Research

Genetic feedback to reduce alcohol consumption in hospital outpatients with risky drinking: feasibility and acceptability

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Article history

Key points

- Communication of DNA-based disease risk estimates may motivate behaviour change
- There have been no trials of genetic susceptibility feedback in relation to alcohol consumption in healthcare settings
- This study suggests that it would be feasible to conduct a methodologically robust trial estimating the effect of genetic susceptibility feedback on alcohol consumption in hospital outpatients with risky drinking

Abstract

Objective: There have been no trials in healthcare settings of genetic susceptibility feedback in relation to alcohol consumption. The purpose of this study was to determine the feasibility and acceptability of conducting a full-scale randomised trial estimating the effect of personalised genetic susceptibility feedback on alcohol consumption in hospital outpatients with risky drinking.

Methods: Outpatients ≥18 years of age who reported drinking more than 14 standard drinks in the past week or in a typical week were asked to provide a saliva sample for genetic testing. Genetic susceptibility feedback was posted to participants 6 months after recruitment. The co-primary outcomes were the proportion of participants who (i) provided a saliva sample that could be genotyped, and (ii) spoke with a genetic counsellor. Secondary outcomes included changes in patients' weekly alcohol consumption; scores on scales measuring readiness to change, importance of changing and confidence in ability to change drinking habits; knowledge about which cancers are alcohol-attributable; and acceptability of the saliva collection procedure and the genetic-feedback intervention. McNemar's test and paired t-tests were used to test for differences between baseline and follow-up in proportions and means, respectively.

Results: Of 100 participants who provided a saliva sample, 93 had adequate DNA for at least one genotyping assay. Three participants spoke to a genetic counsellor. Patients' readiness to change their drinking, their views on the importance of changing and their stated confidence in their ability to change increased between baseline and follow-up. There was no increase in patients' knowledge about alcohol-attributable cancers nor any reduction in how much alcohol they drank 4 months after receiving the feedback. Most participants

(80%) were somewhat comfortable or very comfortable with the process used to collect saliva, 84% understood the genetic feedback, 54% found it useful, 10% had sought support to reduce their drinking after receiving the feedback, and 37% reported that the feedback would affect how much they drink in the future.

Conclusion: Results of this study suggest it would be feasible to conduct a methodologically robust trial estimating the effect of genetic susceptibility feedback on alcohol consumption in hospital outpatients with risky drinking.

Introduction

Consumption of alcohol is causally related to cancer of the oral cavity and pharynx, larynx, oesophagus and upper aerodigestive tract, colorectum, liver and female breast.[1] Alcohol-attributable cancer caused 337 400 deaths globally in 2010, or 4.9 deaths per 100 000 people.[2] The mechanisms by which alcohol consumption increases the risk of cancer are not fully understood, but a genotoxic effect of acetaldehyde from alcohol metabolism in the body has been identified as a likely causal pathway for several alcohol-related cancers.[1] Given the "relationship between alcohol consumption and cancer is monotonic and without threshold",[1] Cancer Council Australia recommends that people limit their drinking to reduce their risk of cancer, and advises individuals who choose to drink alcohol to do so in accordance with the National Health and Medical Research Council (NHMRC) guidelines for reducing the lifetime risk of harm from alcohol consumption.[3,4]

One in five Australians is a risky drinker.[5] To reduce alcohol consumption, the World Health Organization recommends the delivery of alcohol screening and brief intervention in the primary health care setting.[6] This strategy is modestly effective, with reductions in consumption of 13% lasting 12 months among nontreatment-seeking patients with risky drinking.[7] Personalised medicine, defined as "the application of genetic information to predict disease development, influence decisions about lifestyle choices, and tailor preventative intervention or medical treatment to the individual needs of each patient"[8], might be more effective than screening and brief intervention because of its personal salience.[9] Although the findings from a recent systematic review do not support this hypothesis, only four studies met the criteria for a low summary risk of bias and none of these evaluated the effect of genetic feedback on alcohol consumption in healthcare settings.[10]

