Research



bmj.com/podcasts Right or happy

Author Bruce Arroll discusses his paper and its findings

Being right or being happy: pilot study

Bruce Arroll, Felicity Goodyear-Smith, Simon Moyes, Timothy Kenealy

Introduction

Three of the authors are general practitioners who see many patients and couples who lead unnecessarily stressful lives by wanting to be right rather than happy. Mathieu encourages her psychotherapy clients "to try to live in the gray. There are a million shades of gray" (although a recent erotic novel suggests there are only 50) "on the spectrum of white to black, and each provides a much richer telling of a story that is hardly ever as clear as this or that. So, when we looked a bit more closely, we saw that 'right versus happy' was not so much about getting crowned the winner or loser, a genius or fool; it was more about flawed thinking and a desire to want to feel being in control." This might be the first study to systematically assess whether it is better to be right than happy; a Medline search in May 2013 found no similar articles. Our null hypothesis was that it is better to be right than happy.

Participants, setting, and design

To be eligible participants had to be part of a couple and willing to take part in the study. We carried out a parallel trial with one man and one woman in their own home. It was decided without consultation that the female participant would prefer to be right and the male, being somewhat passive, would prefer to be

The male was informed of the intervention while the female participant was not (this form of pre-randomisation is known as the Zelen method²). The female participant was blind to the hypothesis being tested, other than being asked to record her quality of life.

Intervention

The intervention was for the male to agree with his wife's every opinion and request without complaint. Even if he believed the female participant was wrong, the male was to bow and scrape.

Main outcome measure

We measured quality of life with a Likert score of 1 to 10 (10 being the best possible quality

Department of General Practice and Primary Health Care. University of Auckland, Private Bag 92019, Auckland, New

Correspondence to: B Arroll bruce.arroll@auckland.ac.nz



Quality of life by duration of intervention

of life). Although our tool was unvalidated, it was thought to have face validity. It was justified on the grounds that brevity was essential, given that the intervention was administered in a potentially complex domestic environment.

Results

Two participants were eligible and both (100%) were randomised. All participants received the treatment and were analysed for the primary outcome with an intention to treat analysis. Several baseline characteristics differed between the subjects (see appendix).

The data safety monitoring committee stopped the study because of severe adverse outcomes after 12 days. By then the male participant found the female participant to be increasingly critical of everything he did. The situation had become intolerable by day 12. He sat on the end of their bed, made her a cup of tea, and said as much; explained the trial and then contacted the Data Safety Monitoring committee who terminated the trial immediately.

There were three data points in the intervention group and two in the control group (the control participant had become hostile to recording her quality of life). The man's quality of life score had fallen

from 7 out of 10 at baseline to 3 at 12 days; the women's had increased slightly from 8 to 8.5 at six days (figure). The difference between the two participants' QOL scores over time is

significantly different (P=0.004, calculated with a repeated measures generalised linear model). We should treat the results cautiously because we cannot discount causes other than treatment reducing the male participant's score. It seems that being right, however, is a cause of happiness, and agreeing with what one disagrees with is a cause of unhappiness. We cannot discount that the difference in results might be caused by differences between the two treatment groups, which unfortunately we were unable to match by possible confounders such as sex.

The harms were estimated as 100% as all participants who received the intervention reported a serious adverse event.

Discussion

The results of this trial show that the availability of unbridled power adversely affects the quality of life of those on the receiving end.

Strengths and weaknesses

The study has some limitations. There was no trial registration, no ethics committee approval, no informed consent, no proper randomisation, no validated test instrument, and questionable statistical assessment. We used the eyeball technique for single patient trials which, as Sackett says, "more closely matches the way we think as clinicians."3

Generalisability

Many people in the world live as couples, and we believe that it could be harmful for one part-

ner to always have to agree with the other. However, more research is needed to see whether our results hold if it is the male who is always right. Full details including references and competing interests are in the version on bmj.com. Cite this as: BMJ 2013;347:f7398

A statin a day keeps the doctor away: comparative proverb assessment modelling study

Adam D M Briggs, Anja Mizdrak, Peter Scarborough

OBIECTIVE

To model the effect on UK vascular mortality of all adults over 50 years old being prescribed either a statin or an apple a day.

DESIGN

Comparative proverb assessment modelling study.

SETTING

United Kingdom.

POPULATION

Adults aged over 50 years.

INTERVENTION

Either a statin a day for people not already taking a statin or an apple a day for everyone, assuming 70% compliance and no change in calorie consumption. The modelling used routinely available UK population datasets; parameters describing the relations between statins, apples, and health were derived from meta-analyses.

MAIN OUTCOME MEASURE

Mortality due to vascular disease.

RESULTS

The estimated annual reduction in deaths from vascular disease of a statin a day, assuming 70% compliance and a reduction in vascular mortality of 12% (95% confidence interval 9% to 16%) per 1.0 mmol/L reduction in low density lipoprotein cholesterol, is 9400 (7000 to 12500). The equivalent reduction from an apple a day, modelled using the PRIME model (assuming an apple weighs 100 g and that overall calorie consumption remains constant) is 8500 (95% credible interval 6200 to 10800).

CONCLUSIONS

Both nutritional and pharmaceutical approaches to the prevention of vascular disease may have the potential to reduce UK mortality significantly. With similar reductions in mortality, a 150 year old health promotion message is able to match modern medicine and is likely to have fewer side effects.

BHF Health Promotion Research Group, Nuffield Department of Population Health, University of Oxford, Headington, Oxford OX3 7LF, UK Correspondence to: A D M Briggs

adam.briggs@dph.ox.ac.uk

Introduction

"An apple a day keeps the doctor away," a public health message delivered by parents and teachers since the 19th century, is an example of how concise, clear, and accurate Victorian health promotion can truly stand the test of time.

Today in the United Kingdom, lifestyle changes are the recommended first step for primary prevention of vascular disease,2 but calls are being made for greater use of drugs in primary prevention, perhaps the best known example being the polypill.³ In the UK, the only drug class recommended for primary prevention at a population level is statins for people at 20% or greater risk of a cardiovascular event in the next 10 years.² Recent meta-analyses have indicated similar relative benefits to patients with a five year risk of a major vascular event of less than 1% to those at greater than 20% risk. 4 This has led to calls to use statins for cardiovascular disease prevention at the population level, particularly for people aged 50 years and over.5

We set out to test how almost 150 years of Victorian wisdom might compare with the more widespread use of statins in primary prevention. We modelled the effect on vascular mortality of prescribing everybody in the UK aged over 50 either an apple or a statin a day, estimated the number of adverse events, and compared the subsequent drug, or fruit, costs.

