U-Flourish university students well-being and academic success longitudinal study: a study protocol

Sarah Margaret Goodday,1 Daniel Rivera,2 Hannah Foran,2 Nathan King,3 Melissa Milanovic,4 Charles DG Keown-Stoneman,5 Julie Horrocks,5 Elizabeth Tetzlaff,7 Christopher R Bowie,4 William Pickett,3 Kate Harkness,4 Kate E Saunders,8 Simone Cunningham,4 Steven McNevin,9 Anne Duffy*9

ABSTRACT

Introduction Over 30% of Canadians between the ages of 16 and 24 years attend university. This period of life coincides with the onset of common mental illnesses. Yet, data to inform university-based mental health prevention and early intervention initiatives are limited. The U-Flourish longitudinal study based out of Queen’s University, Canada and involving Oxford University in the UK, is a student informed study funded by the Canadian Institute for Health Research Strategy for Patient Oriented Research (CIHR-SPOR). The primary goal of U-Flourish research is to examine the contribution of risk and resiliency factors to outcomes of well-being and academic success in first year students transitioning to university.

Methods and analysis The study is a longitudinal survey of all first-year undergraduate students entering Queen’s University in the fall term of 2018 (and will launch at Oxford University in fall of 2019). In accordance with the CIHR-SPOR definitions, students represent the target population (ie, patient equivalent). Student peer health educators were recruited to inform the design, content and implementation of the study. Baseline surveys of Queen’s first year students were completed in the fall of 2018, and follow-up surveys at the end of first year in the spring of 2019. Extensive student-led engagement campaigns were used to maximise participation rates. The baseline survey included measures of personal factors, family factors, environmental factors, psychological and emotional health, and lifestyle factors. Main outcomes include self-reported indicators of mental health at follow-up and mental health service access, as well as objective measures of academic success through linkage to university administrative and academic databases. A combination of mixed effects regression techniques will be employed to determine associations between baseline predictive factors and mental health and academic outcomes.

Ethics and dissemination Ethical approval was obtained by the Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (HSREB) (#602312) at Queen’s University. Findings will be disseminated through international and national peer-reviewed scientific articles and other channels including student-driven support and advocacy groups, newsletters and social media.

Strengths and limitations of this study

- Collaboration with students at all stages of the research process.
- A strong student-led engagement campaign resulted in a participation rate of almost 60% of the entire first-year undergraduate student body at Queen’s University.
- Findings will inform universal and targeted prevention and early intervention initiatives.
- Comparison of findings across universities (Queen’s and Oxford) will be forthcoming.

INTRODUCTION

The transition to university life coincides with a critical time in psychosocial and biological development. At the same time, the brain is undergoing accelerated growth and has increased sensitivity to risk exposures such as perceived stress, substance use and sleep problems.1 Not surprisingly, the developmental period from 16 to 24 years of age represents a peak period of risk for the onset of psychiatric illness.1–3

Universities have an obligation to provide resources to support student well-being and academic success during this critical transitional period. Yet, there is limited evidence to inform universities as to how to meet the spectrum of need, which ranges from resiliency building and health promotion to supporting students experiencing transient distress and identifying those with emergent psychiatric illness who require referral to specialty services.4

Approximately 1.7 million students were enrolled in universities across Canada in 2017.5 The age at university entry in Canada has been declining since 1980 and the proportion of international compared with domestic students has been increasing, translating...
into a sizeable population of students from varied backgrounds with diverse risk and resiliency profiles.\(^6\)

A recent cross-sectional survey of first-year students at Queen’s University found that 28% self-identified as having a mental illness, over 30% engaged in binge drinking and almost 20% used cannabis within the past 2 weeks.\(^7\) In the same survey, the top ranked reasons reported by students for lower grades in a pivotal assignment or exam were related to mental health including: stress 43%, sleep problems 29%, anxiety 26% and depression 15%.\(^8\) The nationally representative Canadian Health Behaviour in School-Aged Children Study reported findings consistent with this trend, and that poor interpersonal relationships with parents and peers and unhealthy lifestyles behaviours reflect important contributors to mental health problems.\(^8\)

