Is caviar a risk factor for being a millionaire?

Anders Huitfeldt argues that the answer depends on your definition of "risk factor" and calls for greater clarity in research

he risk factor approach to epidemiology was introduced by the Framingham Heart Study investigators, 12 who first alluded to the idea in 1951.3 The first use of the term "factor of risk" appeared in 1961, 4 but it was not precisely defined. The resulting semantic confusion has hindered precise communication about study design and data analysis.

To illustrate the problem, let us suppose that you want to study the causes and distribution of personal wealth. You have a secretive friend, and, among other questions, you are interested in knowing whether he is a millionaire. You are aware that there are some attributes, or risk factors, that are thought to be linked to being a millionaire. You decide to investigate.

#### What is a risk factor?

The first step is to choose your definition of risk factor. Clinical research can generally be divided into four broad objectives based on the intended use of the information obtained by the study: diagnosis, prognosis, treatment effects, and aetiology. Each of these research objectives is associated with a different definition. The table gives examples of how these four definitions of risk factor are used in the scientific literature and shows how each definition describes a different relation between the dependent variable and the independent variable.

Commonly used statistical techniques do not automatically differentiate between the types of relation described in the table,15 and a model adapted to studying one type may not be appropriate for another.16

Therefore, when conducting observational studies. data analysis needs to be designed to match the particular definition that is being considered.

## **Semantics discussion**

Returning to the secretive friend, you decide to find out whether he is a millionaire (diagnosis) by exploring the association between caviar and wealth. You conduct a large scale prediction study to answer this question and confirm that people who eat caviar are more likely to be millionaires. Therefore, when you observe that your dining companion orders a fine beluga, you heighten your suspicion that he is wealthy.

Next, hoping to piggyback off the success of another promising young acquaintance, you turn your interest to predicting whether a person will become a millionaire in the future (prognosis). However, after a follow-up study lasting several years, you conclude that there is little to be gleaned from knowing a person's baseline caviar consumption. Caviar consumption in the present is therefore not a reliable prognostic factor for future wealth.

After falling out with your young friend, you conclude that you will have to make your first million on your own. In looking for insight on

**Semantic** confusion has hindered precise communication about study design and data analysis

what actions you can take to bring about this objective (treatment effects), you conduct several randomised trials to estimate the causal effect of eating caviar. In these trials you recruit a large number of non-millionaires and randomly assign half of them to spend most of their income on caviar whereas the other half avoids it altogether.

Regrettably, you find that not only does caviar not make you a millionaire, it has an unfortunate tendency to bankrupt a person.

After spending a few years resolving some problems with your bank and the institutional review board, you turn your attention to understanding the role of caviar in the mechanism of wealth creation (aetiology).

You suspect that outside randomised trials, people who are susceptible to the detrimental effects of caviar always become addicted to the delicious black stuff and therefore never become millionaires. However, after consulting numerous textbooks on causal inference, you discover that this hypothesis is not testable with currently available statistical theory without strong and often unrealistic assumptions. Therefore, you fail to reach a conclusion.

Your extensive studies have shown that caviar is useful for predicting if

#### **KEY MESSAGES**



The definition of "risk factor" will vary depending on whether a research question is exploring diagnosis, prognosis, treatment effects, or aetiology

Unless a definition is specified, it is not possible for readers of research papers to understand what the investigators attempted to learn or evaluate whether they succeeded in their objectives

Journal editors should require authors to specify the intended use of the research findings and ensure that the methods were appropriate

someone is a millionaire (diagnosis/detection) but not for predicting if they will become a millionaire in the future (prognosis). Furthermore, you conclude that excessive consumption may reduce your probability of becoming a millionaire (treatment effect) but you are unable to answer questions about caviar's role in the mechanism of wealth creation (aetiology) without relying on questionable assumptions.

This brings us to the first crucial point: If scientist A asserts that caviar is a risk factor, it is unclear which type of relation he is referring to. Therefore, if scientist B disagrees but uses a different definition of risk factor, they both may be right.

There is no study design that can resolve this disagreement: the scientists are not arguing about the underlying reality but about who gets to define the term risk factor.