Methods

Data on the effect on vascular mortality of the UK population of a statin a day came from a metaanalysis, which found that statins reduced the relative risk of vascular mortality by 12% (95% confidence interval 9% to 16%) per 1.0 mmol/L reduction in low density lipoprotein cholesterol and that on average this is reduced by 1.08 mmol/L over a year of treatment. 4 We applied this annual reduction to vascular mortality rates for the UK population aged 50 and over who are not taking a statin for primary disease prevention as reported in the Health Survey for England (stratified by sex and five year age categories, with age and sex specific statin uptake for Scotland, Wales, and Northern Ireland assumed to be the same as for England). 6-10 Assuming 70% compliance,11 we calculated the reduction in deaths from vascular disease as the difference between the number of vascular deaths in the population not taking statins, using current age and sex

Table 1 Nutritional composition of 100 g of apple		
Nutritional component	Amount per 100 g of apple	
Energy (kcal)	35.4	
Fat (g)	0.09	
Saturated fatty acids (g)	0.02	
Monounsaturated fatty acids (g)	0.01	
Polyunsaturated fatty acids (g)	0.05	
Cholesterol (mg)	0.00	
Fibre (g)	1.39	
Salt (g)	0.00	

specific mortality rates, and the number of deaths when assuming the new mortality rates.

We modelled the effect on vascular mortality of an apple a day on the entire UK population aged 50 and over by using the PRIME comparative risk assessment model. 12-15 This uses meta-analyses of studies to parameterise the relation between a wide range of nutritional factors and chronic disease mortality. We assumed apples to weigh 100 g. Baseline population diet and the nutritional composition of apples came from the Living Costs and Food Survey 2010 (table 1).16 We held the total calorie intake constant, assuming that the addition of calories consumed in apple form would lead to a proportionate decrease in calories consumed elsewhere. We assumed the effect on health of consuming an extra apple a day to be the same irrespective of baseline apple consumption, as described in meta-analyses describing the relations between fruit and vegetable consumption and cardiovascular disease. 17 18 We assumed compliance to be 70% and prescribing of statins not to change.

We modelled side effects of statins by using reports that statins lead to an excess incidence of myopathy of 0.5/1000 patients over five years, of rhabdomyolysis of 0.1/1000 over five years, and of diabetes diagnoses of 0.1% a year.4 We applied these to the extra population aged over 50 who would be taking statins, assuming 70% compliance, to give an estimated number of additional adverse events per year. Aside from the distress caused by a bruised apple, and the theoretical risk of identifying half a worm inside, apple related adverse events are not widely recognised.

We obtained costs of statins from the British National Formulary. 19 The cost of an apple came from weekly fruit and vegetable prices for the cheapest variety of dessert apple. 20 No costs were estimated for general practice appointments or the management of any side effects.

Sensitivity analyses investigated the effect of prescribing statins or apples to everybody over 30 rather than 50 years; the effect of 90% compliance with apple prescriptions (given that just 10% of the adult population manage less than one portion of fruit and vegetables a day²¹); and removing the assumption that the remainder of the diet, except calorie intake, would be adjusted to compensate for the additional apple.

Results

We estimate that 5.2 million people are eligible for statin treatment in the UK, with an extra 17.6 million people eligible if it became recommended as a primary prevention measure for everyone over 50. Assuming 70% compliance, offering statins to 17.6 million more adults would result in a reduction in the annual number of vascular deaths by 9400 (95% credible interval 7000 to 12500).

Table 2 shows the baseline daily UK diet and the diet after inclusion of an apple a day. ¹⁶ Applying this diet to 70% of the total UK population aged over 50 years (22 million people), we estimate the annual number of vascular deaths averted or delayed to be 8500 (95% credible interval 6200 to 10800). Prescribing statins to everyone over the age of 50 years is predicted to lead to 1200 excess cases of myopathy, 200 cases of rhabdomyolysis, and 12300 diagnoses of diabetes. The total extra cost of statin treatment from the drug alone is estimated at £180m (€217m; \$295m), compared with £260m for apples.

Sensitivity analyses

Prescribing either apples or statins to everybody aged over 30 is estimated to reduce the annual number of vascular deaths by 8800 (6500 to

diet ¹⁶ and diet after introduction of an apple a day				
Nutritional component	Baseline diet	With an apple a day (calorie neutral)	No change except for fruit (sensitivity analysis)	
Energy (kcal)	2027	2027	2027	
Total fat (g)	84.2	82.9	84.2	
Saturated fatty acids (g)	32.5	32.0	32.5	
Monounsaturated fatty acids (g)	31.0	30.4	31.0	
Polyunsaturated fatty acids (g)	15.3	15.0	15.3	
Cholesterol (mg)	230	226	230	
Fibre (g)	13.1	14.3	13.1	
Salt (g)	6.3	6.2	6.3	
Fruit and vegetables (g)	344	440*	444	

^{*}Daily increase in weight of fruit and vegetables consumption is not exactly 100 g, as total calorie consumption is assumed to remain the same meaning a small reduction in consumption from other fruits and vegetables.



Fewer side effects, too

11100) or 9600 (7200 to 12900) respectively, 3% more than prescribing to everybody over 50. The number of adverse events is predicted to double to 2400 cases of myopathy, 400 of rhabdomyolysis, and 24 400 diabetes diagnoses. The cost of statins would be £360m, and that of apples £480m. If compliance with apple prescriptions was 90%, the number of vascular deaths averted would increase to 11000 (8100 to 13900), 29% more than with 70% compliance, and would cost £339m in apples. Finally, if the apple prescription has no effect on the average diet except amount of fruit consumed, annual vascular deaths would reduce by 7100 (5000 to 9400), 20% fewer than if dietary compensation occurs.

Discussion

Prescribing an apple a day or a statin a day is likely to have a similar effect on population vascular mortality. Choosing apples may avoid more than a thousand excess cases of myopathy and more than 12 000 diabetes diagnoses. The basic costs of apples are likely to be greater than those of statins; however, NHS prescription prices and convenience may drive people to purchase their apples from a store, reducing direct NHS costs, or the NHS may be able to negotiate apple price freezes (although defrosted apples may not be so palatable).²²

The strengths of this study lie in the underlying data, which came from meta-analyses of trials and prospective cohort studies.

The reduction in the number of vascular events due to the increased use of statins vastly outweighs the excess incidence of haemorrhagic stroke and diabetes. However, limitations of the meta-analysis have been suggested, including the underestimation of side effects and no effect on all cause mortality for patients at low risk. This would suggest a possible added benefit of apples over statins for all cause mortality.

The predicted effects of a change in national policy to provide statins to everybody aged over 50 could vary for several reasons. Compliance may be less than 70% in a population who may think they do not need the treatment, and may reduce over time, meaning our results could overestimate future benefits and adverse events. We also apply the same treatment effect on vascular mortality to people of all ages, sexes, and cardiovascular risk profiles, but these may differ.²⁴ The estimate of population compliance with an apple a day is less evidence based. Although apples are both delicious and nutritious, this view is not consistently shared across the population. Equally challenging may be the additional time and difficulty associated with consuming an apple compared with a statin.

