2022 Methods Qualifying Exam

Jack Tubbs

August

Instructions

Your exam consists of five parts.

When answering the questions you can use either SAS or R (unless I specify which approach). I do not need nor want to see the same analysis done using both SAS and R.

In some cases the questions are open ended or dependent upon the approach that you take. I am more interested in the approach that you take and your justification for that approach than your answer. I do not want to see your failed attempts to answer the question at hand, nor do I need to see all the steps that you needed to arrive at your final answer (e.g., model selection procedures).

In some cases, the question has been intentionally left vague or open ended. If you encounter these, then tell me what you intend to do, why you did it, and what you found. Do Not redefine your problem so that it is either trivial or overly complex. Use the methods that were presented in STAT 5380/5381. There shouldn't be any Bayesian solutions. Save those for your PPP!. The level of difficulty for this exam is consistent with what one would expect of an MS in Statistics. You are welcomed to use any of the resources given in the methods sequence (or any other resource that does not consume Oxygen).

Answer the questions and present your solutions in a separate document for each question in a similar manner to what I have produced using LaTeX in Overleaf (or your choice of a TeX/LaTeX format). A Word-type document is Not Acceptable!

It is your responsibility to clearly communicate your solution to each of the problems. Make use of cites and labels when referring to output such as tables and graphs or figures. If I have to search or guess at your solution then it is wrong!

You have nearly 7 days in which to work on this exam! Budget your time and use it wisely. I suspect none of the questions can be answered and documented in one sitting. I attack problems of these type by thinking in terms of three disjoint but related tasks. 1. What is the problem, what is my initial approach and do I have the needed resources in place to do what I think will be needed. For example, suppose I think the problem involves ANOVA for which I intend to use SAS. What do I need? How will I try to do it?, etc. 2. The second task involves the analysis. Did my program do what I needed it to do? What are the results? Do I need more since some unexpected issues arose? 3. The third part consists of documenting what I found. Is my explanation clear? Is it relative to what I was attempting to find? etc.

My experience with activities such as this exam is that (10 - 15)% of your time will be spent on part 1. Yet, you can do this anywhere. As you are walking, riding a bike, or drinking coffee, think about your plan. You will be surprised at how valuable this type of activity can be. The analysis should take about 50% of your time. The writing will take the remainder of your time. It is amazing how long it takes to write up your results. I suspect none of you will have an acceptable first draft! So edit and rewrite....