The purpose of this study was to determine the feasibility of conducting a full-scale randomised trial estimating the effect of personalised genetic susceptibility feedback on alcohol consumption in hospital outpatients with risky drinking. This setting was chosen because one in three hospital outpatients report risky drinking[11], compared with one in four primary care patients[12] and one in five Australian adults.[5] We have previously reported that people recruited in the proposed outpatient setting are reluctant to leave their seat for fear of missing their appointment, illustrating the importance of thorough piloting of experimental procedures.[13] Accordingly, one of this study's primary outcomes was the feasibility of collecting saliva samples that could be genotyped. Previous research has shown that the provision of genetic susceptibility results by mail with telephone follow-up for counselling is as effective as in-person counselling[14], but some recent studies have relied on mail alone.[15,16] Therefore, this study's other primary outcome was whether participants expressed the need for genetic counselling by telephone after the provision of genetic susceptibility results by mail.

Methods

This feasibility study was conducted in the outpatient department (Ambulatory Care Centre) of a large public hospital in Newcastle, Australia, which provides services for more than 870 000 people residing in a region the size of England.[17]

Ethical approval for this study was obtained from the Hunter New England Human Research Ethics Committee (13/11/20/4.09) and the University of Newcastle Human Research Ethics Committee (H-2014-0203).

Eligibility, recruitment and screening

Outpatients ≥18 years of age who were capable of completing the screening questionnaire on an iPad, and who reported drinking more than 14 standard drinks in the past week or in a typical week were eligible. We approached potential participants in the waiting area and logged consenting outpatients into the screening questionnaire on an iPad using a unique identifier. Page 1 briefly described the Alcohol Genetic Risk Information Project. Page 2 collected demographic data (gender, age and postcode). Page 3 asked respondents if they had consumed alcohol in the past 12 months (yes or no). Those who had not were excluded at this point. Page 4 comprised a 7-day retrospective drinking diary, and page 5 asked participants to select the number of standard drinks they consumed in a typical week: 1–7, 8–14, 15–21, 22–28, 29–35, 36–42, 43–49, 50–56, 55–63, 64–70 and 71+.

Participants who reported consuming ≤14 standard drinks in the past week and ≤14 standard drinks in a typical week were excluded at this point. Page 6 asked participants questions about their readiness to change their drinking habits, the importance of changing their drinking habits and their confidence in their ability to change their drinking habits.[18] Page 7 assessed participants' knowledge about alcohol-attributable cancers.

Saliva collection

Saliva was collected using a whole-saliva collection device – the Oragene DNA (OG-500) self-collection kit – which has been shown to provide a significantly greater DNA yield than the cytobrush, foam swab and oral rinse methods.[19] Participants are required to spit until the saliva reaches the fill line (2 mL). Participants had the option of providing the saliva sample in the waiting area, one of the nearby rest rooms, or in the consulting room immediately before or after their appointment.

Genotyping assays

DNA samples were genotyped with TaqMan® single nucleotide polymorphism genotyping assays. The choice of assays was based on evidence of increased cancer risk because of altered enzyme activity (increased production of acetaldehyde), as well as the frequency of the risk allele in Caucasians.