# **Ambiguous research objectives**

Determining if an observerational study supports its conclusions depends on what the study's authors are trying to find out: a method that will simultaneously answer questions about diagnosis, prognosis, treatment effects, and aetiology cannot exist.

How could such a method exist, when these questions can have different answers? In other words, the relevant methodological questions the reader engages with to determine if the conclusions are

supported depend on what the authors are trying to achieve—that is, in which definition of risk factor they are interested.

This brings us to the second crucial point. Unless the research objective is clearly defined in terms of an explicitly stated definition of risk factor, it is not possible to evaluate whether the study design and data analysis are appropriate to answer the research questions, and therefore not possible to evaluate the credibility of the study or its conclusions.

## Implications for research

Some have advocated reducing ambiguity by settling on a single definition of risk factor. For example, Miquel Porta's *Dictionary of Epidemiology*<sup>17</sup> defines a risk factor as "a factor that is causally related to the change in the risk of a relevant health process, outcome, or condition." However, this approach can only solve the problem if all researchers agree to use the term only in this sense.

Moreover, this definition implicitly assumes that

Enjoying a fine beluga in the present is not a reliable prognostic factor for future wealth epidemiologists are only interested in causality, to the exclusion of other worthy research objectives such as reducing diagnostic<sup>18</sup> or prognostic<sup>19</sup> uncertainty.

Instead, I suggest that journal editors should enforce a taboo<sup>20</sup> on the term "risk factor," thereby forcing investigators to spell out exactly what they mean by the term. For example, authors could be required to specify whether they are interested in a diagnostic factor, a prognostic factor, an aetiological factor, or a treatment effect.

Only then will it be possible for readers to understand exactly what the investigators intended to learn, and to engage in productive scientific conversation about whether they succeeded in accounting for the biases associated with that particular research objective.

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helpful comments.



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Objectives of clinical research and associated definitions of risk factor					
Research objective	Definition of risk factor*	Suggested term	Example of application	Preferred data analysis or study design	Relevant biases and shortcomings
Diagnosis	Any personal attribute that can be used to make a diagnosis more reliable	Diagnostic factor	Serum cholesterol in people presenting with chest pain <sup>5</sup>	Prediction model with binary outcome variable (measured at the same time as the diagnostic factor)†	Ascertainment of outcome may have imperfect sensitivity and specificity. Model may be overfit to training dataset
Prognosis	Any personal attribute that can be used to make more reliable predictions about future risk of medical conditions	Prognostic factor	Serum cholesterol predicts future cardiovascular disease <sup>6</sup>	Prediction model with time-to-event outcome variable	As above
Treatment effects	An action that may be taken to increase or decrease the probability of the outcome	Treatment effect	Cardiac risk is reduced by lowering serum cholesterol levels <sup>7</sup>	Randomised controlled trials. Observational studies with explicit causal models <sup>8</sup>	Confounding, selection bias, etc
Aetiology	A phenomenon, action, or substance that has a role in the aetiological mechanism	Aetiological factor	Cholesterol is involved in the mechanism behind atherosclerosis <sup>9</sup>	Some aetiological questions can be examined using the same methods as for treatment effects (eg, mendelian randomisation). <sup>10</sup> For others, there is no consensus on preferred study design. Relevant concepts include reverse causal inference, <sup>11</sup> excess fraction, <sup>12</sup> aetiological fraction, <sup>13</sup> and sufficient component cause models <sup>14</sup>	Imprecisely stated research questions because of current state of statistical methods

<sup>\*</sup>Note that not all commonly accepted risk factors for cardiovascular disease meet all four definitions. For example, family history is valid both as a prognostic factor and as a diagnostic factor, but if you attempt to reduce your patient's coronary risk by starting their parents on primary prevention, you are likely to be struck from the register. Some variables even have opposite effects depending on whether we are interested in prediction or causation. For example, if the patient's clinical history shows that he has had a coronary artery bypass graft, your risk estimate increases for the purposes of both diagnosis and prognosis, although the procedure itself almost certainly reduced his risk. †Such models are often termed "detection models" in the data mining literature, where they are used to detect fraud.