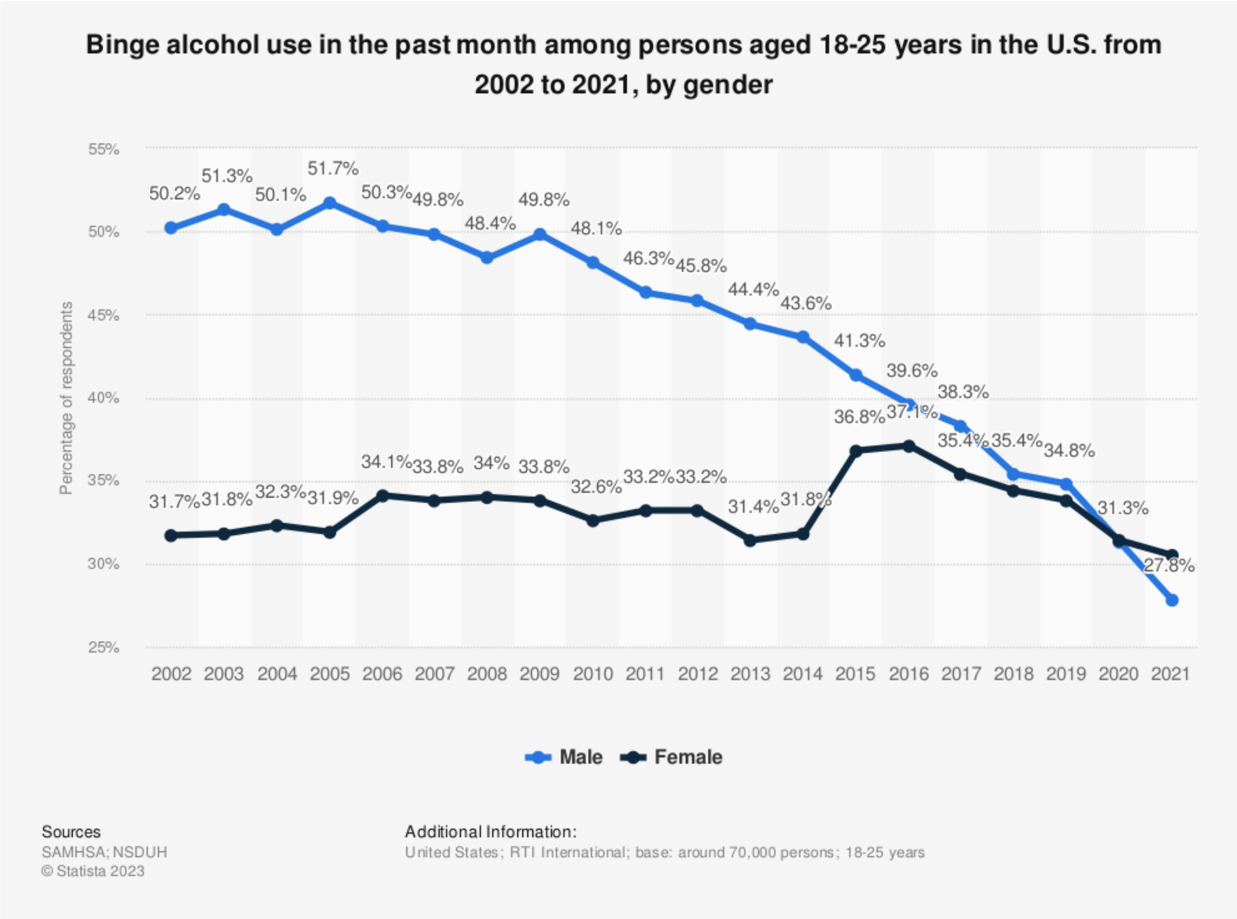
When I grade the exam, I often think the performance was at one of three levels. 1) great job - hire as soon as possible, 2) promising work, needs more experience and time but certainly worthy of consideration when a job opening becomes available, 3) encourage this person to take the LSAT!

Turn your exam in via BOX. Share a folder entitled, PE2023 - your name, on your BOX account with me. The exam is due at 5:00 pm on Monday August 21.

Exam

Part 1 – Binge alcohol use in persons aged 18-25 years in US

Alcohol use has always been an issue with older teens and younger adults. They tend to binge drink at parties and on weekends rather than daily use. The following chart illustrate this phenomena during the early part of this century and up to and including the Covid-19 pandemic in the US.



This chart suggests a story, what story would you tell? One can probably safely say that a greater percentage of males participate in this type of behavior than females. This is certainly true in 2002. Yet, by 2020 the two groups have nearly identical percentages. Choose appropriate statistical methods for answering the following.

1. When is the earliest that the percentage of binge drinking is statistically the same for both genders?
2. What is the data suggesting in terms of binge drinking after 2016? Can you think of a statistical method to help with your case?[1]
3. Hint: consider the percentages as rates or probabilities and look at relative rates or ratios. At each year, you have a 2 x 2 table for gender and binge drinking (yes or no).

[1] It may appear that I want a yes or no response, I don't. Demonstrate and justify everything that you do!

Part 2 – APSTAT Clinical Study

The following is taken from a free response question on an AP STAT exam. Go ahead an pretend that you are still in high school and answer the questions given in part (a) and (b)

4. The anterior cruciate ligament (ACL) is one of the ligaments that help stabilize the knee. Surgery is often recommended if the ACL is completely torn, and recovery time from the surgery can be lengthy. A medical center developed a new surgical procedure designed to reduce the average recovery time from the surgery. To test the effectiveness of the new procedure, a study was conducted in which 210 patients needing surgery to repair a torn ACL were randomly assigned to receive either the standard procedure or the new procedure.