The ADH1B*2, ADH1C*1 and ADH7*2 alleles increase acetaldehyde production through increased enzyme activity of 40-, 2.5- and 100-fold, respectively.[20] Caucasians have a 50% ADH1C*1 allele (rs1693482) frequency and a 10% ADH*2 allele (rs1573496) frequency.[20] The ADH1B*1 allele (rs1229984) was also included, because this allele is associated with head and neck cancer in epidemiological studies and has almost 100% allele frequency in Caucasians.[21]
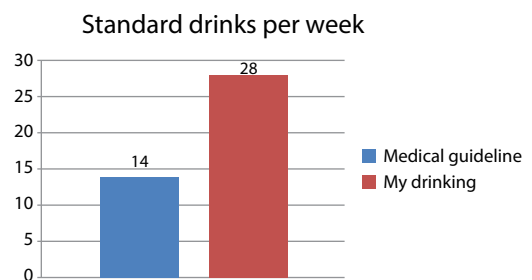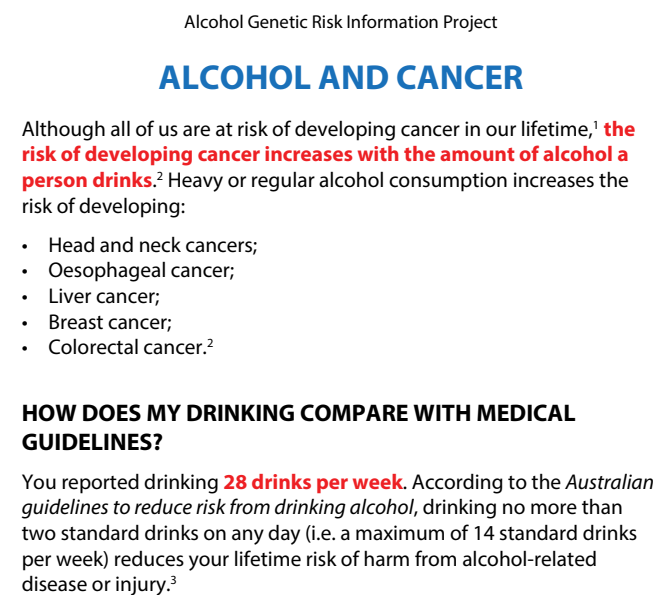
Intervention

Personalised behavioural and genetic susceptibility feedback was posted to participants 6 months after recruitment (Figure 1). The expressed need for genetic counselling by telephone after the provision of genetic susceptibility results by mail was assessed by randomly allocating participants to receive one of:

- A letter enclosed with their feedback encouraging them to call the research team to organise a telephone appointment with a genetic counsellor
- A telephone call from the research team shortly after their feedback had been posted.

During the telephone call, participants received a brief explanation of the feedback and were offered a telephone appointment with a genetic counsellor. Participants were also asked how they felt about getting their results in the post, whether it was useful to have someone call to explain the results, and if they thought it might be necessary for participants to have a face-to-face meeting with a genetic counsellor.

Figure 1. Example of personalised behavioural and genetic feedback

Alcohol Genetic Risk Information Project

ALCOHOL AND CANCER

Although all of us are at risk of developing cancer in our lifetime,[1] **the risk of developing cancer increases with the amount of alcohol a person drinks**.[2] Heavy or regular alcohol consumption increases the risk of developing:

- Head and neck cancers;
- Oesophageal cancer;
- Liver cancer;
- Breast cancer;
- Colorectal cancer.[2]

HOW DOES MY DRINKING COMPARE WITH MEDICAL GUIDELINES?

You reported drinking **28 drinks per week**. According to the *Australian guidelines to reduce risk from drinking alcohol*, drinking no more than two standard drinks on any day (i.e. a maximum of 14 standard drinks per week) reduces your lifetime risk of harm from alcohol-related disease or injury.[3]

AM I AT INCREASED RISK OF AN ALCOHOL-RELATED CANCER?

Summary

- There are 3 main enzymes involved in processing alcohol in the body.

- We tested you for 6 different versions of the genes that make these enzymes.

- Your genetic profile indicates that you have 3 versions that reduce your ability to process alcohol.

- This increases your risk of head and neck cancer, colon cancer, liver cancer, and breast cancer, when you drink too much alcohol.

- Your risk can be reduced by adhering to the medical guidelines which state that, for healthy men and women, drinking no more than:

  a) two standard drinks on any day reduces the lifetime risk of harm from alcohol-related disease or injury.

  b) four standard drinks on a single occasion reduces the risk of alcohol-related injury arising from that occasion.

Follow-up

Four months after the genetic susceptibility feedback had been posted, we sent participants a letter on university stationery (with a $20 supermarket voucher redeemable irrespective of further participation) advising them they would receive a follow-up questionnaire in the next few days. Participants who provided an email address were sent a message embedded with a unique hyperlink to the follow-up questionnaire, and the remainder were sent a paper copy. Reminders were sent at 2-week intervals. The first was sent by email or post as per the initial contact, and the second by post because offering different response modes sequentially (web then post) has been shown to improve response rates.[22] After a further 2 weeks, telephone follow-up was attempted and participants were invited to complete the questionnaire by telephone when contact was made.