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ORIGINAL RESEARCH Genome-wide association study of asparagus anosmia

# Sniffing out significant "Pee values"

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**Objective** To determine the inherited factors associated with the ability to smell asparagus metabolites in urine.

Design Genome-wide association study.

**Setting** Nurses' Health Study and Health Professionals Follow-up Study cohorts.

Participants 6909 men and women of European-American descent with available genetic data from genome-wide association studies.

Main outcome measure Participants were characterised as asparagus smellers if they strongly agreed with the prompt "after eating asparagus, you notice a strong characteristic odour in your urine," and anosmic if otherwise. We calculated per-allele estimates of asparagus anosmia for about nine million single nucleotide polymorphisms using logistic regression. P values <5×10<sup>-8</sup> were considered as genome-wide significant.

Results 58.0% of men (n=1449/2500) and 61.5% of women (n=2712/4409) had anosmia. 871 single nucleotide polymorphisms reached genome-wide significance for asparagus anosmia, all in a region on chromosome 1 (1q44: 248139851-248595299) containing multiple genes in the olfactory receptor 2 (*OR2*) family. Conditional analyses revealed three independent markers associated with asparagus anosmia: rs13373863, rs71538191, and rs6689553.

Conclusion A large proportion of people have asparagus anosmia. Genetic variation near multiple olfactory receptor genes is associated with the ability of an individual to smell the metabolites of asparagus in urine. Future replication studies are necessary before considering targeted therapies to help anosmic people discover what they are missing.

#### Introduction

Benjamin Franklin once remarked, "a few stems of asparagus eaten, shall give our urine a disagreeable odour." For those who can detect the distinctive odour it must seem, as the chemist Louis Lémery wrote in 1702, "They [asparagus spears] cause a filthy and disagreeable smell in the urine, as everybody knows."

But not everybody does seem to know, as a subset of the population is unable to smell the methanethiol and S-methyl thioesters metabolites produced after asparagus consumption. It was uncertain whether this phenomenon<sup>5</sup> was a failure to produce the metabolites or a specific anosmia. Foundational research found that the prevalence differs between people and across populations. 6-8 Studies have shown that those who cannot smell the odour in their own urine are also unable to smell it in the urine of known producers, <sup>79</sup> lending credence to the anosmia hypothesis. The phenotypic distribution, however, suggests a genetic component.67

Few scientists have examined the inherited factors associated with asparagus anosmia. The results of a genome-wide association study<sup>10</sup> showed that a single nucleotide polymorphism (SNP)—an individual genetic variation in DNA—rs4481887 located near olfactory receptor 2M7 (OR2M7) was statistically significantly associated with participant reported asparagus anosmia. We carried out a genome-wide association study of asparagus anosmia among two large and well characterised US based cohorts.

#### Methods

This study was conceived during a meeting attended by several of the coauthors, where it became apparent that some of us were unable to detect an unusual odour in our urine after consuming asparagus. To further examine this phenomenon we sought epidemiological studies, and found the Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS). We included participants of European descent from these cohorts with available genomewide data from nested case-control studies. 11

# Definition of asparagus anosmia

The main outcome was asparagus anosmia, which was collected by questionnaire administered in 2010. Participants were asked: "After eating asparagus, you notice a strong characteristic odour in your urine." Those who responded "Strongly agree" were categorised as being able to smell asparagus and those who responded "Moderately agree," "Slightly agree," "Slightly disagree," "Moderately disagree," and "Strongly disagree" were categorised as having asparagus anosmia.

# Statistical analysis

We carried out multivariable logistic regression analyses, modeling SNPs as ordinal variables and asparagus anosmia as the outcome. Models were adjusted for age, sex, smoking status (never, former, and current), and the first three principal components of genetic variation (to adjust for potential confounding by ethnicity). The analyses were conducted separately for the genotyping platforms and combined the estimates using fixed effects meta-analysis. We considered two sided P values <5×10<sup>-8</sup> to indicate genome-wide significance. <sup>12</sup>

To further explore the association between genetic variation and asparagus anosmia, we performed sequential conditional analysis using GCTA-COJO, a tool for genome-wide complex trait analysis. <sup>13</sup> <sup>14</sup> This method allows adjustment for SNP-B when evaluating the association between SNP-A and anosmia to determine if they have independent effects or are both associated with the outcome through correlation.