   (a) Based on the design of the study, would a statistically significant result allow the medical center to conclude that the new procedure causes a reduction in recovery time compared to the standard procedure, for patients similar to those in the study? Explain your answer.

   (b) Summary statistics on the recovery times from the surgery are shown in the table.

Type of Procedure	Sample Size	Mean Recovery Time (days)	Standard Deviation Recovery Time (days)
Standard	110	217	34
New	100	186	29

   Do the data provide convincing statistical evidence that those who receive the new procedure will have less recovery time from the surgery, on average, than those who receive the standard procedure, for patients similar to those in the study?

The objective of this question for the AP students is to perform a two sample test when the randomization assures the independence of the two treated groups, standard and new. But does randomization insure that the assumptions hold? What might you suggest as a reasonable (I'm the judge) alternative trial when the primary objective is post-op recovery time for ACL surgery? To assist with your new trial design, let me pose some questions or thoughts.

- What is the research hypothesis for the APSTAT trial? what is it for your trial?
- Since ACL surgeries are not rare, what do you think is known about the post-op recovery time using the standard procedure as compared with the new procedure?
- Since the sample sizes are 11 to 10 (favoring the standard treatment) rather than 1 to 1, is this potentially problematic? If so, how and why?
- What unreported factors (variables) do you think affects post-op recovery time for ACL surgery aside from the surgical method used? Does your random sample allocation fix this issue? What would you propose while retaining the same clinical trial budget?
- There is no analysis here, just talk! and I'm not accepting a Bayesian designed trial!

Part 3 – Out of Hospital CPR Survival Rates

The following is a chatGPT dialog concerning survival when using CPR for out of hospital incidents, such as the recent episode with Brony James, son of LeBron James.

What are the survival rates for those who receive CPR?

ChatGPT

The survival rates for those who receive CPR (cardiopulmonary resuscitation) can vary depending on several factors, including the cause of the cardiac arrest, the location where it occurs, and the promptness and quality of the CPR performed. It's important to note that CPR is typically administered in situations where the person's heart has stopped beating, and it is intended to provide temporary support until more advanced medical care can be given.

Survival rates can be influenced by factors such as:

1. Immediate response: The sooner CPR is initiated after cardiac arrest, the better the chances of survival. Prompt initiation of CPR helps maintain blood flow to vital organs until professional medical help arrives.

2. Early defibrillation: In cases of cardiac arrest caused by certain heart rhythm abnormalities like ventricular fibrillation, defibrillation (an electric shock to the heart) can be crucial. The use of automated external defibrillators (AEDs) by trained individuals or medical professionals significantly improves survival rates.

3. Bystander intervention: If bystanders are trained in CPR and can perform it effectively, it can greatly improve the chances of survival. Bystander CPR can be critical in maintaining blood circulation until professional help arrives.

Survival rates can vary widely, but here are some general statistics:

1. Out-of-hospital cardiac arrest: The survival rates for out-of-hospital cardiac arrest vary, but studies have shown that overall survival rates range from 8% to 10%. However, this can increase significantly if early bystander CPR and rapid defibrillation are provided.

2. In-hospital cardiac arrest: Survival rates for in-hospital cardiac arrest tend to be higher than those for out-of-hospital cardiac arrest. According to studies, survival rates for in-hospital cardiac arrest can range from 20% to 24%. It's important to remember that these statistics are general estimates and may vary based on individual circumstances. The effectiveness of CPR and the chances of survival are influenced by various factors. It is always recommended to seek immediate medical help in case of an emergency and to receive proper training in CPR techniques to improve the chances of a positive outcome.

What are some studies that support these findings concerning out-of-hospital arrests?

ChatGPT

There have been several studies conducted on out-of-hospital cardiac arrest (OHCA) and survival rates following CPR. Here are a few notable studies that support the findings mentioned earlier:

Resuscitation Outcomes Consortium (ROC) study: The Resuscitation Outcomes Consortium is a large collaborative research network that conducted a study on OHCA survival rates. The study involved multiple regions across North America and aimed to evaluate the impact of interventions, including bystander CPR and public access defibrillation. The findings showed that survival rates for

OHCA varied between regions but ranged from 8% to 12%. The study emphasized the importance of bystander CPR and early defibrillation in improving survival outcomes.