Primary outcomes

Feasibility of collecting saliva samples that can be genotyped

The feasibility of collecting saliva samples was measured as the proportion of eligible consenting outpatients who reported consuming >14 standard drinks in the past week or in a typical week, and who provided a saliva sample that could be genotyped.

Expressed need for telephone counselling

The expressed need for genetic counselling by telephone after the provision of genetic susceptibility results by mail was measured as the proportion of participants with a saliva sample that could be genotyped and who spoke with a genetic counsellor.

Secondary outcomes

Weekly alcohol consumption

A 7-day retrospective diary was used to measure the volume of alcohol consumed in the past week.[23]

Readiness to change, importance of changing and confidence in ability to change drinking habits

Visual analogue scales ranging from 1 to 100 were used to measure participants' readiness to change, importance of changing and confidence in ability to change drinking habits. The questions were:[18]
- How ready are you to change your drinking habits?
- How important is it for you right now to change your drinking?
- If you decide to change your drinking habits, how confident are you that you would succeed?

Knowledge

Participants were asked "Which of the following cancers is related to a person's alcohol consumption?" The response options were 'no', 'yes', and 'don't know' for each of the following cancers: bladder, breast, colon and rectal, mouth and throat, kidney, liver, lung, ovarian, pancreatic, and prostate.

Acceptability

Participants were asked:
- How comfortable did you feel when providing the saliva sample? (very comfortable, somewhat comfortable, somewhat uncomfortable, very uncomfortable)
- Did you understand the genetic risk information? (no, yes)
- Did you find the genetic risk information useful? (very useful, quite useful, somewhat useful, not useful at all)
- Have you sought support to reduce your drinking as a consequence of receiving the genetic risk information? (no, yes)
- Will the genetic risk information affect how much you drink in the future? (no, yes)

Survey on attitudes to genetic susceptibility testing

We briefly surveyed outpatients' attitudes to genetic susceptibility testing. We told participants that "Some genes put people at a higher risk of developing an alcohol-related cancer. The test for these genes involves providing a saliva sample". We then asked them "If you could be tested for these genes while waiting for your appointment here today, would you want to get the test done?" After participants had provided a yes or no response, they were asked to provide one or more reasons for their decision.
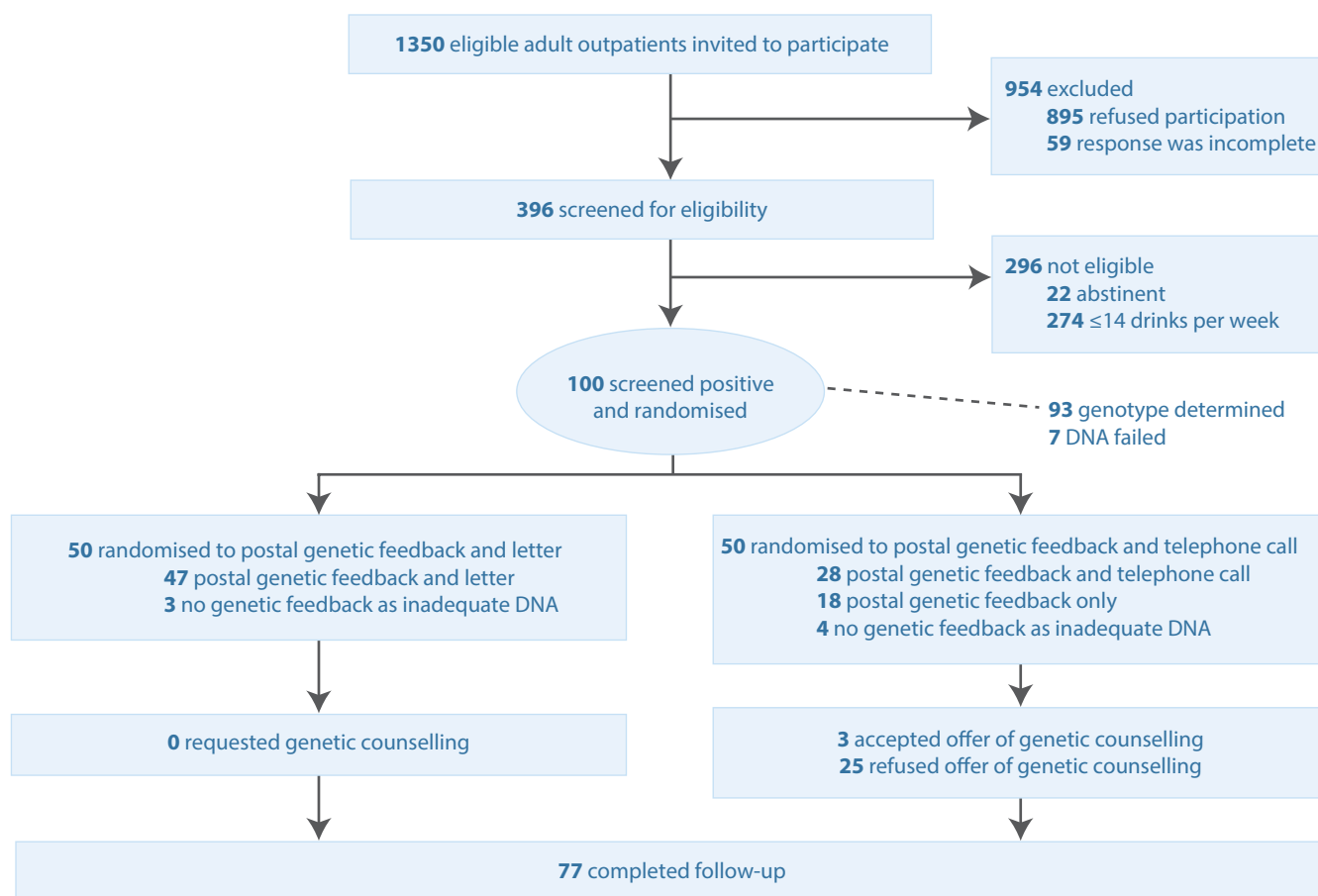
Data analyses