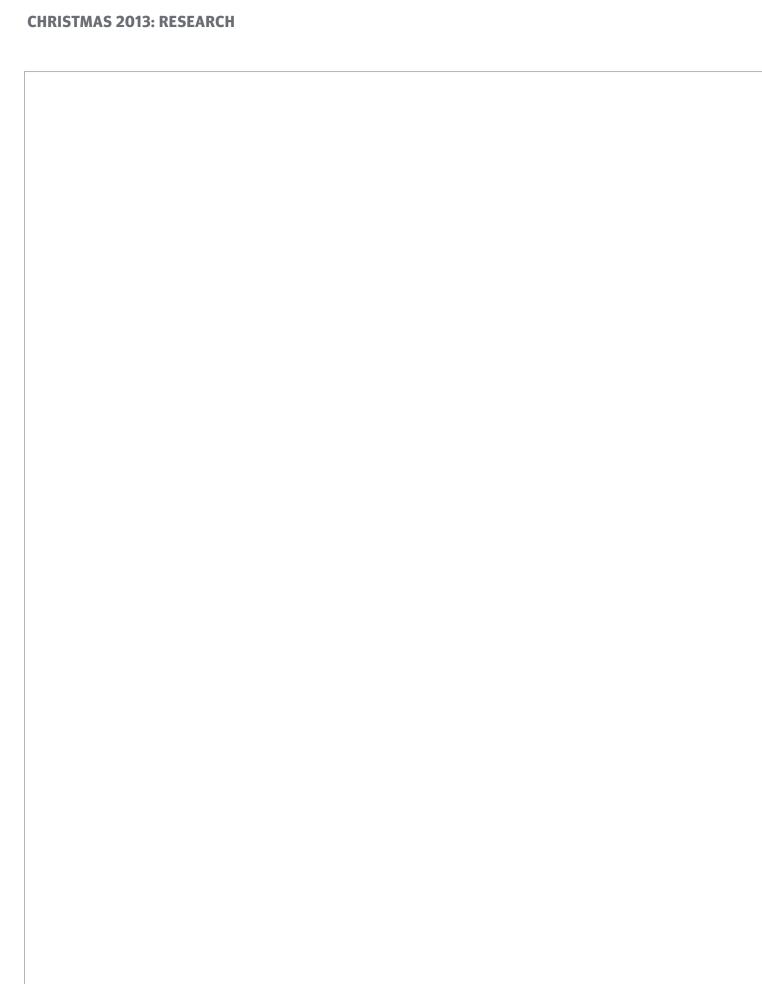
Further limitations are that fruit costs were taken in the autumn but are likely to vary around the year. Total calories consumed are assumed to remain the same in the apple model,²⁵ but what people may substitute their apple for is unclear. We assumed that the nutritional components of the average diet (table 2) would proportionately reduce by the increase in calories from 100 g of apple, but people might choose to remove other fruits from their diet instead. People may also choose to consume fewer total calories by replacing foods with a higher energy density with the low energy dense apple, potentially leading to even greater benefits on vascular mortality through reduced body mass index.26

Finally, we have not estimated the potential wider benefits of more than 12 million extra statin prescriptions to the drug industry and the jobs that would create, the boost to the apple farming industry of around 22 million extra daily requests for apples, or the effect on quality of life of fewer non-fatal cardiovascular events.

This study shows that small dietary changes as well as increased use of statins at a population level may significantly reduce vascular mortality in the UK. The five a day campaign to increase fruit and vegetable consumption has the potential to deliver significant population health benefits, ²⁷ ²⁸ but the UK is yet to adopt drug prescribing as a population level approach to primary prevention. This research adds weight to calls for the increased use of drugs for primary prevention of cardiovascular disease, as well as for persevering with policies aimed at improving the nutritional quality of UK diets.

We find that a 150 year old proverb is able to match modern medicine and is likely to have fewer side effects. Now to model the effect of inquisitiveness on feline mortality rates.

Full details including references and competing interests are in the version on bmj.com.



The survival time of chocolates on hospital wards: covert observational study

Parag R Gajendragadkar, ¹ Daniel J Moualed, ² Phillip L R Nicolson, ³ Felicia D Adjei, ¹ Holly E Cakebread, ¹ Rudolf M Duehmke, ¹ Claire A Martin ¹

OBJECTIVE

To quantify the consumption of chocolates in a hospital ward environment.

DESIGN

Multicentre, prospective, covert observational study.

SETTING

Four wards at three hospitals (where the authors worked) within the United Kingdom.

PARTICIPANTS

Anyone eating Quality Street and Roses chocolates.

INTERVENTION

Observers covertly placed two 350 g boxes of Quality Street and Roses chocolates on each ward (eight boxes were used in the study containing a total of 258 individual chocolates). These boxes were kept under continuous covert surveillance, with the time recorded when each chocolate was eaten.

MAIN OUTCOME MEASURE

Median survival time of a chocolate.

RESULTS

The median survival time of a chocolate was 51 minutes (39 to 63). The model of chocolate consumption was non-linear, with an initial rapid rate of consumption that slowed with time. An exponential decay model best fitted these findings (model R²=0.844, P<0.001), with a survival half life of 99 minutes. Quality Street chocolates survived longer than Roses chocolates (hazard ratio for survival of Roses *v* Quality Street 0.70, 95% confidence interval 0.53 to 0.93, P=0.014). The highest percentages of chocolates were consumed by healthcare assistants (28%) and nurses (28%), followed by doctors (15%).

CONCLUSIONS

Chocolate survival in a hospital ward was relatively short, and was modelled well by an exponential decay model. Roses chocolates were preferentially consumed to Quality Street chocolates in a ward setting. Chocolates were consumed primarily by healthcare assistants and nurses, followed by doctors. Further practical studies are needed.

¹Department of Cardiology, Bedford Hospital, Bedford MK42 9DJ, UK

²Department of Ear, Nose and Throat Surgery, Great Western Hospital, Swindon, UK

³Department of Haematology, University Hospital of North Staffordshire, Stoke-on-Trent, UK

Correspondence to: PR Gajendragadkar gajendragadkar@gmail.com

Introduction

We have noted that chocolate boxes empty quickly on wards and that determining which healthcare professionals ate the most chocolates was a common source of workplace conflict.

We carried out an exploratory study to provide quantitative data on patterns of chocolate consumption in a hospital environment. Specifically we estimated the survival time of a chocolate in a ward setting, modelled mathematically any pattern of chocolate consumption observed, estimated if survival time was affected by chocolate brand, and investigated differences in healthcare professionals' chocolate consumption stratified by job type.

Methods

The study was prospective and conducted across three UK sites and four different wards. Observations took place in the last week of August 2013.

We chose to study a 350 g box of Quality Street chocolates (Nestlé, Switzerland) and a 350 g box of Roses chocolates (Cadbury, United Kingdom), on the basis that they are commonly given as gifts and are two of the leading brands of chocolates. Pilot data showed that these two brands contained similar numbers of chocolates (30 to 35 on average).

At approximately 10 am an observer (a doctor familiar with the study ward) covertly placed the boxes side by side in a prominent location in the main nursing or reception area, where gifts are normally placed. The observers covertly recorded what time each box was opened, and at what time individual chocolates were taken from each box. The observers used a preprinted data collection form to record, in an anonymised fashion, the role of the person eating the chocolate (for example, doctor), ensuring that the chocolates were kept under continuous surveillance as much as was practical. The observation period was a minimum of two hours up to approximately four hours. Before leaving, the observers were asked to record the numbers of leftover chocolates by brand.

The primary outcome was the median survival time of a chocolate. The main secondary outcome

was the mean time taken for a box of chocolates to be opened when placed on the ward.