Swedish Cardiac Arrest Registry (SCAR): The SCAR is a nationwide registry in Sweden that collects data on cardiac arrests.

A study published in the New England Journal of Medicine analyzed data from the registry and found that bystander CPR significantly improved the chances of survival following OHCA. The study reported survival rates of 10.5% when bystander CPR was performed compared to 4.0% when it was not.

American Heart Association (AHA) statistics: The American Heart Association provides regular updates on cardiovascular disease statistics, including survival rates for cardiac arrest. According to the AHA's 2020 statistics, the overall survival rate for OHCA in the United States was around 10.8%. The AHA also emphasizes the critical role of bystander CPR and early defibrillation in improving outcomes.

These studies and data provide insights into the survival rates for OHCA and the impact of interventions such as bystander CPR and early defibrillation. It's important to note that survival rates can vary depending on many factors, and advancements in emergency medical care and public awareness can contribute to improving outcomes over time.

The following questions use data from a meta analysis concerning survival for out of hospital incidents of cardiac arrest and CPR usage. The studies cover separate investigations during the 1984 - 2008 time frame in which considerable attention has been paid to improving one's training in administering CPR. The question of interest is, "Has the survival rate for out of hospital usage of CPR improved for cardiac arrest?" The primary endpoint is survival rates in the time period covered by the studies in the meta analysis. A secondary endpoint is patient survival to hospital admission (not dead on arrival).

I have included SAS code and a resultant data set as a *.csv file. My SAS code is a very elementary and simple look at the analysis. You should convert the ideas given in the SAS code to R-script and perform whatever analysis you deem necessary to answer these question for both endpoints using R or RStudio. Describe and justify your solution. (I suspect a major part of your solution will be the added breath and graphics for the analysis).

Were you surprised by the size of the survival rate? Explain.

The SAS Code is

```
    libname ldata '/home/jacktubbs/my_shared_file_links/jacktubbs/2022_Exam';
options center nodate pagesize=120 ls=80;

title 'Meta Studies for CPR Survival';

/***************************************************
***************************************************
Variables are;

Author      names for the study
Year      date of when the study was published
Total     total number of cases
No_Res      no response to cpr (death)
Surv_to_Adm   survived to admission in hospital
Sur_to_Dis    survived to discharge from hospital (Ultimate success)
Surv_Rate_Dis survival rate = Sur_to_Dis / Total

