Travel Medicine and Infectious Disease 14 (2016) 621–624

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: www.elsevierhealth.com/journals/tmid

How low an effect of a preventive measure against diarrhoea are travellers willing to pay for?: A survey of Norwegian travellers

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ARTICLE INFO

Article history:
Received 12 November 2015
Received in revised form
13 October 2016
Accepted 14 October 2016
Available online 21 October 2016

Keywords:
Traveller's diarrhoea
Prophylaxis
Vaccine
Willingness to pay

ABSTRACT

Background: Traveller's diarrhoea (TD) is the most common infectious problem for travellers, and we lack effective ways of preventing it, apart from antibiotic prophylaxis. This study aims to quantify the risk reduction of a hypothetic TD vaccine Norwegian travellers are willing to pay for.
Methods: 1204 clients at Reiseklinikken responded to a questionnaire asking what level of effectiveness would be required of a hypothetical vaccine against TD costing US$65.
Results: 18.7% of the respondents would buy the vaccine even if it was only 20% effective. Among respondents older than 50 years, the proportion was 28.8%.
Conclusions: Our findings should encourage the development of vaccines and other preventive measures against travellers' diarrhoea.

1. Introduction

Traveller's diarrhoea (TD) affects 20–90% of travellers to high risk regions in Africa, Asia and Latin America and lasts 4 days on average [1]. The incidence of diarrhoea is highest in the beginning of the traveller's stay: 62% of TD cases occur within the first week. General precautions have no documented effect [2]. Prophylactic use of antibacterial agents is cost-effective for short-term travel [3], but the use of antibiotics may increase the risk of acquiring multiresistant bacteria: Kantele et al. [4] found an odds ratio of 4.2 for carrying ESBL (Extended Spectrum Beta Lactamase) producing bacteria after having been treated with antibiotics for TD while travelling ($P < 0.001$). Antibiotic treatment of uncomplicated TD, which is mostly a self-limiting disease, should therefore be discouraged [5]. Furthermore, a recent review showed that antibiotics are not superior to loperamide in treating mild and moderate TD [6]. In general, Scandinavian countries have a restrictive attitude to the use of antibiotics, and Norwegian health authorities do not recommend TD prophylaxis with antibiotics. Vaccines against TD would be an environmentally friendly type of prophylaxis. However, the development of a universal TD vaccine seems far ahead because of the high number of agents that cause TD. A combined vaccine, preventing infections with all the Salmonella, Shigella, Campylobacter and the enterotoxigenic, enteroaggregative and enteropathogenic *Escherichia coli* would be needed to achieve a general protection of 60–80% (calculated from Shah, DuPont and Ramsey, 2009 [7]). The most common pathogen causing TD is enterotoxigenic *Escherichia coli* (ETEC), accounting for 30.4% of all TD cases [7]. There are two types of enterotoxin produced by *E. coli*: thermo labile (LT) and thermo stabile (ST) enterotoxin. An oral cholera vaccine, Dukoral®, which contains inactivated cholera vibriones and cholera toxin-B-subunit rCTB, is claimed to protect against LT ETEC [8], but a Cochrane analysis from 2013 concluded that "There is currently insufficient evidence to support the use of the oral cholera vaccine Dukoral® to protect travellers against ETEC diarrhoea." [9]. The prevalence of the different ETEC strains varies tremendously between countries, but overall, 55% of wild-type strains of ETEC in travellers are either LT or LT/ST producing [10], indicating that an effective LT ETEC vaccine could give a 15–20% reduction of the incidence of TD. The protective effect of cholera toxin-B-subunit vaccine on TD lasts for only three months [8]. A recent study of a dermal patch vaccine against LT enterotoxin failed to show any protective effect against TD [11].

Increasing the number of beneficial bacteria in the gut has been suggested to reduce the risk of TD. This can be achieved either by consuming probiotics, which are live bacteria, or prebiotics, which are defined as "non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species already resident in

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http://dx.doi.org/10.1016/j.tmaid.2016.10.005
1477-8939/

the colon" [12]. Prophylaxis with probiotics (e.g., *Saccharomyces boulardii*, *Lactobacillus acidophilus* and *Bifidobacterium bifidum*) has a minor effect on the risk of TD. A meta-analysis of probiotic prophylaxis showed a TD Risk Ratio of 0.85 ($p < 0.001$) [13]. A small, double-blind study comparing a prebiotic galacto-oligosaccaride with placebo showed a 39% reduction of the risk of TD in the treatment group versus the control group ($P < 0.05$) [14].

Given the large number of pathogens causing TD, it is unlikely that one single measure will give 100% protection. When deciding to take a TD prophylaxis, its efficacy, effort, side effects, ecological impact, and price may be considered. Given the high incidence of TD, even a small protective effect could be cost effective. We wanted to assess travellers' willingness to pay for a hypothetical vaccine preventing TD. In the case of TD, where all the cost of prevention is paid by the travellers, and the TD has little impact on the society after return, this individual approach would in our opinion be much more relevant than a public health approach. As no insurance company in Norway provides coverage of travel vaccines, the issue of travel insurance was not addressed. We did not include any adverse effect of the hypothetical vaccine, and we specified the length of vacation to two weeks in order to avoid bringing possible long-term protection into the calculation. To our knowledge, no study has attempted to quantify the value of a day on vacation without TD. The results of this study may be relevant to decision makers who evaluate prioritising the development of vaccines and other preventive measures in travel medicine.