Data were analysed using Stata 11.1 (StataCorp, College Station, TX, US). Descriptive statistics (frequencies and percentages for discrete variables, and medians with interquartile ranges for continuous variables) were used to summarise participants' characteristics at baseline (gender, age, alcohol consumption). McNemar's test and paired t-tests were used to test for differences between baseline and follow-up in proportions and means, respectively.

Results

Of the 1350 outpatients invited to participate, 895 (66%) refused and 59 (4.4%) did not complete the screening process because they were called for their appointment. Of the 396 participants who completed the screening questions, 296 (75%) were excluded – 274 (69%) reported drinking ≤14 drinks in the past week or in a typical week, and 22 (5.6%) reported not drinking any alcohol in the past year. Of the 100 (25%) who

Figure 2. Recruitment, enrolment and retention

reported drinking >14 standard drinks in the past week or in a typical week, 87 were male, their mean age was 45.7 years (standard deviation 17.4), and the median (25th and 75th percentile) number of standard drinks they consumed was 22 (17, 32). Most participants (77/100) completed the follow-up questionnaire (Figure 2). There were no significant differences between participants observed and unobserved at follow-up with regard to gender, age and number of standard drinks consumed in the past week or in a typical week at baseline.

Primary outcomes

Feasibility of collecting saliva samples that can be genotyped

Of the 100 saliva samples collected, 93 contained adequate DNA for at least one genotyping assay.

Expressed need for telephone counselling

Of the 93 participants who provided adequate DNA for at least one genotyping assay, 47 were allocated to the letter arm of the study and 46 were allocated to the telephone arm. None of the participants allocated to the letter arm called to organise an appointment with a genetic counsellor. We were unable to offer 18 of

the 46 participants allocated to the telephone arm an appointment with a genetic counsellor because:
• Nine did not answer any of our calls
• Six said we had called at an inconvenient time and failed to answer when we called back at the nominated suitable time
• Three advised us that they were no longer interested in participating (one person was in hospital, one was "beyond the age of worrying" and one gave no reason).