```

```
****************************************************
**************************************************/;


data survival_data1;
length Author $20.;
input Author $ Year Total No_Res Surv_to_Adm Sur_to_Dis Surv_Rate_Dis;
if 2000 le year le 2004 then c_year = 2000;
if 2005 le year le 2009 then c_year = 2005;
datalines;
Citerio 2002 178 0 . 10 5.6
Fan 2002 320 82 . 4 1.3
Lim 2002 93 0 15 1 1.1
Myerberg 2002 738 0 . 51 6.9
Smith 2002 436 778 82 35 8.0
Goto 2003 203 227 . 20 9.9
Grmec 2003 216 . 128 44 20.4
Haukoos 2003 575 0 . 25 4.3
Nishiuchi 2003 974 176 236 50 5.1
Ong 2003 351 . 30 7 2.0
Horsted 2004 219 233 82 25 11.4
Rudner 2004 147 150 43 15 10.2
Davies 2005 172 4 . 39 22.7
Handel 2005 84 79 26 12 14.3
Hayashi 2005 179 0 . 2 1.1
White 2005 326 0 158 85 26.1
Drezner 2006 9 0 . 1 11.1
Kellum 2006 358 169 . 39 10.9
Pleskot 2006 560 144 149 53 9.5
Davis 2007 1095 46 197 47 4.3
Daya 2007 7478 6052 . 568 7.6
Dunne 2007 471 51 28 1 0.2
Estner 2007 412 277 180 47 11.4
Fairbanks 2007 539 277 . 27 5.0
Herlitz 2007 38413 . . 2114 5.5
Hostler 2007 9886 . . 727 7.4
Iwami 2007 12437 . . 433 3.5
Jasinskas 2007 62 10 11 . .
Ma 2007 1423 86 242 80 5.6
Morrison 2007 4673 40 671 239 5.1
Vadeboncoeur 2007 1097 . . . .
Fleischhackl 2008 62 . . 17 27
;
run;

data survival_data0;
length Author $20.;
input Author $ Year Total No_Res Surv_to_Adm Sur_to_Dis Surv_Rate_Dis;
if 1980 le year le 1989 then c_year = 1985;
if 1990 le year le 1994 then c_year = 1990;
if 1995 le year le 1999 then c_year = 1995;
if 2000 le year le 2004 then c_year = 2000;
datalines;
Wilson 1984 126 0 28 11 8.7
Smith 1985 893 0 79 29 3.2
Aprahamanian 1986 319 126 94 42 13.2
Bachman 1986 512 . 24 14 2.7
Bonnin 1989 232 7 56 22 9.5
Becker 1991 3221 . 241 55 1.7
Brison 1992 1510 . 143 38 2.5
```

```
Bonnin 1993 1461 0 . 92 6.3
Kellermann 1993 1068 0 267 85 8.0
Pepe 1993 2404 0 . 193 8.0
Richless 1993 96 0 14 3 3.1
Tresch 1993 196 0 37 10 5.1
Van_der_Hoeven 1993 257 0 39 6 2.3
Kass 1994 599 0 113 24 4.0
Lombardi 1994 2329 . . 52 2.2
Schneider 1994 211 125 50 19 9.0
Crone 1995 1069 0 240 135 12.6
Hodgetts 1995 100 82 . 2 2.0
Rainer 1995 455 0 105 52 11.4
Giraud 1996 113 146 22 8 7.1
Killien 1996 78 2 31 17 21.8
Kuisma 1996 255 68 98 44 17.3
Adams 1997 8651 . . 612 7.1
Fischer 1997 464 82 185 74 15.9
Kuisma 1997 162 43 45 8 4.9
Mitchell 1997 275 . . 27 9.8
Stapczynski 1997 311 0 46 19 6.1
Valenzuela 1997 7635 0 . 1086 14.2
Valenzuela 1997 665 0 . 46 6.9
De_Vreede 1998 288 350 . 47 16.3
Joyce 1998 322 0 83 26 8.1
Kette 1998 344 . 60 23 6.7
Lindholm 1998 832 0 . 67 8.1
Tadel 1998 337 511 78 19 5.6
Waalewijn 1998 1046 400 165 134 12.8
Absalom 1999 260 0 59 26 10.0
Bottinger 1999 338 243 129 48 14.2
Kuilman 1999 898 0 441 276 30.7
Lui 1999 744 0 89 12 1.6
Stiell 1999 5335 0 366 197 3.7
Sunde 1999 326 573 96 30 9.2
Swor 2000 2608 108 538 189 7.2
Valenzuela 2000 148 0 71 56 37.8
Finn 2001 1293 . . 85 6.6
Groh 2001 388 0 61 21 5.4
Jennings 2001 115 96 22 6 5.2
Rea 2001 7265 . . 1112 15.3
;
run;
proc sort data=survival_data0; by year; run;
proc sort data=survival_data1; by year; run;

data survival_data; merge survival_data0 survival_data1; by year;
run;

data survival_data; set survival_data;
if surv_rate_dis ne '.';
run;

*proc print data=survival_data; run;

title2 'Survival Rates to Discharge';

proc sgplot data=survival_data;
scatter y=Surv_Rate_Dis x=year;
loess y=Surv_Rate_Dis x=year;
reg y=Surv_Rate_Dis x=year;
```

```
run;

proc sgplot data=survival_data;
histogram Surv_Rate_Dis;
density Surv_Rate_Dis/type=kernel;
run;

proc sgplot data=survival_data;
*  xaxis discreteorder=data;
  yaxis label="Survival Rate (%)";
*  scatter y=c_year x= Surv_Rate_Dis/jitter;
  vbox Surv_Rate_Dis/ group=c_year;* / lineattrs=(color=blue thickness=2);
*  highlow y = c_year low=q1 high=q3;
*  scatter y=Time_Period x=Survival_Rate / markerattrs=(symbol=circlefilled color=blue size=8);
run;


/* Create example dataset with OHCA survival rates by 5-year time periods */;
proc sort  data=survival_data;by c_year;run;
proc means data=survival_data n q1 median q3;
output out=a n=n q1=q1 median=median q3=q3; var Surv_Rate_Dis;  by c_year;
run;

proc means data=survival_data n q1 median q3;
output out=b n=n q1=q1 median=median q3=q3; var Surv_Rate_Dis;
run;


data b; set b; c_year=2015; run;

data ohca; set a b; by c_year; run;


title "OHCA Survival to Hospital Discharge";

proc sgplot data=ohca;
  yaxis discreteorder=data;
  xaxis label="Survival Rate (%)";
*  scatter y=c_year x= Surv_Rate_Dis/jitter;
  scatter y=c_year x=median;* / lineattrs=(color=blue thickness=2);
  highlow y = c_year low=q1 high=q3;
*  scatter y=Time_Period x=Survival_Rate / markerattrs=(symbol=circlefilled color=blue size=8);
run;
```

