- 6. Stockwell, T., Zhao, J., Greenfield, T., Li, J., Livingston, M., and Meng, Y., Estimating under- and over-reporting of drinking in national surveys of alcohol consumption: identification of consistent biases across four English-speaking countries. Addiction, 2016. 111(7): p. 1203-1213.
- 7. Gallus, S., Tramacere, I., Boffetta, P., Fernandez, E., Rossi, S., Zuccaro, P., *et al.*, Temporal changes of under-reporting of cigarette consumption in population-based studies. Tobacco Control, 2011. 20(1): p. 34-39.
- 8. Livingston, M. and Callinan, S., Underreporting in Alcohol Surveys: Whose Drinking Is Underestimated? Journal of Studies on Alcohol and Drugs, 2015. 76(1): p. 158-164.
- 9. Hernández, F., Castiglioni, S., Covaci, A., de Voogt, P., Emke, E., Kasprzyk-Hordern, B., *et al.*, Mass spectrometric strategies for the investigation of biomarkers of illicit drug use in wastewater. Mass Spectrometry Reviews, 2016: p. n/a-n/a.
- 10. Ort, C., van Nuijs, A.L.N., Berset, J.-D., Bijlsma, L., Castiglioni, S., Covaci, A., *et al.*, Spatial differences and temporal changes in illicit drug use in Europe quantified by wastewater analysis. Addiction, 2014. 109(8): p. 1338-52.
- 11. EMCDDA, <u>http://www.emcdda.europa.eu/publications/insights/assessing-drugs-in-</u> <u>wastewater</u>. Assessing illicit drugs in wastewater: advances in wastewater-based drug epidemiology, 2016.
- 12. Reid, M.J., Langford, K.H., Mørland, J., and Thomas, K.V., Analysis and Interpretation of Specific Ethanol Metabolites, Ethyl Sulfate, and Ethyl Glucuronide in Sewage Effluent for the Quantitative Measurement of Regional Alcohol Consumption. Alcohol Clin Exp Res, 2011. 35(9): p. 1593-1599.
- 13. Ryu, Y., Barceló, D., Barron, L.P., Bijlsma, L., Castiglioni, S., de Voogt, P., *et al.*, Comparative measurement and quantitative risk assessment of alcohol consumption through wastewater-based epidemiology: An international study in 20 cities. Sci Total Environ, 2016. 565: p. 977-83.
- 14. Boogaerts, T., Covaci, A., Kinyua, J., Neels, H., and van Nuijs, A.L.N., Spatial and temporal trends in alcohol consumption in Belgian cities: A wastewater-based approach. Drug and Alcohol Dependence, 2016. 160: p. 170-176.
- 15. Rodríguez-Álvarez, T., Rodil, R., Cela, R., and Quintana, J.B., Ion-pair reversed-phase liquid chromatography–quadrupole-time-of-flight and triple-quadrupole–mass spectrometry determination of ethyl sulfate in wastewater for alcohol consumption tracing. J Chromatogr A, 2014. 1328: p. 35-42.
- 16. Mastroianni, N., Lopez de Alda, M., and Barcelo, D., Analysis of ethyl sulfate in raw wastewater for estimation of alcohol consumption and its correlation with drugs of abuse in the city of Barcelona. J Chromatogr A, 2014. 1360: p. 93-99.
- 17. Andrés-Costa, M.J., Escrivá, Ú., Andreu, V., and Picó, Y., Estimation of alcohol consumption during "Fallas" festivity in the wastewater of Valencia city (Spain) using ethyl sulfate as a biomarker. Sci Total Environ, 2016. 541: p. 616-622.