Family factors have been associated with mental health and academic outcomes in students. Specifically, a history of mental illness in first-degree relatives is a major risk factor for emerging mental illness in youth.\(^9\)\(^,\)\(^10\) Current models suggest the risk of mental illness in youth is in part caused by an interaction between genetic predisposition and experience of early adversity (e.g. childhood abuse), early life stress, and trauma, compounded by more proximal risk exposures, such as peer support and social connectedness, perceived stress and substance use.\(^11\)\(^-\)\(^13\) Evidence supports that parental attitudes also influence student well-being and academic success.\(^14\) For example, a student’s perception of parental beliefs shapes their assessment of how appropriate and achievable their academic goals are. In addition, students who perceive greater parental warmth appear to work harder to pursue their academic goals and believe more strongly in reward important to academic success and have been assessed through self-efficacy, locus of control and perceived competence.\(^15\)\(^-\)\(^17\) Expectancy beliefs are also important to academic success and have been assessed through self-efficacy, locus of control and perceived competence.\(^15\)\(^-\)\(^17\) Specifically, it appears that students are more likely to set higher academic goals and feel more motivated to achieve these goals when they believe success is based on their own effort and that they are competent to achieve these goals. The literature also supports that student ability to self-regulate sleep and study habits are important contributors to academic success.\(^15\)\(^-\)\(^17\)

We currently lack adequate data on the collective contribution of risk factors to mental health and academic outcomes in students transitioning to university. We therefore launched the U-Flourish study—a longitudinal study of all incoming first-year undergraduate students, and those entering first-year professional schools of law and medicine. The aim of the research is to understand why some university students flourish and others do not in the transition to university life in terms of their academic and mental health outcomes. Specific objectives include to:

1. Partner with students in research to improve mental health and academic outcomes.
2. Describe the mental health needs of university students.
3. Identify risk and resiliency profiles pertaining to student outcomes.
4. Determine the individual and collective contribution of family, personal and environmental factors on outcomes of well-being and academic success in university students to inform resource and service development.
5. Understand the longitudinal relationship between mental health and academic outcomes.

**METHODS AND ANALYSIS**

**Patient and public involvement**

This is a student-informed research effort. Peer health educators (PHEs) are included at all stages of the research from design to implementation and we will include the student perspective in the interpretation and dissemination of findings.

**Setting**

The U-Flourish Survey is a longitudinal study based at Queen’s University in Kingston, Ontario, Canada (https://www.queensu.ca/about/). Queen’s is a public undergraduate education-intensive university founded in 1841 via a Royal Charter issued by Queen Victoria. The majority of its almost 19,000 undergraduate students currently come from surrounding major cities in Canada (e.g., Toronto, Ottawa and Montreal) and regions across the province of Ontario, with a lesser number of students coming from other provinces in the country. The proportion of international students is increasing but remains around 10% of the undergraduate student body. The majority (over 85%) of first-year students entering Queen’s live in small towns or rural areas.
residence on campus. The U-Flourish study will launch at a partner site, Oxford University in the fall of 2019. This will allow comparison across two different universities, both with high rates of students living in college.

**Target population and stakeholder involvement**

The Canadian Institutes for Health Research Strategy for Patient-Oriented Research initiative defines patients as: ‘anyone who has personally lived the experience of a health issue as well as their informal caregivers including family and friends’ (http://www.cihr-irsc.gc.ca/e/documents/spor_panel-en.pdf). Under the SPOR theme, students as ‘patients’ represented the target population for potential interventions that might develop from the research. We included PHEs as key stakeholders to inform the design, content and implementation of the survey.

**Procedure**

All first-year students were invited to take part including first-year students entering professional schools of business, medicine and law. Any newly enrolled first-year undergraduate student consenting to the study was eligible to participate. There were no exclusion criteria in order to maximise representativeness of the sample of undergraduate students.

We launched the Queen’s University baseline survey approximately 2 weeks into the fall 2018 term (figure 1). We sought to maximise participation through an ambitious student-designed and student-led engagement campaign, creating a study brand and logos now trademarked with the Canadian Government (online supplementary information). While we targeted a minimum participation rate of 30% for an adequately powered study, we achieved a response rate of 58% of all first-year Queen’s students completing the baseline survey resulting in a cohort 3029 out of a possible 5242 (figure 2). About 64% of students participating in the baseline survey completed the follow-up survey resulting in a completed 1-year study sample of 1952 students with time 1 and time 2 observations. There were 32 additional students who started but did not complete the time 1 survey but did complete the follow-up time 2 survey putting the total number of students with outcome data to 1984.

The launch of the baseline survey was announced on each student’s e-learning platform (D2L). All first-year students were sent a link to complete the survey via their university email. The portal to complete the survey was open for 2 weeks after the launch. Those completing the survey were credited with $5 Flex dollars donated by the University Division of Student Affairs that could be used at campus venues such as a café or dining hall.