# WHAT IS ALREADY KNOWN ON THIS TOPIC

- Asparagus tends to endow human urine with a distinctive odour
- The ability to smell asparagus metabolites in urine varies across people and populations

#### **WHAT THIS STUDY ADDS**

 This study provides important knowledge of the inheritance of asparagus anosmia, and genetic variation was identified near multiple olfactory receptor genes

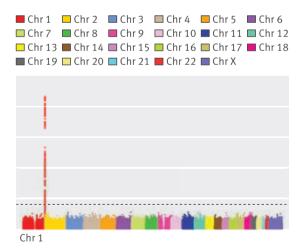


#### Results

Among 6909 participants, 39.8% (n=2748) strongly agreed that they could perceive an odour in their urine after eating asparagus and 60.3% (n=4161) said they could not (see table 1 on thebmj.com). The proportion of participants unable to detect the odour was slightly lower among men in the HPFS compared with women in the NHS.

Overall, 871 SNPs reached genome-wide significance  $(P<5\times10^8)$  for asparagus anosmia. The figure displays a Manhattan plot in which each dot represents an SNP laid out across the chromosomes from left to right. The height of the peaks corresponds to the strength of association with asparagus anosmia. The large peak represents a 0.46 Mb region on chromosome 1 (248139851-248595299). This region was split into two subregions by a recombination hotspot and contained multiple members of the olfactory receptor 2 (OR2) gene family. The SNP identified previously in one study 10 and validated in another 9 (rs4481887) was also significantly associated with asparagus anosmia in this population  $(P=1.41\times10^{-43})$  and is located in the same 1944 region identified in this analysis.

Sequential conditional analysis revealed three loci independently associated with asparagus anosmia in this region (rs13373863, rs71538191, and rs6689553) (see table 2 on thebmj.com). After conditioning on these three SNPs, no other SNP reached genome-wide significance.



Manhattan plot showing results of genome-wide association studies for asparagus anosmia. Chr=chromosome

#### Discussion

Anosmia for the urinary metabolites of asparagus is common. In this study of 6909 European-American men and women, three in five were unable to detect the odour in their urine. Linking information from genome-wide association studies with the anosmia trait, we found 871 unique SNPs reaching genome-wide significance. All were located on chromosome 1, containing multiple members of the olfactory receptor 2 gene family.

Our analyses included imputed SNPs from the 1000 Genomes Project, which allowed us to more thoroughly identify novel SNPs that might interact with the previously identified SNP to produce the anosmic phenotype. The previous genome-wide association studies of asparagus anosmia identified an association with rs4481887, 8993 base pairs upstream of *OR2M7*. After efforts to refine the signal, we identified three independent association signals in this region, tagged by rs13373863, rs71538191, and rs6689553. Although we did not conduct a further replication study of the genome-wide signals, our findings validate and extend the previously reported associations between *OR2* and asparagus anosmia.

The molecular basis of human olfaction is not fully understood. Research has investigated specific anosmias and hyperosmias as a key to understanding olfaction, often focusing on the genetic determinants of these phenomena to better understand the overall functional relation.

Women in the NHS were more likely to report asparagus anosmia than men in the HPFS, despite the fact that women have been shown to more accurately and consistently identify smells. <sup>23 24</sup> We hypothesise that this unexpected result might be due to under-reporting by modest women who loathe to admit their urine smells. It is possible that women are less likely than men to notice an unusual odour in their urine because their position during urination might reduce their exposure to volatile odorants. That we rely on self report of perception rather than on an objective measurement of olfactory stimulation highlights a weakness of our study design. Our study is also limited by a one-off measure of ansomia.