- 18. Rodríguez-Álvarez, T., Racamonde, I., González-Mariño, I., Borsotti, A., Rodil, R., Rodríguez, I., *et al.*, Alcohol and cocaine co-consumption in two European cities assessed by wastewater analysis. Sci Total Environ, 2015. 536: p. 91-98.
- 19. Gatidou, G., Kinyua, J., van Nuijs, A.L.N., Gracia-Lor, E., Castiglioni, S., Covaci, A., *et al.*, Drugs of abuse and alcohol consumption among different groups of population on the Greek Island of Lesvos through sewage-based epidemiology. Science of The Total Environment, 2016. 563–564: p. 633-640.
- 20. Castiglioni, S., Senta, I., Borsotti, A., Davoli, E., and Zuccato, E., A novel approach for monitoring tobacco use in local communities by wastewater analysis. Tob Control, 2014: p. doi:10.1136.
- 21. van Wel, J.H.P., Gracia-Lor, E., van Nuijs, A.L.N., Kinyua, J., Salvatore, S., Castiglioni, S., *et al.*, Investigation of agreement between wastewater-based epidemiology and survey data on alcohol and nicotine use in a community. Drug Alcohol Depend, 2016. 162: p. 170-5.
- 22. Wang, D.-G., Dong, Q.-Q., Du, J., Yang, S., Zhang, Y.-J., Na, G.-S., *et al.*, Using Monte Carlo simulation to assess variability and uncertainty of tobacco consumption in a city by sewage epidemiology. BMJ Open, 2016. 6(2).
- 23. Mackulak, T., Birošová, L., Grabic, R., Škubák, J., and Bodík, I., National monitoring of nicotine use in Czech and Slovak Republic based on wastewater analysis. Environmental Science and Pollution Research, 2015. 22(18): p. 14000-14006.
- 24. Rodríguez-Álvarez, T., Rodil, R., Rico, M., Cela, R., and Quintana, J.B., Assessment of local tobacco consumption by liquid chromatography-tandem mass spectrometry sewage analysis of nicotine and its metabolites, cotinine and trans-3'-hydroxycotinine, after enzymatic deconjugation. Anal Chem, 2014. 86(20): p. 10274-81.
- 25. Lopes, A., Silva, N., Bronze, M.R., Ferreira, J., and Morais, J., Analysis of cocaine and nicotine metabolites in wastewater by liquid chromatography–tandem mass spectrometry. Cross abuse index patterns on a major community. Sci Total Environ, 2014. 487: p. 673-680.
- 26. ABS, Australian Standard Geographical Classification (ASGC). Australian Bureau of Statistics (ABS), 2011.
- 27. Lai, F.Y., O'Brien, J., Bruno, R., Hall, W., Prichard, J., Kirkbride, P., *et al.*, Spatial variations in the consumption of illicit stimulant drugs across Australia: A nationwide application of wastewater-based epidemiology. Science of The Total Environment, 2016. 568: p. 810-818.
- 28. Ort, C., Lawrence, M.G., Reungoat, J., and Mueller, J.F., Sampling for PPCPs in wastewater systems: comparison of different sampling modes and optimization strategies. Environ. Sci. Technol. , 2010. 44: p. 6289-6296.
- 29. Castiglioni, S., Thomas, K.V., Kasprzyk-Hordern, B., Vandam, L., and Griffiths, P., Testing wastewater to detect illicit drugs: state of the art, potential and research needs. Sci Total Environ, 2014. 487: p. 613-20.
- 30. Been, F., Bijlsma, L., Benaglia, L., Berset, J.-D., Botero-Coy, A.M., Castiglioni, S., *et al.*, Assessing geographical differences in illicit drug consumption-A comparison of results from epidemiological and wastewater data in Germany and Switzerland. Drug Alcohol Depend, 2016. 161: p. 189-199.
- 31. Australian Bureau of Statistics (ABS). 3235.0 Population by Age and Sex, Regions of Australia, 18 August 2016. ABS, Canberra. 2016; Available from: <u>http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3235.02015?OpenDocument</u>.
- 32. AIHW, Australian Institute of Health and Welfare (AIHW) 2014. National Drug Strategy Household Survey detailed report 2013. Drug statistics series no. 28. Cat. no. PHE 183. Canberra: AIHW., 2014.
- 33. Australian Government Taxation, Department of Health, 2013. Available from <u>http://www.health.gov.au/internet/main/publishing.nsf/content/tobacco-tax</u>.
- 34. Scollo, M. and Bayly, M., 10.2 The manufacturing industry in Australia. In Scollo, MM and Winstanley, MH [editors]. Tobacco in Australia: Facts and issues. Melbourne: Cancer Council

Victoria 2016., 2016: p. Available from <u>http://www.tobaccoinaustralia.org.au/chapter-10-tobacco-industry/10-2-the-manufacturing-industry-in-australia</u>.