2. Methods

Reiseklinikken (Oslo Travel Clinic) is a private travel clinic providing vaccination and pre-travel advice to approximately 11,000 travellers per year, the vast majority being recreational travellers. During the study period from July to November 2011, approximately 2900 travellers visited the clinic. The clients were presented to a questionnaire asking the following hypothetical questions: "If the risk of ruining 3–6 days of a two weeks' vacation from diarrhoea is 20–30%, and you were offered a vaccine against diarrhoea that costs NOK 500 (which is equivalent to approximately US$65 in 2015), would you buy the vaccine if it reduced the risk of contracting diarrhoea by at least 20%, 40%, 60%, 80% or 100%?" The respondents could also choose, "I wouldn't buy it in any case". The price of the hypothetical vaccine was deliberately set equal to the price of Dukoral®, which in practice also would give protection for only one vacation. The form was anonymous, and no clinical data were collected. Age, sex and income (three ordinal alternatives: <US$29,000, US$29,000–53,000 and> US$53,000) were registered. We estimated the proportion of people preferring each of the six alternatives. A 95% confidence interval for each proportion was estimated using the Clopper and Pearson method [15]. Possible effects of age, sex and income were assessed by using the Kruskal-Wallis rank sum test and Fisher's exact test. The analyses were performed in the statistical software R [16].

3. Results

During the study period, 1207 people responded to the questionnaire, which was 42% of all travel vaccine clients during the period. Three respondents gave an ambiguous answer to the vaccine effect question and were hence excluded from further analyses. Of the remaining 1204 respondents, 1162 entered their age. The majority were young people between 20 and 35 years old (64%), but the travellers' age ranged from 16 to 75 (Fig. 1).

Of the 1204 respondents answering the vaccine effect question, 18.7% would require at least a 20% effect to decide to buy the vaccine, 13.3% required at least a 40% effect, 20.2% required at least a 60% effect, 20.8% required at least an 80% effect, 15.7% required a 100% effect, and 11.4% would not buy the vaccine in any case (Fig. 2). An effect of age was found. Grouping the 170 respondents aged 51 years or older, we found that 28.8% would buy the vaccine even if it gave only a 20% reduction in the incidence of TD, while only 16.6% of those younger than 51 years old would have bought it ($P = 0.00036$) (Fig. 3). No significant difference was found between men and women, or between the different income categories.

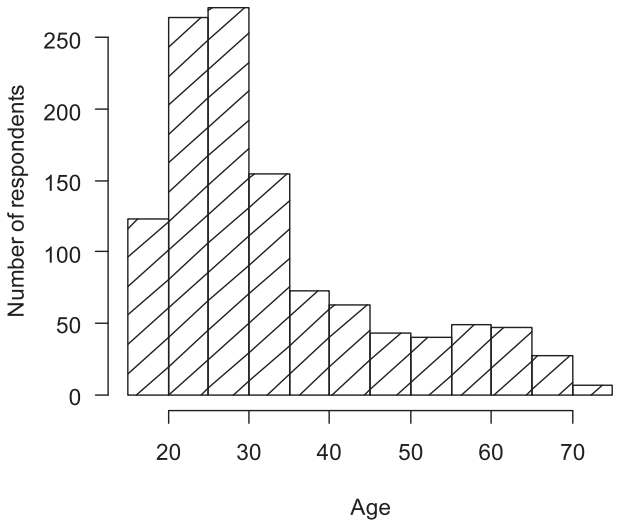

Fig. 1. Age distribution of the respondents. First bar: 16–20 years, second bar: 21–25 years, etc. 42 respondents did not enter their age.

4. Discussion

A possible bias of the study may be the seemingly low response rate. However, the form could only be presented to the clients when the receptionists had time to do so, and few of the clients refused to fill the form. The most frequent reason for not completing the form,

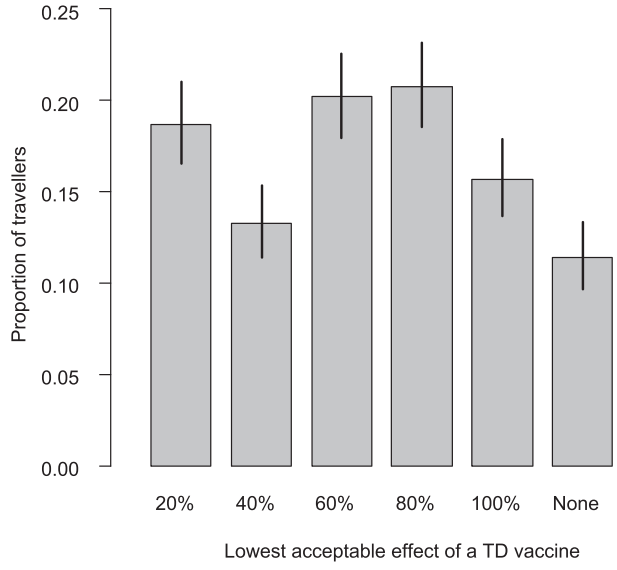

Fig. 2. The proportion of travellers willing to pay US$65 for a vaccine against traveller's diarrhoea (*y*-axis), given various levels of the vaccine's effect (*x*-axis). The right-most bar shows the proportion of travellers who would not have bought the vaccine in any case. (Error bars: 95% CI).