Outstanding questions on this topic remain; first and foremost perhaps is why a delicacy such as asparagus results in such a strong odour? Why does genetic variation across the olfactory receptor genes exist that leads to susceptibility to asparagus anosmia? What selective pressures drive different populations of people to have the ability to smell the metabolites of asparagus and others to not? And, will scientists take the results of our study and apply gene editing techniques to convert smellers to non-smellers?<sup>25</sup>

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#### **ORIGINAL RESEARCH**

Prospective cohort study of unsolicited and unwanted academic invitations

# We read spam a lot

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Objectives To assess the amount, relevance, content, and suppressibility of academic electronic spam invitations to attend conferences or submit manuscripts.

Design Prospective cohort study.

**Setting** Email accounts of participating academics.

**Participants** Five intrepid academics and a great many publishers, editors, and conference organisers.

**Intervention** Unsubscribing from sender's distribution lists.

Main outcome measures Number of spam invitations received before, immediately after, and one year after unsubscribing from senders' distribution lists. The proportion of duplicate invitations was also assessed and the relevance of each invitation graded to the recipient's research interests. A qualitative assessment of the content of spam invitations was conducted.

Results At baseline, recipients received an average of 312 spam invitations each month. Unsubscribing reduced the frequency of the invitations by 39% after one month but by only 19% after one year. Overall, 16% of spam invitations were duplicates and 83% had little or no relevance to the recipients' research interests. Spam invitations were characterised by inventive language, flattery, and exuberance, and they were sometimes baffling and amusing.

**Conclusions** Academic spam is common, repetitive, often irrelevant, and difficult to avoid or prevent.



#### Introduction

Unsolicited and unwanted (spam) electronic invitations to speak at or attend conferences, or to write for or edit journals are a burgeoning aspect of academic life. Colleagues regard such invitations with wry amusement, intense frustration, or resignation.

Few studies have focused on academic spam. In the Academic Spam Study we investigated the amount, relevance, content, and suppressibility of academic spam emails.

# WHAT IS ALREADY KNOWN ON THIS TOPIC

 Anecdotal and limited published evidence suggests that spam academic invitations to publish or present research might be common and irritating

#### **WHAT THIS STUDY ADDS**

- Academic spam invitations are common and irritating, with 2.1 invitations received daily by each investigator
- The incidence of spam invitations is modestly reduced in the first month after unsubscription but the effect wanes after one
- 16% of spam invitations were duplicates and 83% were of little relevance to the recipient

#### Methods

# Academic participants

In a deftly ironic twist, AG emailed five prospective collaborators to invite them to participate in the study. Invitations addressed the recipient as "Eminent Professor," included five or more exclamation marks, and lacked an option to unsubscribe. Non-response to an invitation prompted a flurry of follow-up emails. Inclusion criteria were personal acquaintance with the first author, a sense of humour, a relentless wish to conduct leading edge research, desperation for academic outputs, and an inability to say "no." The exclusion criterion was application of a personal email spam filter. Four of the invited academics agreed to participate; one invitee lacked the inability to say "no."

# Collation and analysis of spam and non-spam emails

We defined academic spam as unsolicited and unwanted email invitations to attend or present at a conference or to write or edit for a journal. We included all emails the recipients considered to be spam. The investigators collected

spam emails received between 1 February 2014 and 30 April 2014. During May 2014, the investigators unsubscribed from the mailing lists of organisations distributing spam. During June 2014 and

void or prevent.

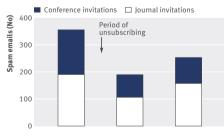


Unsolicited and unwanted (spam) electronic invitations are a burgeoning aspect of academic life

April 2015, the investigators again collected spam emails.

We assessed the number of spam emails received in each collection phase. The investigators rated their spam invitations as being of no, low, medium, or high relevance to their academic careers.

Between 1 February 2014 and 30 April 2014, the investigators collated invitations to speak at academic meetings or write for journals that they did not regard as spam.



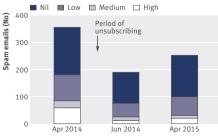


Fig 2  $\mid$  Number of spam invitations by type and relevance to recipient

## RESULTS

The Academic Spam Study investigators are mid-career, modestly productive, and conduct research across several disciplines (table 1, see thebmj.com). On the basis of salutations contained in emails received during the study period, each investigator is highly esteemed. Modesty precludes a systematic description of the height of the esteem but according to these emails each investigator has "made important contributions," is a "distinguished expert," and has "great expertise," sometimes in disciplines surprisingly remote from the primary academic focus.