- 35. Australian Bureau of Statistics (ABS), Apparent Consumption of Alcohol, Australia, 2011-2016. ABS, 2015. Available from: <u>http://www.abs.gov.au/ausstats/abs@.nsf/mf/4307.0.55.001/</u>.
- 36. Lai, F.Y., Ort, C., Gartner, C., Carter, S., Prichard, J., Kirkbride, P., *et al.*, Refining the estimation of illicit drug consumptions from wastewater analysis: Co-analysis of prescription pharmaceuticals and uncertainty assessment. Water Res, 2011. 45(15): p. 4437-48.
- 37. Castiglioni, S., Bijlsma, L., Covaci, A., Emke, E., Hernández, F., Reid, M., *et al.*, Evaluation of uncertainties associated with the determination of community drug use through the measurement of sewage drug biomarkers. Environ Sci Technol, 2013. 47(3): p. 1452-1460.
- 38. Høiseth, G., Bernard, J.P., Stephanson, N., Normann, P.T., Christophersen, A.S., Mørland, J., *et al.*, Comparison between the urinary alcohol markers EtG, EtS, and GTOL/5-HIAA in a controlled drinking experiment. Alcohol and Alcoholism, 2008. 43(2): p. 187-191.
- 39. Lai, F.Y., Bruno, R., Hall, W., Gartner, C., Ort, C., Kirkbride, P., *et al.*, Profiles of illicit drug use during annual key holiday and control periods in Australia: wastewater analysis in an urban, a semi-rural and a vacation area. Addiction, 2013. 108(3): p. 556-565.

	Nicotine		Cigarettes		Alcohol	
	Range	Mean (SE)	Range	Mean (SE)	Range	Mean (SE)
ACT	1210-1280	1430 (1160)	1360-1450	1610 (1400)	7.40-16.0	13.0 (11.0)
QLD-A	1950-2540	1950 (940)	2200-2870	2200 (1190)	11.0-24.0	16.0 (7.60)
QLD-B	130-1690	1620 (760)	1500-1900	1830 (960)	9.10-24.0	14.0 (8.10)
NSW-A	1150-3900	1960 (1230)	1300-4400	2210 (1500)	7.30-36.0	12.0 (11.0)
NSW-B	750-1340	1210 (780)	850-1510	1360 (950)	9.50-21.0	16.0 (6.50)
NSW-C NSW-D	350-1370	750 (460)	390-1540	850 (560)	6.00-12.0	8.20 (3.60)
5 NSW-D	520-820	790 (690)	580-920	890 (830)	3.70-15.0	6.90 (5.30)
NT-B	1610-2990	2380 (1090)	1820-3370	2680 (1380)	14.0-43.0	23.0 (15.0)
SA	1830-1960	1900 (720)	2070-2210	2140 (940)		
VIC-A	1740-2010	1850 (710)	1960-2260	2080 (920)	9.30-18.0	11.0 (5.50)
VIC-B	2010-2300	2010 (860)	2270-2590	2260 (1100)	8.60-23.0	12.0 (7.40)
WA	1590-1760	1650 (630)	1800-1980	1860 (820)	7.80-12.0	9.70 (3.90)
_ QLD-C	1160-1720	1430 (590)	1310-1940	1620 (760)	7.70-15.0	11.0 (4.70)
QLD-C	2460-3150	2680 (1050)	2780-3550	3020 (1360)	12.0-27.0	17.0 (7.90)
NT-A	2930-3500	3020 (1270)	3300-3940	3400 (1630)	16.0-37.0	24.0 (13.0)

Table 1: Population-normalised (per 1000 people) nicotine use (mg/day) and its equivalent number of cigarettes and alcohol (L/day) in the studied communities.

SE: standard error; -----: not available.

Nationwide average daily use of nicotine/cigarette	Estimated from cotinine	Estimated from hydroxycotinine
Nicotine (kg)	40.5	38.1
No. of cigarette (million)	45.7	43.0
Nicotine (mg/day/capita aged 15-79 years)	2.23	2.10
Cigarette ¹ (numbers/day/capita aged 15-79 years)	2.52	2.37