Part 4 – Halloween Candies Study

The internet site Fivethirtyeight.com conducted an online survey of Halloween candies. Respondents were asked to rate which candy they prefer out of a random pairing of 2 candies selected from a full list of 85. About 269,000 candy comparisons were presented to respondents spanning 8,371 unique IP addresses. From these comparisons, an ultimate preference score was calculated as the percentage of times each candy was chosen as the better of the pair, recorded as the win percent in the data. Additional independent variables included sugar percentage, price, and the presence of various candy components. The data in this file contains the results for 85 candy choices. Answer the following using your random sample of 50 candies chosen from the original sample of 85. (Each student will have his/her own data set in which to answer the questions).

1. Model the win percentage as a continuous normally distributed variable and determine which

factors are used when creating a predictive model. There are multiple approaches, including multiple regression and CART/RF methods. Use methods from both areas.

2. Determine which independent characteristics of a HALLOWEEN candy best predict the event that a candy falls into the top 15% of the win percentage category.

3. (New method) Repeat # 1 above assuming that the win percentages are continuous decimal ($win_{dec} = win/100$) variables on the interval (0,1). Use the GLM for the Beta model[2]. Summarize your findings. How do these results compare with what you found in part # 1 above? There is no reason to repeat the machine learning parts you used in # 1, why? Explain.

Part 5 – Experimental Study Opioid Use

The results of a recent trial concerning opioid use for relief of mild upper and lower back pain was published in Lancet Journal[3]. A copy of the paper is included with the exam material.

Selected material has been included here.

Methods

OPAL was a triple-blinded, placebo-controlled randomised trial that recruited adults (aged ≥ 18 years) presenting to one of 157 primary care or emergency department sites in Sydney, NSW, Australia, with 12 weeks or less of low back or neck pain (or both) of at least moderate pain severity. Participants were randomly assigned (1:1) using statistician-generated randomly permuted blocks to guideline-recommended care plus an opioid (oxycodone–naloxone, up to 20 mg oxycodone per day orally) or guideline-recommended care and an identical placebo, for up to 6 weeks. The primary outcome was pain severity at 6 weeks measured with the pain severity subscale of the Brief Pain Inventory (10-point scale)[4], analysed in all eligible participants who provided at least one post-randomisation pain score, by use of a repeated measures linear mixed model. Safety was analysed in all randomly assigned eligible participants. The trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12615000775516).