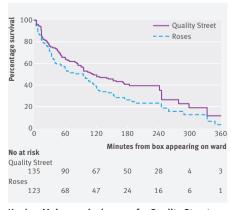
Statistical analysis

We estimated that a total of 210 chocolates would be needed to provide 80% power (P<0.05, two sided) to detect a 50% change in the hazard ratio between brands, assuming a median survival of 60 minutes for an individual chocolate, and follow-up of four hours maximum. Assuming a 350 g box contained 30 choco-

lates, we estimated that we would need eight boxes, totally around 240 chocolates.

Once the observers left the ward,

we deemed any leftover chocolates to be "lost to follow-up." We analysed the primary outcome using Kaplan-Meier survival analysis and Cox regression. The data were also pooled and analysed separately by type of chocolate. Other continuous variables were analysed by two sided independent sample *t* tests, with a significance level of <0.05. After excluding leftover chocolates, we performed regression curve fitting and estimation to generate a potential mathematical model of chocolate consumption by using statistical software, with an independent variable of survival time and a dependent variable of the proportion of chocolates remain-



Kaplan-Meier survival curves for Quality Street and Roses chocolates across all wards



ing. We used regression curve fitting to test a variety of models (linear, logarithmic, quadratic, cubic, and exponential). The model with the highest R^2 value and an F statistic with a two sided significance level of <0.05 was chosen as the best fit. Survival half life was calculated as the time taken until 50% of the chocolates remained ($t_{1/2}$ =[ln 0.5]/ λ ; where λ was the decay constant). Differences in preference between the two brands (modelled as a continuous variable of percentage of total chocolate consumption) were calculated using a one sample t test with a null hypothesis test value of 0.5 (that is, equal preference), repeated separately for each professional group.

Results

Overall, 191 chocolates out of a possible 258 (74%) were eaten. The remainder were lost to follow-up. The mean observation period was 254 minutes (95% confidence interval 179 to 329). No adverse events occurred.

The median survival time of a chocolate was 51 minutes (95% confidence interval 39 to 63). Regression curve fitting suggested that the rate of emptying of a box of chocolates was best explained by an exponential decay curve with equation C_p =e $-\lambda t$; where C_p is the proportion of chocolates remaining, t is the time in minutes, and λ is the decay constant, which was -0.007 for our model (model R^2 =0.844, P<0.001). Across the whole dataset, the survival half life (time taken for 50% of chocolates to be eaten) was 99 minutes.

The mean time taken for a box of chocolates to be opened after being placed on the ward was 12 minutes (95% confidence interval 0 to 24). The time to opening of Quality Street and Roses boxes did not differ significantly (19 v 5 minutes, 95% confidence interval for difference –19 to 46 minutes, P=0.35). Quality Street chocolates survived longer than Roses chocolates (hazard ratio for survival of Roses v Quality Street 0.70, 95% confidence interval 0.53 to 0.93, P=0.014, figure).

Healthcare assistants and nurses each accounted for 28% of the total chocolates consumed (54 out of 191 chocolates consumed by each group). Doctors were the third biggest consumers, accounting for 15% (29 out of 191) of the total chocolates consumed. There was a trend that healthcare assistants and nurses preferred Roses chocolates, whereas doctors preferred

Quality Street chocolates, but, examining each job type separately, preference for one type of chocolate was not statistically significant (see bmj.com).

Discussion

Chocolates left on wards for staff are consumed rapidly. An exponential decay model best explained how a box of chocolates was consumed in a ward environment. Overall, ward chocolate consumers preferred Roses chocolates over Quality Street chocolates. Taken as a group, healthcare assistants and nurses were the largest consumers.

To our knowledge, our observational study is the first to provide quantitative data on patterns of chocolate consumption within a hospital environment, was appropriately powered to detect a difference between two leading chocolate brands, and was conducted robustly over multiple sites and in multiple specialty situations, to have as much external validity as possible. Bias was minimised by using a similar start time and ensuring that all observers were familiar with the study protocol. Qualitatively, the observers all commented that when a box was first opened the initial phase of chocolate consumption was rapid, followed by a steadier and ever slowing consumption over time. This was confirmed by our exponential decay model. The behavioural or anthropological basis of this model needs further investigation, although similar patterns are seen in a variety of biological processes.

Although we noted that healthcare assistants and nursing staff consumed a larger proportion of the total

portion of the total chocolates, wards have higher numbers of nurses and healthcare assistants compared with other groups. The chocolates were placed at the nurses' station or reception as these areas were easily accessible to all staff and the commonest place for keeping gift chocolates. None the less, taken as a group, the nurses and healthcare assistants consumed the majority of the chocolates.

Being novel, the study was exploratory in nature and thus had a limited sample size and observational methodology. As we explored two types of chocolate products that were artificially placed in a hospital environment, we cannot comment on whether the quantitative data apply to other brands of

chocolates. The observers were all doctors, which may introduce a degree of bias, although this was minimised by using a clear proforma for data capture. Coincidentally, the trial was conducted during Ramadan, and so some healthcare professionals did not eat chocolate. However there are likely to be seasonal influences on chocolate consumption all year round (increased availability leading up to Christmas and Easter, decreased consumption owing to New Year dieting), so it is unclear whether there is truly any representative time for doing such research.

Differences in consumption habits were noted between ward and specialty, but we did not think that single observations were sufficient to draw conclusions on these, and instead we chose to focus on the pooled results.

A meta-analysis investigated the link between chocolate consumption and cardiometabolic disorders.3 It found significant heterogeneity in the reporting of chocolate consumption, so only compared highest with lowest consuming groups. The highest consuming groups consumed chocolate more than once weekly or more than 7.5 g/day, and showed a pooled reduction in the odds of developing any cardiovascular disease and stroke. The studies included in the meta-analysis were highly variable in defining chocolate consumption and cocoa content, so it is difficult to relate these to our study findings.3 None the less, a single chocolate from our study weighed approximately 9 g, which is above the 7.5 g/day threshold reported in the meta-analysis. Commercially available chocolate has a high sugar and fat content and it is likely that excessive consumption will lead to deleterious effects on population health, outweighing any potential

benefits.

Conclusions

The median survival time of a chocolate in this study was just 51 minutes.

In keeping with many biological processes, the way a box of chocolates is consumed seems to follow an exponential decay process, with an initial rapid "grab" phase. Given the short half life of a box of chocolates, to ensure that all healthcare staff get benefits from consistent chocolate consumption it is the authors' opinion that the frequency of chocolates delivered to wards needs to be increased and manufacturers lobbied to stop further shrinkage of chocolate boxes.

Full details including references and competing interests are in the version on bmj.com.

Were Bond's drinks shaken because of alcohol tremor?

Graham Johnson, ¹ Indra Neil Guha, ² Patrick Davies ³

OBIECTIVE

To quantify James Bond's consumption of alcohol as detailed in the series of novels by Ian Fleming.

DESIGN

Retrospective literature review.

The study authors' homes, in a comfy chair.

PARTICIPANTS

Commander James Bond, 007; Mr Ian Lancaster Fleming.

MAIN OUTCOME MEASURES

Weekly alcohol consumption by Commander Bond.

METHODS

All 14 James Bond books were read by two of the authors. Contemporaneous notes were taken detailing every alcoholic drink taken. Predefined alcohol unit levels were used to calculate consumption. Days when Bond was unable to consume alcohol (such as through incarceration) were noted.