Three of the 28 participants we contacted chose to speak with a genetic counsellor. One participant declined because he didn't have time (59-year-old man) but most felt it was not needed – for example:

I don't really need it. I know and I understand. (61-year-old woman)

Don't have a need for that. (25-year-old man)

All of the participants we spoke to felt postal feedback was acceptable – for example:

Nice to have a hard copy. Time to think about it and digest. Or email. (55-year-old man)

Some participants found the follow-up telephone call helpful – for example:

I didn't realise that about the gene so thank you that's very helpful to get a call. (48-year-old man)

Table 1. Change in weekly alcohol consumption and psychological constructs between baseline and follow-up among retained participants[a]

Measure (range)	Baseline median (25th, 75th percentiles)	Follow-up median (25th, 75th percentiles)	Mean change	95% confidence interval	*p* value[b]
Number of standard drinks consumed in the past week	21 (17, 31)	21 (15, 34)	–0.29	–4.26, 3.69	0.89
Readiness to change drinking habits (1–100)	21 (0, 45)	25.5 (5, 58)	9.43	3.26, 15.61	<0.01
Importance of changing drinking habits (1–100)	16 (0, 48)	26 (7.5, 70.5)	10.82	3.93, 17.70	<0.01
Confidence in ability to change drinking habits (1–100)	54 (23, 80)	68 (38, 90)	8.92	0.96, 16.89	0.03

a Seventy-seven participants completed both questionnaires
b Statistical significance was determined by paired t-tests

Some found it useful from a confirmatory point of view – for example:

Put my mind at ease that I read it right. (71-year-old woman)

Others thought it was unnecessary – for example:

Someone might not understand, but I had no problem understanding. (35-year-old man)

Most participants did not express the need for a face-to-face meeting with a genetic counsellor, but thought others might – for example:

Some people maybe. (44-year-old man)

Depends on the person. (64-year-old man)

I wouldn't personally want that. (66-year-old man)

Secondary outcomes

Weekly alcohol consumption

The volume of alcohol consumed in the past week did not decrease between baseline and follow-up (Table 1).

Readiness to change, importance of changing and confidence in ability to change drinking habits

Participants' scores on scales measuring readiness to change, importance of changing and confidence in ability to change drinking habits increased between baseline and follow-up (Table 1).

Knowledge

There was no increase in the proportion of participants who correctly identified which cancers are related to alcohol consumption and which are not between baseline and follow-up.

Acceptability

Participants' responses to questions about acceptability are shown in Table 2. Positive feedback

Table 2. Findings regarding acceptability among retained participants[a]

Questions	Available answers	n (%)
How comfortable did you feel when providing the saliva sample?	Very comfortable	35 (46)
	Somewhat comfortable	26 (34)
	Somewhat uncomfortable	9 (12)
	Very uncomfortable	6 (7.9)
Did you understand the genetic risk information?	No	12 (16)
	Yes	63 (84)
Did you find the genetic risk information useful?	Very useful	12 (16)
	Quite useful	28 (38)
	Somewhat useful	25 (34)
	Not useful at all	9 (12)
Have you sought support to reduce your drinking as a consequence of receiving the genetic risk information?	No	66 (90)
	Yes	7 (10)
Will the genetic risk information affect how much you drink in the future?	No	44 (63)
	Yes	26 (37)

a Seventy-seven participants responded at follow-up

provided in the comments section of the follow-up questionnaire included:

It has made me rethink my drinking problem and act on fixing it. (48-year-old man)

It has made me stop drinking; I only drink about every 1–2 months. (52-year-old woman)

Some of the less positive feedback provided in the comments section included:

Thought this would be good, but it's a waste of time. Did it because I thought I would get an idea of risk of cancer but didn't tell me anything. Don't know if I'm at risk of colon cancer or specific details, just an increased risk from drinking alcohol. (45-year-old man)

I didn't read it very carefully. Off-hand I don't think it was a very good result. And I prefer not to know the risks. (48-year-old man)

Survey on attitudes to genetic susceptibility testing

Of the 100/138 (73%) outpatients who consented, 26/100 (26%) said they would not agree to have the genetic susceptibility testing. The reasons given were no or low alcohol use (14 participants), no family history of cancer (5 participants), worry about result (4 participants), inconvenience of test (3 participants), concerns about privacy (2 participants), not worried about cancer (1 participant) and too old (1 participant).

