

## Introduction

- Helicobacter Eradication Aspirin Trial (HEAT) is a double-blind placebo controlled randomised trial of the effects of *H. pylori* eradication on subsequent ulcer bleeding in infected patients who age  $\geq 60$  years old and taking aspirin  $\leq 325$ mg daily. The eradication therapy consists of one week of lansoprazole 30mg, clarithromycin 500mg and metronidazole 400mg twice daily<sup>1</sup>.
- Many common side effects associate with the eradication therapy.
- Withdrawal reasons are recorded during the trial. However, factors that associate with withdrawal occurring are not concluded.
- The objective of this project is to analyse the side effects and withdrawal of the trial.

## Method

- Currently, the treatment allocation remains blinded and there are 2741 randomised, *H. pylori* positive participants. The information of participants is kept in Queen's Medical Centre's database.
- Transcription of the information from the database into Excel format is performed.
- Participants' characteristics is analysed by using descriptive statistics.
- The probability of a side effect occurring and withdrawal occurring is modelled using probit regression.
- In both regression models, the controls include: gender, age, treatment adherence, side effects, smoking and alcohol status.

## Results

**Table 1 Participants' characteristics at baseline**

	Durham (n=351)	Nottingham (n=826)	Oxford/ Birmingham (n=744)	Southampton (n=820)	Combined (n=2741)
<b>Gender, %</b>					
Male	72.9	73	73.8	72.7	73.1
Female	27.1	27	26.2	27.3	26.9
<b>Age, mean (SD), y</b>	72.5 (7)	73.1 (7)	73.9 (7)	73.9 (7)	73.5 (7)
<b>Treatment record form returned, %</b>	84.62	83.41	84.14	81.71	83.25
<b>History of smoking, %</b>					
Ex-smoker	54.7	52.4	52.8	55.3	53.7
Non-smoker	38.7	39.8	39.8	38.9	39.4
Smoker	6.3	7.7	7.4	5.1	6.7
<b>Alcohol units per week (SD)</b>	8.0 (10.0)	7.8 (11.1)	8.9 (11.5)	7.8 (10.7)	7.3 (11.0)

- Age of participants is considered high.
- Relatively low number of participants in Durham is observed.
- H. pylori* infection rate is higher in male than female.
- 18.29% of participants in Southampton do not have their treatment record forms returned.

## Discussion

- One study shows that a higher active *H. pylori* infection in male than in female (14.5% vs 12.3%,  $p < 0.05$ ), after stratifying the age<sup>2</sup>.
- One abstract shows that female is associated with an increased risk of admission into hospitals for an adverse drug reaction<sup>3</sup>.
- As the age of participants is considered high, poor memory of remembering to take medicines possibly explains that they are more likely to miss the doses, causing non-adherence to the treatment and subsequently withdraw from the trial.
- One study demonstrates that 246 out of 274 responders (89.8%) do not adhere to the erythromycin regimen due to adverse drug reaction<sup>4</sup>.
- Adverse drug reaction is the main reason that is responsible of 58.3% of withdrawers from Nottingham region withdraw from the trial.
- As smokers have reduction of sensitivity of taste, they tend to not report side effects or withdraw the treatment.

## Reference

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**Table 2 Model of probability of a side effect occurring, controlling for gender, age, treatment adherence, smoking and alcohol status (n=2741)**

	Coefficient	P-value	95% Confidence interval
Gender	0.187	0.001	0.073 to 0.301
Age	-0.003	0.338	-0.010 to 0.004
Ex-smoker	-0.086	0.103	-0.190 to 0.017
Smoker	-0.174	0.103	-0.383 to 0.035
Alcohol	0.000	0.899	-0.004 to 0.005
Non-adherence	1.185	0.000	0.942 to 1.427
Region			
Nottingham	-0.039	0.639	-0.204 to 0.125
Oxford/Birmingham	-0.016	0.855	-0.183 to 0.152
Southampton	-0.056	0.505	-0.221 to 0.109

- Diarrhoea, unpleasant taste and abdominal discomfort are the three most frequent reported side effects.
- Gender and treatment adherence are significant factors at  $p < 0.05$  and both show positive estimated coefficient.
- Therefore, females are more likely to experience side effect than males; participants who do not adhere to their assigned treatment are more likely to experience side effect.
- No regional difference is observed.

**Table 3 Model of probability of withdrawal occurring, controlling for treatment adherence, side effects, gender, age, smoking and alcohol status, in condition of having treatment record forms (n=2282)**

	Coefficient	P-value	95% Confidence interval
Non-adherence	1.517	0.000	1.226 to 1.808
Side effects	0.519	0.001	0.207 to 0.830
Gender	-0.129	0.414	-0.440 to 0.181
Age	0.031	0.002	0.011 to 0.051
Ex-smoker	-0.062	0.649	-0.328 to 0.204
Smoker	-0.567	0.210	-1.452 to 0.318
Alcohol	0.004	0.521	-0.008 to 0.015
Region			
Nottingham	0.536	0.038	-0.282 to 0.739
Oxford/Birmingham	0.003	0.992	-0.548 to 0.553
Southampton	0.229	0.379	0.030 to 1.041

- Treatment adherence, side effects and age are significant factors for withdrawal occurring at  $p < 0.05$ . Their estimated coefficients are also positive.
- Participants who do not adhere to their assigned treatment tend to withdraw the treatment.
- The likelihood of withdrawal occurring is greater in participants who experience side effects.
- Older participants are more likely to withdraw their treatment than younger participants.
- In comparison with other regions, participants from Nottingham withdraw their treatment at significant level of  $p < 0.05$ .

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