RESULTS

After exclusion of days when Bond was unable to drink, his weekly alcohol consumption was 92 units a week, over four times the recommended amount. His maximum daily consumption was 49.8 units. He had only 12.5 alcohol free days out of 87.5 days on which he was able to drink.

CONCLUSIONS

James Bond's level of alcohol intake puts him at high risk of multiple alcohol related diseases and an early death. The level of functioning as displayed in the books is inconsistent with the physical, mental, and indeed sexual functioning expected from someone drinking this much alcohol. We advise an immediate referral for further assessment and treatment, a reduction in alcohol consumption to safe levels, and suspect that the famous catchphrase "shaken, not stirred" could be because of alcohol induced tremor affecting his hands.

¹Emergency Department, Royal Derby Hospital, Derby ²NIHR Nottingham Digestive Diseases Biomedical

Research Unit, University of Nottingham

³Paediatric Intensive Care Department, Nottingham University Hospitals NHS Trust, Nottingham Correspondence to: P Davies

patrick.davies@nuh.nhs.uk

In the entertainment world drinking alcohol is often portrayed in a positive, even glamorous, light. Of particular note are the drinking habits of James Bond, the quintessential British spy, in the novels by Ian Fleming. He is renowned for enjoying cigarettes, alcohol, and women, with a catchphrase of "vodka martini-shaken, not stirred."

Bond is admired for his performance under pressure and his ability to be master of all situations he encounters. His alcohol consumption is high, and we wondered whether he would have the capacity to perform. Despite his requests to the contrary, Bond's drink of choice, vodka martinis, should be stirred, not shaken. That he would make such an elementary mistake in his preferences seems incongruous with his otherwise impeccable mastery of culinary etiquette. Could Bond have been unable to stir his drinks because of persistent shaking from alcohol induced tremor, making it more socially acceptable to ask for his drinks "shaken, not stirred"?

Methods

Two authors each read seven original James Bond books and noted all alcohol consumption, as documented in the books. Alcohol intake was calculated by the number of days on which action was described in units of alcohol (10 ml or 8 g of pure ethanol). When drinks were shared, an equal split was presumed at all times. Data were then analysed by day. When days were not described or described in only brief detail, they were not taken into account. Days when Bond was unable to drink (usually because of incarceration or injury) were logged. We excluded The Spy Who Loved Me and Octopussy and The Living Daylights as stylistic outliers.

Results

Across the 12 books studied, 123.5 days were described, though Bond was unable to consume alcohol for 36 of these because of external pressures (admission to hospital, incarceration, rehabilitation). During this time he was documented as consuming 1150.15 units of alcohol. Taking into account days when he was unable to drink, his average alcohol consumption was 92 units a week (1150 units over 87.5 days). Inclusion of the days incarcerated brings his consumption down to 65.2 units a week. His maximum daily consumption was 49.8 units (From Russia with Love day 3). He had 12.5 alcohol free days out of the 87.5 days on which he was able to drink.

Discussion

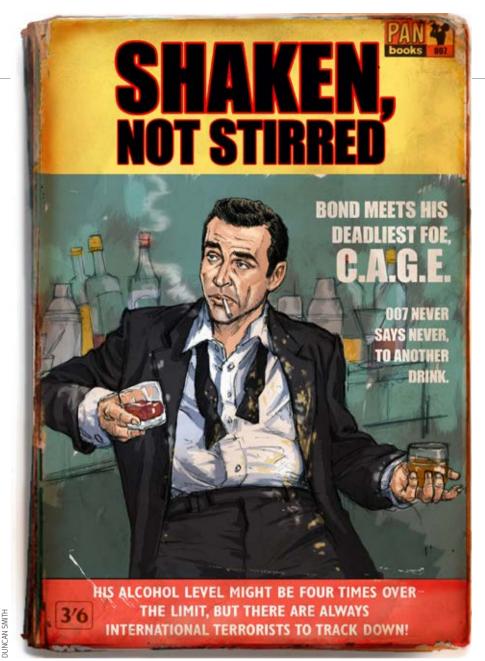
While on active service James Bond's alcohol consumption is, on average, between 65 and 92 units a week. People generally underestimate their alcohol consumption by around 30%, implying that Bond's could be as high as 130 units a week. UK recommendations for alcohol consumption state that an adult male should drink no more than 21 units a week, with no more than 4 units on any one day, and at least two alcohol free days a week. Bond's drinking habits are well in excess of each of these, and his consumption puts him in the highest risk group for malignancies, depression, hypertension, and cirrhosis. He is also at high risk of sexual dysfunction, which would considerably affect his womanising.

Data on the average life expectancy of real world secret agents are, not surprisingly, difficult to find. In Moonraker, Bond reflects that he would probably be killed before the age of 45 (the age of mandatory retirement from the "00" section of MI6). Should he not be "killed in action," his risk of developing many serious pathologies is high.

Bond has a relative risk of developing liver cirrhosis of between 7 and 16 compared with a lifetime abstainer. His relative risk of all cause mortality is greater than 1.74, particularly from stroke and alcohol related causes. Presuming survival despite the high risk nature of his profession, we anticipate that Bond's life expectancy would be significantly reduced.

Alcohol increases the risk of driving related incidents. Throughout the books Bond is noted to have several drinks and then drive. In Casino Royale he drinks over 39 units before engaging in a high speed car chase, losing control, and spending 14 days in hospital. We hope that this was a salutatory lesson. Such behaviour is typical of Bond. Despite his alcohol consumption, he is still described as being able to carry out highly complicated tasks and function at an extraordinarily high level. This is likely to be pure fiction.

If we apply the CAGE questions to Bond, we would score him 3 out of 4 (two yes responses should prompt further investigation). In Thunderball he recognises his high alcohol intake and that he feels better drinking less. He also admits to having an eye opener on some mornings. Also in Thunderball and in The Living Daylights he becomes annoyed when challenged about his drinking by his boss "M." It is likely that an international spy and assassin cannot spend too much time worrying about remorse, so we are



In Casino Royale he drinks over 39 units before engaging in a high speed car chase, losing control, and spending 14 days in hospital

not surprised that there are no documented instances of alcohol associated guilt.

Shaking (not stirring)

Cerebellar lesions are well known to cause an intention tremor and cerebellar tremor is considered a distinct clinical entity. While strokes are a more common cause of cerebellar lesions, chronic exposure to toxins, such as alcohol, that cause more generalised damage to the cerebellum can also cause a cerebellar tremor. Bond's alcohol intake is of sufficiently high frequency and duration to cause such cerebellar damage.

Conclusion

James Bond's weekly alcohol intake is over four times the advisable maximal alcohol consumption for an adult male. He is at considerable risk of developing alcoholic liver disease, cirrhosis, impotence, and other alcohol related health problems, together with being at serious risk of injury or death because of his drinking. Although we appreciate the societal pressures to consume alcohol when working with international terrorists and high stakes gamblers, we would advise referral for further assessment of his alcohol intake and reduce his intake to safe levels.

We conclude that James Bond probably couldn't stir his drinks, even if he wanted to, because of probable alcohol induced tremor.