#### **BULK SPAM**

Unsurprisingly, therefore, we received many spam invitations. Between 1 February 2014 and 30 April 2014, 936 spam invitations were received: an average of 312 for each calendar month (fig 1, see thebmj.com).

Spam invitations outnumbered non-spam invitations (n=11) during this period by more than 80-fold. After unsubscribing from the mailing lists of organisations distributing spam during May 2014, the number of invitations received

in June 2014 decreased by 39%, to 190. In April 2015, the number of spam invitations had increased to 253.

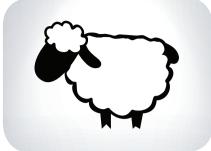
The proportions of spam invitations to write manuscripts and attend conferences were similar before and after unsubscribing (fig 2). Consistently, more than 75% of spam invitations were of no or low relevance to the recipient.

# REHEATED SPAM

In April 2014, June 2014, and April 2015, 74 of 356 (21%), 30 of 190 (16%), and 27 of 253 (11%) of spam emails, respectively, were duplicates. The higher proportion in April 2014 was attributable to the receipt by one investigator of 29 duplicate messages from the Korean Society for Bone and Mineral Research, 19 of which arrived within 72 seconds on one frenetic evening and the other 10 within 57 seconds on a different evening.

#### SPAM DISTRIBUTORS

During April 2014, four publishers each distributed more than 10 spam invitations to write a manuscript or edit a journal (table 2, see thebmj.com). These publishers have previously been labelled "predatory." Three—Bentham Science, Herbert Publications, and Science Domain—provided an option to unsubscribe. Spam emails from Bentham Science and Herbert Publications almost completely ceased after the month of unsubscribing.



#### SPAM DRESSED AS LAMB

We identified some eye catching subject lines. We learnt that good times happen at oral health conferences ("Learn and Have Fun at the International Conference on Orthognathic Surgery and Orthodontics"). We were tempted by "Cracking the Mysterious Psychiatric Disorders at Euro Psychiatry 2015," and to "Unleash (y)our research ideas at Orthopedics and Rheumatology 2014." We were interested in "Biologically signifying the clinical molecule," and extremely interested in "Special Issue on Wine Health"—sadly, no offers to recruit mid-career academics to studies of wine were apparent.

#### **TASTY SPAM**

We found several memorable examples of tasty academic spam (box 1). We were impressed by the great enthusiasm of the invitations, featuring up to six exclamation marks! Flattery and inventive turns of phrase were prominent.

#### STIR FRIED SPAM

Sometimes we found scrambled spam. We were unsure what to make of the session at the 3rd Annual World Congress of Geriatrics and Gerontology 2015 that "can provide you with a best promotion channels in partner seeking, investor relation retreatment and talent search." Rather too many invitations were disrespectful of our eminent selves—for example, "Dear Dr.MJ Mark JMJ Mark J," "Dear Dr. Name, Greetings for the day!," and "Dear Dr. {firstname}."

#### PREMIUM SPAM

Some spam was almost too delicious to ignore. Box 2 lists journals and conferences that we found especially intriguing.



the **bmj** | 17-31 December 2016 **481** 

#### Box 1 | Examples of tasty academic spam

#### Friendly and exuberant

"We would be really happy to anchor with you"

"Let your wisdom enkindle others"

"Looking forward for an everlasting scientific relationship!"

"I would like to extend my sincere congratulations on the publication of your highly cited original article, <Prevalence and clinical factors associated with gout in patients with diabetes and prediabetes, in the field of diabetes. As of today, this article has been cited more than 4 times"."

"It gives us immense pleasure to share this moment of happiness that *Journal of Global Economics* is planning to release continuous issues every month"

"The purpose of this letter is to solicit your gracious presence as a speaker..."