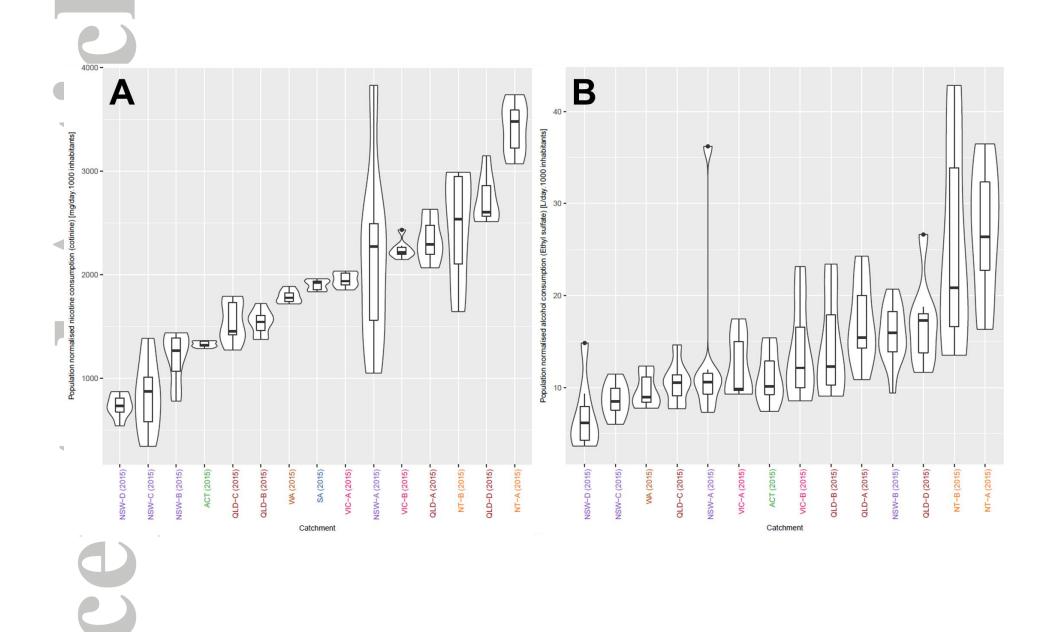
Table 2: Nationwide estimation of nicotine, cigarette and alcohol consumption.

¹Sale data in 2015 = 2.48 cigarettes/day/capita aged 15-79 years.

		Ethanol ² (mL/day/capita aged 15-79	
Nationwide average daily use of alcohol	Pure ethanol (L)	years); standard drinks ³	
Monday	322,000	18.0; 1.44	
Tuesday	297,000	16.6; 1.33	
Wednesday	280,000	15.7; 1.25	
Thursday	301,000	16.9; 1.35	
Friday	360,000	20.1; 1.61	
Saturday	420,000	23.5; 1.88	
Sunday	442,000	24.7; 1.98	
Weekly	346,000	19.3; 1.55	

²Sale data in 2015 for daily use = 26.3 mL/day/capita aged +15 years.

³One standard drink in Australia = 12.5 mL of alcohol.



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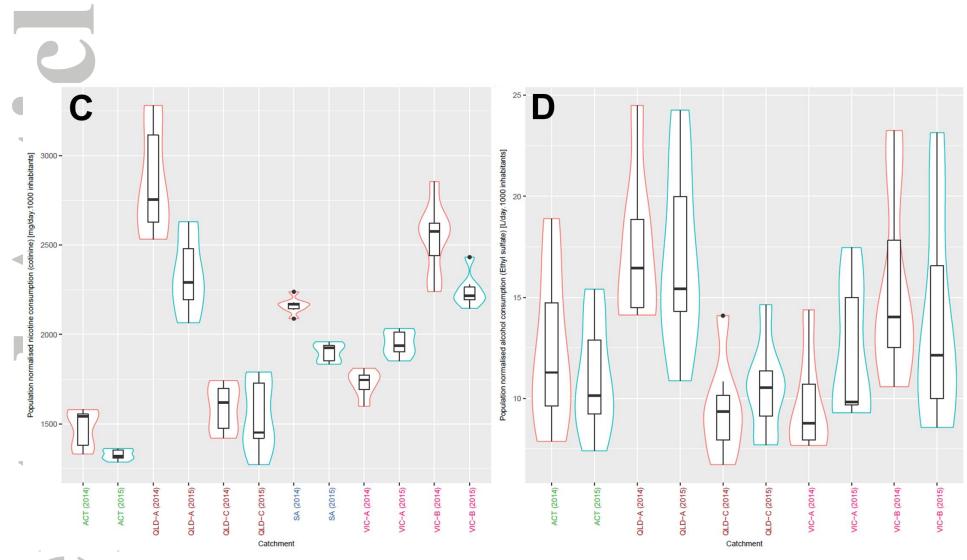
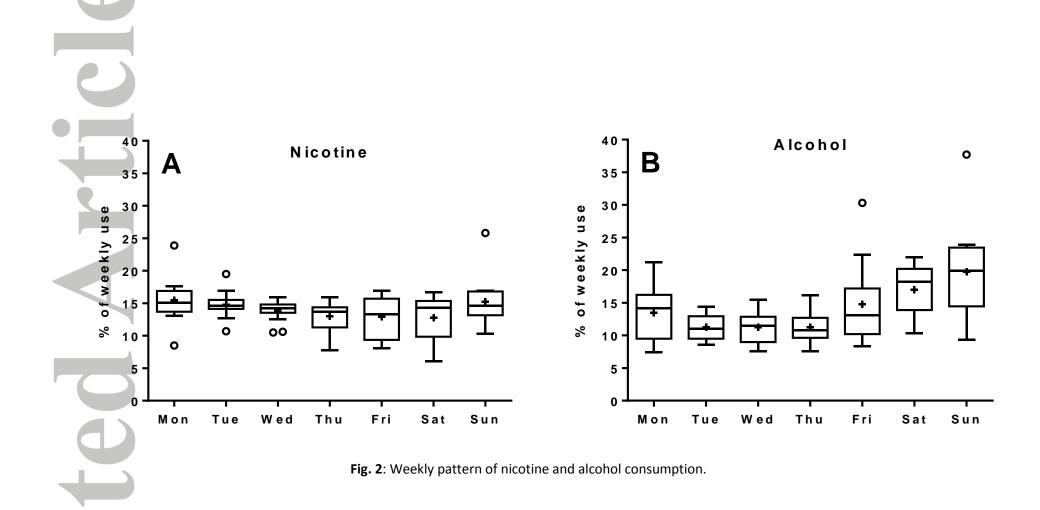