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Die another day

One Tuesday in April we were confronted by a very upset patient on our rheumatology ward round. He was happy with his treatment and reported that he had received exemplary care from the hospital staff. However, the ward equipment was not supportive of our multidisciplinary effort. The patient declared "the clock is telling me to die." Turning to the wall we confirmed that the clock indeed said "DIE" (figure). We discovered that the radio controlled clock had reverted to German and was displaying an abbreviation of "Dienstag" (Tuesday). We quickly rectified this by pressing several buttons to show the English abbreviation "TUE." Fortunately, it was not the patient's time to die after all.

Stuart Carter rheumatology academic clinical fellow specialist trainee year 4, Rheumatology Department, Royal Hallamshire Hospital, Sheffield S10 2JF, UK stuartjcarter@sky.com Fiona Fawthrop rheumatology consultant, Rheumatology Department, Rotherham Hospital, Rotherham, UK

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Research

New evidence for nominative determinism in patients' health: population based cohort

John J Keaney, ¹ John D Groarke, ¹ Zita Galvin, ² Catherine McGorrian, ¹ Hugh A McCann, ¹ Declan Sugrue, ¹ Edward Keelan, ¹³ Joseph Galvin, ¹³ Gavin Blake, ¹ Niall G Mahon, ¹ James O'Neill ¹³⁴



OBJECTIVE

To ascertain whether a name can influence a person's health, by assessing whether people with the surname "Brady" have an increased prevalence of bradycardia.

DESIGN

Retrospective, population based cohort study.

SETTING

One university teaching hospital in Dublin, Ireland.

PARTICIPANTS

People with the surname "Brady" in Dublin, determined through use of an online telephone directory.

MAIN OUTCOME MEASURE

Prevalence of participants who had pacemakers inserted for bradycardia between 1 January 2007 and 28 February 2013.

RESULTS

579 (0.36%) of 161 967 people who were listed on the Dublin telephone listings had the surname "Brady." The proportion of pacemaker recipients was significantly higher among Bradys (n=8, 1.38%) than among non-Bradys (n=991, 0.61%; P=0.03). The unadjusted odds ratio (95% confidence interval) for pacemaker implantation among individuals with the surname Brady compared with individuals with other surnames was 2.27 (1.13 to 4.57).

CONCLUSIONS

Patients named Brady are at increased risk of needing pacemaker implantation compared with the general population. This finding shows a potential role for nominative determinism in health.

¹Cardiology Department, Mater Misericordiae University Hospital, Dublin 7, Ireland

²Liver Centre, Mater Misericordiae University Hospital, Ireland

³ James Connolly Memorial Hospital, Blanchardstown, Dublin, Ireland

⁴Royal College of Surgeons in Ireland, Dublin, Ireland

Correspondence to: JJ Keaney ikeaney@mgh.harvard.edu

Weedon and Splatt's paper¹ on the urethral syndrome in the *British Journal of Urology* is often cited not only for its obvious scientific merit, but also as a great example of nominative determinism. The term nominative determinism describes how certain people seem compelled towards a particular profession because of the influence of their surname. It was first coined by *New Scientist* journalist John Hoyland in 1994.² This is not to suggest that the theory is a recent one. Over 40 years before Hoyland, in 1952, Swiss analytical psychologist Carl Jung had noted "the sometimes quite gross coincidence between a man's name and his peculiarities or profession."

We rarely need to search for too long for great examples—Marie Harte was a cardiologist in Dublin for many years—but the growth of the internet has increased the ease with which we can now find cases of nominative determinism (table 1). ⁴⁻¹⁷ A newspaper article on the subject identified a dermatologist called Rash, a rheumatologist named Knee, and a psychiatrist named Couch, through use of the American Directory of Physicians. ¹⁸

Obviously, science does not have a monopoly on nominative determinism. Was it a surprise that during the London 2012 Olympics, a man who shares his name with lightning became the fastest man in the world? Usain Bolt ran the 100 metre final in 9.63 seconds, faster than anyone else in history. It is also somewhat predict-

Table 1 | Examples of nominative determinism in

scientific publications		
Publication author surname	Subject	
Fear ⁴	Mental health symptoms	
Ache ⁵	Muscle activity	
Sehgal ⁶	Alaskan birds	
Snowman ⁷	The polar regions	
Fountain ⁸	Water flow	
Spray ⁹	Fresh water	
Bone ¹⁰	Osteoporosis	
Flood ¹¹	Incontinence	
Harte ¹²	Cardiac arrhythmias	
Byrne ¹³	Burns	
Seymour ¹⁴	Visual cortex	
Sun ¹⁶	Solar cells	

Pelvic pain

Payne¹

able that Bulgarian hurdler Vania Stambolova would, well, stumble over as she did, unfortunately falling at the first hurdle in her heat. On a more sombre note, Will Drop was a Montreal window cleaner who died in a fall, and on the same day in October 1941, two inmates of the Florida state prison, Willburn and Frizzel, were sent to the electric chair.

Of course, the above examples could be pure chance, devoid of any scientific basis; but there are some supportive claims within the field of psychology. Pelham and colleagues concluded in a paper that people have a preference for things "that are connected to the self," and are disproportionately more likely to find careers with a label closely related to their name. Indeed, psychologists have shown that as well as influencing your own personal actions, a name also affects how others treat us. This effect may range from preferential grading of a student with a more pleasant name by their teacher²⁰ to more favourable findings by jurors.²¹

We sought to determine whether a person's name could influence their health. To investigate our theory we used the example surname "Brady," and sought to establish whether people with that name in Dublin had an increased incidence of bradycardia.

Methods

The percentage of the population in Dublin, Ireland, with the surname Brady was determined through use of online residential telephone listings. ²² The prevalence of bradyarrhythmia in the general population is unknown. Sinus bradycardia, particularly in young people, can be entirely asymptomatic, but symptomatic bradycardia is a class IB indication for permanent pacemaker insertion. ²³ Therefore, we used pacemaker insertion as a marker of bradycardia. We used the pacemaker database at a university teaching hospital in Dublin to calculate the proportion of pacemakers implanted in patients named Brady in our institution over 61 months (from 1 January 2007 to 28 February 2013).

We presented categorical data as percentages and continuous, non-normally distributed data



This increased bradyphenomenon in Bradys could be attributable to increased levels of bradykinin

as medians with interquartile ranges. We compared baseline characteristics by surname (Brady ν other surnames) using Fisher's exact test for binary variables and Wilcoxon rank sum test for non-normally distributed continuous variables. The relation between the likelihood of pacemaker implantation and the name Brady was presented as a crude odds ratio with associated 95% confidence intervals. A confidence interval for this measure of effect that did not contain the null value of 1 was considered as evidence of a significant association between the surname Brady and pacemaker implantation. We did all analyses using SAS version 9.3. A two tailed value of P<0.05 was considered statistically significant.

Results

Of 161967 residential telephone listings in the Dublin area, 579 (0.36%) Bradys were listed. During the study, 1012 pacemakers were implanted in the teaching hospital in Dublin; 13 patients with names other than Brady were excluded from analyses owing to missing data. Of 999 pacemaker recipients remaining, 557 (55.8%) were male with a median age of 77 years (interquartile range 70-83). Eight (0.8%) of the devices were implanted in patients named Brady. Among pacemaker recipients with Brady as a surname (n=8, 0.8%) and those with other surnames (n=991, 99.2%), age did not differ significantly (table 2 on bmj.com). However, there was a non-significant tendency for Brady recipients to be male (n=7, 87.5%) compared with recipients with other names (n=550, 55.5%; P=0.08).