"We have been through your articles and we are enthralled to know about your reputation and commitment in the field"

"We have chosen selective scientists who have enormously contributed to the scientific community to have their work publish in our journal

#### Aspirational and dedicated

"Aspire to clear all the barriers in dissemination of information and knowledge around the world"

"We aim to enlighten the lamp of information across the sphere especially in the areas of science and technologies"

"Ommega Publishers welcomes you to the newest chapter in the long history of scientific manuscript publication"

"International Journal of Cardiovascular Research, a new frontier among the peerreviewed scholarly Journals..."

"GBC 2015 will...draw together both novice and veterans from the biotechnological front from all over the world to herald avenues to innovations and advancements in the biotechnology sphere both at regional and global level"

"We are creating a kind of mind storming forum to create a new therapeutic approaches"

"Our dedicated proofreaders, cheerfully labor on your manuscripts in a speedy way, with high quality standards on the back of their minds and offer you very appropriate content improvisation wherever required"

"The scientific program paves a way to gather visionaries through the research talks and presentations and put forward many thought provoking strategies"

"Hence the need for integrating the research into the fast paced era needs the a source of rapid dissimilation with a reliable platform. We invite you to be a part of this modern perception by going open access with us"

#### **Thematic**

Lipids 2015—"Solving the impetus of innovations in lipid world"

World Congress of Oral and Dental Medicine—"Keep the door of lives"

The 7th Annual International Congress of Cardiology—"Bring new vitality into life"

\*Emphasis is ours.

#### **Discussion**

The Academic Spam Study shows that midcareer academics in New Zealand receive on average 2.1 spam invitations each day to publish papers and attend conferences. Unsubscribing had a modest and short lived effect on the quantity of received spam, 83% were of little or no relevance to the recipient. Some organisations send spam invitations without an unsubscribe option, or persist despite recipients requesting unsubscription.

#### Strengths and weaknesses of this study

Our study has limitations. Some invitations were removed by the institutional spam filter, so we might have underestimated the amount of spam. Our sample of researchers was too small to be representative of the academic community. New Zealand is a small, remote country that might not be targeted by academic spam distributors, even though we have held the Rugby World Cup since 2011, and the *Lord of the Rings* movies were filmed here. <sup>3</sup>

#### Comparison with other studies

Published research on academic spam is limited. Some senders of spam journal invitations are bad eggs, 4 who misrepresent their locations and are usually open access publishers. 5 Spam invitations are often issued by predatory organisations, 1 the modus operandi of which threatens academic integrity. 6 Vigorous responses to spam invitations might generate humorous outcomes but not stop the invitations. Attempts to unsubscribe from spam invitations are only moderately successful, but stringent email filtering or threatening recidivist organisations with legal action might stop further communications.

# Implications and future research

We suggest further research on academic spam: "Nobel and prestigious colleagues,

We are enthralled by prospect of novel research focus of academic spam so we make a proposition to improve enlightenment of evidence. We wish greatly to start journal and convene scientific meeting that focus on academic spam, so illustrious colleagues can form interdisciplinary web of scientific rigour to advance knowledge. Maybe we will christen soon *Journal of Advances in Interdisciplinary Academic Spam* and launch with alacrity the First Annual International Symposium on Academic Spam (Spam-2017). Once we identify publisher and conference organiser we will email academics to join this exciting novel venture! Honourable colleagues, stay tuned!!!!!!"

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Find this at: http://dx.doi.org/10.1136/bmj.i5383

#### Box 2 | Premium spam, featuring intriguing journals and conferences we wish we had attended

## **Journals**

International Journal of Advances in Case Reports Hair: Therapy and Transplantation

Therapeutic Hypothermia and Temperature Management Journal of Investigative Medicine High Impact Case Reports Journal of Ancient Diseases and Preventive Remedies Journal of Laboratory Automation

 $Interdisciplinary {\it Journal} of {\it Microinflammation}$ 

#### Conferences

Friends of Israel Urological Symposium 2014

Global 1000: Meet | Partner | Deal: Showcase + Conference Sept 2014

Conference of the Global Innovation and Knowledge Academy (GIKA): "Turning Kurt Lewin on his head: Nothing is so theoretical as a good practice"

World Congress on Controversies in Bovine Health, Industry and Economics 2015 International Conference on Steel and Composite Structures