Discussion

This study suggests that it would be feasible to conduct a methodologically robust trial estimating the efficacy of genetic susceptibility feedback in hospital outpatients with risky drinking, despite the three main problems we encountered.

First, the consent rate was low. This would inflate the cost of a trial by increasing the time required to recruit enough participants for adequate study power. The low consent rate may also reduce the generalisability (external validity) of effect estimates. The findings of this study facilitate the design of a trial with high internal validity by increasing the duration of recruitment. Given that approximately 500 people attend outpatient appointments at the Ambulatory Care Centre each day, we estimate it would take 12 months to recruit the required number of people in this setting.

Second, 7% of saliva samples obtained using the Oragene DNA (OG-500) collection system did not contain adequate DNA because the participants were unable to produce the required 2 mL of saliva. The oral rinse method, which involves swishing vigorously with 10 mL of mouthwash for 45 seconds before expectorating the mouthwash into a clean specimen cup, provides high-quality DNA, but it requires immediate processing, which is not practical.[19] Another option is the use of DNA from blood, but this is invasive and likely to be inconvenient, because participants would need to visit the pathology collection centre before leaving the hospital. Given that the Oragene DNA (OG-500) self-collection system remains the best option, outpatients would be eligible for inclusion in a trial only if their saliva sample can be genotyped. This approach may reduce

the generalisability of the effect estimates, but it would preserve internal validity, which must be the priority in an efficacy trial.[24]

Third, we were unable to contact many of the participants by telephone. It should be noted that:
- Only 3 of the 28 participants we contacted chose to speak with a genetic counsellor
- The other participants declined because they understood the feedback
- No-one in the group allocated to receive a letter encouraging them to call the research team to organise a telephone appointment with a genetic counsellor did so.

These results suggest that genetic counselling by telephone after the provision of genetic susceptibility results by mail is not needed. Since expressed need may underestimate actual need, it may be prudent to provide participants in a trial with the option of speaking to a genetic counsellor.

There was no reduction in alcohol consumption between baseline and follow-up. This is not surprising, because the study was not powered to detect a clinically meaningful change in alcohol consumption. The finding that patients' readiness to change their drinking, their views on the importance of changing, and their stated confidence in their ability to change increased between baseline and follow-up is encouraging, given that high readiness, high importance and high confidence have been shown to predict reductions in alcohol consumption.[18,25] Participants' knowledge as to which cancers were alcohol-attributable did not increase after receiving information about these associations. This arguably suggests that the focus of public health messages should be on the alcohol–cancer link per se, rather than on specific cancers. There may be value in undertaking interviews with participants to investigate how they process this information and what would help increase retention.

Limitations

The study was not powered to detect a clinically meaningful change in alcohol consumption. Furthermore, the lack of a control group prevents inferring a relationship between the intervention and any changes in drinking. The purpose of the study was to examine the acceptability of the intervention to the target population of patients, and to gather data that would inform a decision about the feasibility of a large, robust efficacy trial, and the design of such a trial.

Conclusion

Results of this study suggest it would be feasible to conduct a methodologically robust trial estimating the efficacy of genetic susceptibility feedback in hospital outpatients with risky drinking. If efficacy is shown, there is a high potential for health benefits, but if the

intervention is found to be ineffective, policy makers and the health research community will have valuable information about where not to invest scarce resources.[26]

Acknowledgements

Competing interests

AD is seconded by the NSW Ministry of Health to work as the Chief Addiction Medicine Specialist. Payment is to his employer, the Hunter New England Local Health District.

Author contributions

NJ, KK, JA, MM and AD conceived the research and were responsible for the design of the intervention. JA and MM were responsible for the selection of the single nucleotide polymorphisms and the provision of genetic counselling to participants. JL was responsible for data collection, management and analysis. RS oversaw the genetic analysis. All authors reviewed and approved the final manuscript.

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