Using residential telephone listings as a crude indicator of overall proportions of Bradys and non-Bradys within the catchment area of the study centre, the proportion of pacemaker recipients among Bradys (eight (1.38%) of 579) was significantly higher than among non-Bradys (991 (0.61%) of 161 388; P=0.03, using Fisher's exact test). The unadjusted odds ratio for pacemaker implantation among individuals with the

surname Brady compared with other surnames was 2.27 (95% confidence interval 1.13 to 4.57).

Discussion

This study shows a link between people's names and their health. The underlying mechanisms through which people with the name Brady have a higher incidence of bradycardia than the general public are at present unclear. Genetic mutations causing familial sinus bradycardia have been described, particularly affecting the HCN4 cardiac ion channel, ²⁴⁻²⁶ and a familial genetic predisposition could explain the increased rates of pacemaker insertion in our Brady cohort.

The high percentage of male patients in the Brady pacemaker group was also noteworthy, although not statistically significant. It suggests that the effect of the name Brady on your conduction system is likely only to be seen in people born as Brady rather than those who become Brady when they get married. Indeed, the number of true Bradys with pacemakers may have been underestimated, because female patients with pacemakers whose maiden name was Brady were not determined in this study.

This increased bradyphenomenon in Bradys could be attributable to increased levels of bradykinin. Some animal studies have shown bradykinin to reduce heart rate. ²⁷⁻²⁹ Bradykinin seems to elicit this bradycardiac effect by centrally controlling the baroreflex heart rate. ³⁰ However, these studies have been contradicted in other animal studies, ³¹⁻³⁴ and have not been replicated in humans.

Limitations

This single centre, retrospective analysis had several limitations. We did not have information on whether the patients were related; therefore, genetic predisposition in one single family could have biased the data. However, four male Bradys have the same first name, which makes it more unlikely that these particular patients, at least, were first degree relatives.

Geographical biases could have influenced the results. There are eight hospitals in the greater Dublin area in which pacemakers are implanted.

If there is a greater proportion of Bradys in our catchment area compared with the rest of the city, the implantation rates for Bradys in our institution would be artificially elevated. However, we found no evidence that such a cluster of Bradys exists in north central Dublin.

Social biases include use of landline telephones and private health insurance by Bradys. If Bradys are less likely to attend private hospitals, implantation rates in our university hospital—which is a public hospital—would be artificially high. The use of landline telephones in Ireland has fallen substantially over recent years. If technology savvy Bradys have abandoned the traditional landline in favour of mobiles more frequently than non-Bradys, this difference could lead to a telephone bias.

Conclusion

We have shown that the influence of a person's name not only affects their professional career or how others may treat them, but can also extend to determining aspects of their health. Further research could include investigating increased rates of obesity in the Fatt family or depression in people whose surname is Lowe. We believe that this finding could have an important role in public health medicine, and screening programmes that are name specific could be developed for families at risk.

Full details including references and competing interests are in the version on bmj.com.

Stem cells of mouse and whale: does size matter?

Martin J Hoogduijn, ¹ Johanna C van den Beukel, ¹ Lidewij C M Wiersma, ² Jooske Ijzer³

OBJECTIVE

Compare the morphology and size of stem cells from two mammals of noticeably different body size.

DESIGN

Observational study.

SETTING

The Netherlands.

PARTICIPANTS

A humpback whale (*Megaptera novaeangliae*) and a laboratory mouse (*Mus musculus*).

MAIN OUTCOME MEASURES

Morphology and size of mesenchymal stem cells from adipose tissue.

RESULTS

Morphologically, mesenchymal stem cells of the mouse and whale are indistinguishable. The average diameter of 50 mesenchymal stem cells from the mouse was 28 (SD 0.86) μ m and 50 from the whale was 29 (SD 0.71) μ m. The difference in cell size between the species was not statistically significant. Although the difference in body weight between the species is close to two million-fold, the mesenchymal stem cells of each were of similar size.

CONCLUSION

The mesenchymal stem cells of whales and mice are alike, in both morphology and size.

Introduction

The class Mammalia contains species of extensively different phenotype and body size. The family Cetacea contains the largest mammals, whales. Cetaceans vary in body size, with the rare porpoise species vaquita (Phoeoena sinus) measuring 1.5 m in length and with a body weight of 55 kg and the blue whale (Balaenoptera musculus)—the largest animal ever known to have lived—measuring up to 30 m in length and with a body weight of 180000 kg. Mice (genus Mus) represent the other end of the mammalian size spectrum, with the common house mouse measuring about 8 cm in length, with a tail of approximately the same length, and a body weight on average of 20 g. The common laboratory mouse (C57BL/6, or the "black 6" mouse) is of the same size and weight. Although organs are sized in proportion to the size of the animal, suborgan structures do not reflect this difference. For instance, capillaries in all mammals range from 5 to 10 µm, the optimal size for oxygen exchange.

¹Department of Internal Medicine, Erasmus MC, Rotterdam, Netherlands

²Department of Virology, Erasmus MC, Rotterdam, Netherlands

³Department of Pathobiology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, Netherlands

Correspondence to: M J Hoogduijn, Nephrology and Transplantation, Department of Internal Medicine, Dr Molewaterplein 50, 3015 GE, Rotterdam, Netherlands m.hoogduijn@erasmusmc.nl

In recent decades interest in stem cells has been growing, both from a basic biological and a therapeutic perspective. In response to this, we compared the morphology and size of mesenchymal stem cells from two mammalian species of noticeably different body size.

Methods

The whale

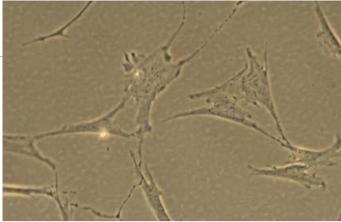
The humpback whale (*Megaptera novaeangliae*) is a baleen whale (contains special structures in its mouth that enable it to filter food from the water) of the subfamily Balaenopteridae, and ranges in length from 12 m to 16 m with a body weight of approximately 36 000 kg.

On 12 December 2012 a humpback whale became stranded on a sandbank near Texel on the Dutch coast. After several failed attempts to get the whale back in the sea, it died on 16 December and necropsy was performed two days later.