Findings

Between Feb 29, 2016, and March 10, 2022, 347 participants were recruited (174 to the opioid group and 173 to the placebo group). 170 (49%) of 346 participants were female and 176 (51%) were male. 33 (19%) of 174 participants in the opioid group and 25 (15%) of 172 in the placebo group had discontinued from the trial by week 6, due to loss to follow-up and participant withdrawals. 151 participants in the opioid group and 159 in the placebo group were included in the primary analysis. Mean pain score at 6 weeks was $2 \cdot 78$ (SE $0 \cdot 20$) in the opioid group versus $2 \cdot 25$ ($0 \cdot 19$) in the placebo group (adjusted mean difference $0 \cdot 53$, 95% CI $-0 \cdot 00$ to $1 \cdot 07$, p=$0 \cdot 051$). 61 (35%) of 174 participants in the opioid group reported at least one adverse event versus 51 (30%) of 172 in the placebo group (p=$0 \cdot 30$), but more people in the opioid group reported opioid-related adverse events (eg, 13 [$7 \cdot 5$%] of 174 participants in the opioid group reported constipation vs six [$3 \cdot 5$%] of 173 in the placebo group).

Interpretation

[2]There will likely be many occasions in the future in which you are ask to do something for which you have never been exposed or taught. Get busy or get another job!

[3]Opioid analgesia for acute low back pain and neck pain (the OPAL trial): a randomised placebo-controlled trial - 28 June 2023

[4]0-no pain, 10-extreme pain

Opioids should not be recommended for acute non-specific low back pain or neck pain given that we found no significant difference in pain severity compared with placebo. This finding calls for a change in the frequent use of opioids for these conditions.

Special items of interest include:

- Participants were masked and randomly assigned (1:1) to the opioid or placebo group.
- Data were collected at baseline, then at weeks 2, 4, 6, 12, 26, and 52 by use of a REDCap database. Outcomes and adverse events were measured via participants completing online surveys, or by research assistants over the phone if preferred by the participant.
- The primary endpoint was pain intensity (measured on a 0–10 scale by the Brief Pain Inventory Pain Severity Subscale) at 6 weeks after randomisation.
- A detailed a-priori statistical analysis plan was published before database lock.19 A sample size of 173 participants per group (346 total) had 90% power to detect a between-group difference of 1 on a 10-point pain scale at 6 weeks assuming a SD of $2 \cdot 5$ and an α of 5%, and allowing for 5% dropout and 10% non-compliance. We estimated that 1 on a 10-point scale would be the minimal clinical difference.
- The primary treatment effect was estimated as the adjusted mean difference in pain severity at the week 6 visit between groups and its 95% CI. The same model was used to estimate the effect of the treatment at weeks 12 and 52, as part of the pre-specified analyses.
- This study found there was no benefit of an opioid compared with placebo in people receiving guideline care for acute non-specific low back pain or neck pain. No significant difference was found in pain severity at the primary timepoint (6 weeks); however, we could not exclude a small benefit favouring placebo. The difference in pain scores between the groups increased over time until week 52, at which time there was a small but significant difference favouring placebo.
- This is the first blinded, placebo-controlled, multicentre trial of an opioid for acute non-specific spinal pain to measure treatment effects including short-term harms (adverse events) and long-term harms (opioid misuse risk). The trial was prospectively registered, and the trial design, conduct, analysis, and reporting have been transparent and independent. A limitation is that approximately 25% of data were missing at the primary timepoint, which reduced the power of the trial and could introduce bias if the data were not missing at random. This limitation was managed by analysing all participants with at least one post-baseline measurement using a repeated-measure model, thus reducing the proportion of excluded participants to 10% of all randomised participants. Sensitivity analyses using multiple imputations and tipping point analyses supported the robustness of the main findings and showed that the findings were unlikely to have been affected by the missing data. This rate of missing data is common in trials of opioids versus placebo.

Questions (Justify and support your answers.)

1. What is the research hypothesis for this paper? Can this be tested?
2. What is the null hypothesis that should be tested when the active treatment is known to have addictive side effects when misused? Should this null ever be two-sided when the active treatment is known to have addictive side-effects when using a placebo control? Explain your answer.

3. At week 6, they report that the results are inconclusive. Do you agree? Your answer will likely depend upon how you answered the previous question. Explain.
4. The original study was powered at 90% and the sample sizes anticipated some dropouts. What is the effective power when using the reported sample sizes in the study?
5. Under what initial assumptions could the authors have found that the placebo is more effective in reducing pain as considered in the study. This is not a hard question, so don't make it into one!