Fig. 1: Spatial patterns for population-normalised consumption of (A) nicotine (mg/day/1000 people) and (B) alcohol (L/day/1000 people) in the studied communities in 2015. Temporal trends of 2014 (red) and 2015 (turquoise) for population-normalised consumption of (C) nicotine (mg/day/1000 people) and (D) alcohol (L/day/1000 people). Catchment: ACT (green), QLD (reddish brown); NSW (purple); NT (orange); SA (blue); VIC (pink); WA (brown).

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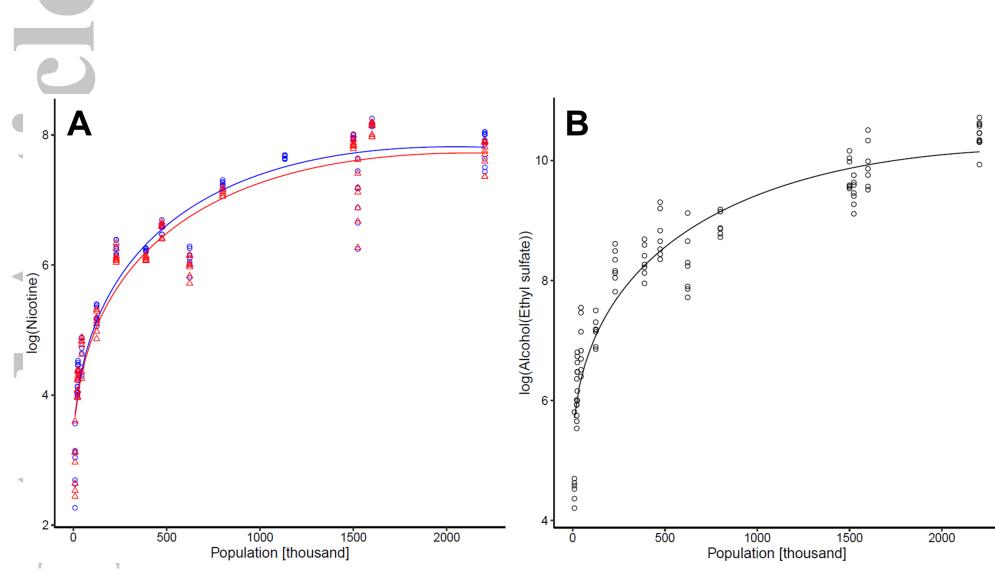


Fig. 3: The best fit model (square root function) for the consumed amount of (A) nicotine (blue: cotinine; red: hydroxylcotinine) and (B) alcohol against the population size across the studied catchment in 2015. For representation purposes, only the fixed effect model for alcohol consumption estimates is shown here.