Sample collection

Samples of blubber, subcutaneous adipose tissue, and visceral adipose tissue were removed from the whale, stored in phosphate buffered saline, transferred to the laboratory at the Erasmus MC, and kept overnight at 4°C. The next day we sectioned and stained the tissues with haematoxylin and eosin (see fig 1 in full paper on bmj.com). Multiple small muscle-like struc-







Investigators with access to

beached blue whales or with

the African pygmy mouse or

bumblebee bat: please call

mesenchymal stem cells from

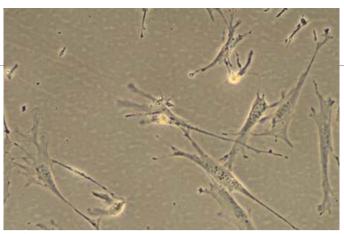


Fig 2 | Morphology of cultured mouse mesenchymal stem cells after four subcultures

tures were seen in the blubber sections. These were not observed in the subcutaneous adipose tissue. Owing to severe autolysis of the carcass, the visceral adipose tissue was of poor quality. Under continuous shaking we minced up and digested the three tissues with sterile 0.5% collagenase type IV (Sigma-Aldrich, St Louis, MO) solution for 30 minutes at 37°C. After washing the digested material, we seeded the cell suspensions in culture flasks in a minimum essential medium (Lonza, Verviers, Belgium) supplemented with combined penicillin and streptomycin and 15% fetal bovine serum (Lonza). The cell suspensions were kept at 37°C in 5% carbon dioxide and 20% oxygen, and at 95% humidity. We changed the medium every three or four days. After two days we stopped culturing the visceral adipose tissue

because of a bacterial infection. After three weeks we stopped culturing blubber because of the absence of living cells in the cultures. However, in the culture derived from subcutaneous

adipose tissue we observed a few living cells that resembled mesenchymal stem cells (fig 1). We subcultured these cells when confluency was 90%. For further experiments we used cells that had been subcultured four times.

The mouse

The house mouse (*Mus musculus*) is one of the most common mammalian species in the world. In 1921, an American researcher, Clarence Cook Little, inbred the C57BL/6 mouse strain from the house mouse. This strain provides consistent data in experiments.

On 2 January 2013 we collected, sectioned, and stained interscapular brown adipose tissue, subcutaneous fat, and abdominal fat from a laboratory mouse (see fig 1 on bmj.com). We isolated mesenchymal stem cells from the abdominal fat using the same procedures as for the humpback whale. In the culture we observed cells that resembled the morphology of both human mesenchymal stem cells and cells cultured from the humpback whale adipose tissue (fig 2).

Mesenchymal stem cells

Mesenchymal stem cells are the precursor cells

of mesenchymal tissues. They can be expanded in culture, and differentiated into osteogenic, adipogenic, chondrogenic, and myogenic lineages in culture.² Mesenchymal stem cells have been identified in nearly all tissues,3 with adipose tissue being the most accessible. Mesenchymal stem cells are usually routinely cultured from human or mouse adipose tissue, but there are reports on cells derived from ovine and pig adipose tissue. A study from 2011 showed that mesenchymal stem cells can be isolated from adipose tissue of the brown bear. 4 Although fierce, the brown bear is only a mediocre species to use for comparison of the size of mesenchymal stem cells from small and large mammals. Comparing cells from a mouse with those from a whale covers a far larger body size spectrum and is there-

fore more informative.

In addition to their capacity for differentiation, mesenchymal stem cells have trophic properties and support the survival, proliferation, and differentiation

of other cell types. Furthermore, they have potent immunomodulatory properties and inhibit the proliferation of activated T cells, modulate the differentiation of B cells, and promote the differentiation of macrophages into a regulatory phenotype.5-7 These beneficial properties make mesenchymal stem cells candidates for application in regenerative medicine and immune therapy. Early clinical trials are exploring this in conditions such as graft versus host disease8 and Crohn's disease, 9 and in organ transplantation. 10 As mesenchymal stem cells need to be administered in relatively large numbers, obtaining sufficient cells of good quality is challenging. A universal source of mesenchymal stem cells is a potential solution to this problem.

The size of mesenchymal stem cells from mouse and whale is of general biological interest. We therefore trypsinised the fourth subculture of mesenchymal stem cells from both species and placed a sample of the cell suspension in a counting window. The cells were then photographed and their size measured using Axiovert software (Zeiss, Oberkochen, Germany).

Results

The average diameter of 50 mesenchymal stem cells from the mouse and 50 from the whale was 28 (SD 0.86) μm and 29 (0.71) μm , respectively. The difference in size of the cells between the species was not statistically significant. Despite these mammals differing in body weight close to two million-fold, their mesenchymal stem cells were of similar morphology and size.

Discussion

Mice and whales have noticeably different body sizes, but their mesenchymal stem cells are of equal morphology and size in culture.

Species that differ vastly in size and are far apart on the phylogenetic tree are known to have molecular machinery of similar proportions. Bacteria use adenine, guanine, cytosine, and thymine to replicate their genetic code, as do whales. At a cellular level we now know that the size of mesenchymal stem cells between small and large mammals does not differ. Size starts to matter only beyond the level of the single mesenchymal stem cell. The whale's body weight is approximately two million times that of the mouse. Does the whale also have two million times more mesenchymal stem cells? If this was the case, and if mouse or whale adipose tissue were being considered for study or perhaps for veterinary therapeutic applications, the option would be to breed a large number of mice, or wait for a whale to become stranded on a beach.

Every study can be improved and even the present study does have limitations. The study could be further improved by obtaining mesenchymal stem cells from a larger whale species, preferably the blue whale, and from a smaller mouse species. The authors therefore call on investigators with access to beached blue whales or with mesenchymal stem cells from the African pygmy mouse or bumblebee bat, to come forward and collaborate with us.

We thank Naturalis Biodiversity Center, Leiden, Netherlands, for its support of this study and all members of the necropsy teams for their extensive technical assistance.

Full details including references and competing interests are in the version on bmj.com.

The haiku as a research medium



Long and winding road, decaffeinated trucker: No happy ending Francis Toolis

Alert! Truck driver!
Coffee or Red Bull may well
Make a safer drive
Simon Power

Use of caffeinated substances and risk of crashes in long distance drivers of commercial vehicles *BMJ* 2013;346:f1140



To your heart be true An egg with your morning kiss May help not harm you Wendy-Jane Walton

What a stroke of luck An egg a day's safe, but still One egg is un oeuf Andrew Fox-Lewis

Egg consumption and risk of coronary heart disease and stroke BMJ 2013;346:e8539



Love, my burning child signals to winter wisdom false traffic lights here Jo Richardson

Improve the NICE guide for under 5s with fever Urinalysis Brian Attock

Accuracy of the "traffic light" clinical decision rule for serious bacterial infections in young children with fever *BMJ* 2013;346:f866

Could research results be shrunk to fit the conventions of the haiku, and still retain their meaning? Here are the winners of our competition, which received 293 entries and was judged by **Sandy Goldbeck-Wood** and **Richard Lehman.**



Drug reps pay for lunch. Goodwill gesture, or a bribe? Leave gifts for Christmas Jonathan Hackett

If they can't bribe you You won't sell their drugs, but still I hate buying pens Andrew Fox-Lewis

Medical school gift restriction policies and physician prescribing of newly marketed psychotropic medications *BMJ* 2013;346:f264



Recession saves lives, says our man in Havana, by slimming waistlines David Strachan

Easy come, easy Go. A moment on the lips An early MI Andrew Fox-Lewis

Population-wide weight loss and regain in relation to diabetes burden and cardiovascular mortality in Cuba 1980-2010 *BMJ* 2013;346:f1515



For healthy old age
Be active, eat greens, don't smoke
Carry on drinking
David Grant

Fit, fruit-fed, no cigs: Old able. Autumn leaves fall Slowly, gracefully Jeremy Holmes

Unhealthy behaviours and disability in older adults *BMJ* 2013;347:f424 Cite this as: *BMJ* 2013;347:f7391 CATONIE