The same engagement procedure was used for the follow-up survey. Specifically, 1 month prior to the end of the spring term, a second media and engagement campaign led by the PHEs was launched. Two weeks prior to the end of spring term classes at the end of March, students who opened the link to the baseline study were sent a link via their university email to complete the follow-up survey. The portal remained open for a 2-week period. As an incentive, students completing the time 2 survey were credited with $5 Flex dollars again donated by Student Life and offered the opportunity to enter a draw to win 1 of 10 iPads (see below and figure 1).

---

**Figure 1** Study design and timing of engagement activities, survey launches and email reminders (R).

---

<table>
<thead>
<tr>
<th>Month</th>
<th>Engagement Activities</th>
<th>Survey Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aug</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oct</td>
<td></td>
<td>R R R</td>
</tr>
<tr>
<td>Nov</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr</td>
<td></td>
<td>R R R</td>
</tr>
</tbody>
</table>

*social media messages; website newsletters; digital posters; information booths; in class presentations by faculty and peer health educators (PHE R=reminders via social media and email )
Qualtrics survey software was used as the electronic platform for the survey. Once students click on the link, they are brought to the introduction page which displays a Letter of Information detailing the name of the study, study funder, investigators and the aims of the research. Drop-down menus and branching logic were used to facilitate the ease of completion of the e-survey. The baseline survey took approximately 12 min to complete while the follow-up survey took approximately 8 min to complete.

**Student engagement: orientation week**

Student engagement began in the 2018 fall semester orientation week during which student PHEs were present at two separate club fairs and three orientation week presentations run by various faculties. The orientation week presentations were part of the Concurrent Education, Kinesiology and Off-Campus student orientation weeks. The PHEs were able to provide information about the fall baseline survey, answer student questions, and encourage participation to a considerable proportion of the 5242 incoming students.

**Student engagement: branding and advertising**

U-Flourish graphics and branding were presented to students and PHEs to determine the most effective for engagement. Print and digital posters (online supplementary information) were placed at various public locations across campus including three dining halls, two student centres and numerous other dining locations on campus prior to and while the survey was open. A messaging campaign was established via the university’s social media accounts that released nine distinct posts with information about the survey along with a professionally created and branded graphics similar to the posters placed around the campus (online supplementary information—social media posts). Emphasis was placed on the use of student-centric language and phrases that urged students to ‘have their say’ and contribute to the conversation about what was needed to support well-being and academic success through partaking in the study. A total of four campus booths were set up during the survey period and staffed by PHEs. At these booths, students were able to show an electronic receipt for completing the baseline survey and receive a free pizza lunch, as well as small branded items such as stress balls and laptop stickers. Students, regardless of status of survey completion, were able to interact with the student PHE’s who provided information about the study and its relevance to student life.

**Student engagement: in-class presentations**

In the first and second week of classes, 19 in-class talks were given by the study investigators (faculty at the Queen’s University) and PHEs targeting the largest first-year classes in each programme. These presentations included informative slides and a standardised script to share information about the aims of the study (online supplementary information).

**Student engagement: incentives**

A $5 credit applied to student’s accounts was offered to students completing each of the baseline surveys and follow-up surveys. Information on how to earn and access the $5 credit was described during in-class presentations and on the websites. In addition, branded postcards announcing the study along with laptop stickers with the U-Flourish logo were distributed in drawstring bags that are given to every incoming student at the beginning of the orientation week. The Division of Student Life at Queen’s University provided the $5 Flex credit incentive as a donation in kind to the project.

**Student engagement: university web-platforms**

The U-Flourish team worked with campus-based film production service and student volunteers to make engaging brief video clips introducing the survey and posted on the first-year student D2L learning platform and U-Flourish study website (http://www.queensu.ca/studentwellness/health-promotion/u-flourish-student-health-project).

**Student engagement: reminders**

A total of three reminder emails were sent to students to participate and redeem their rewards for survey completion 1 week after the survey launch, at the beginning of the second week after the launch, and 48 h prior to the close of the survey (figure 1). Messages containing important survey information were sent to incoming
students through programme newsletters, student residence newsletters and the online learning platforms used by large first-year classes (online supplementary information). A message to all respondents was sent out thanking them for their initial participation and wishing them luck with their final examinations. They were also encouraged to participate in the follow-up survey and stay vigilant for updates on the study webpage.

**Follow-up survey engagement**

The general procedure and methods used to engage students with the baseline survey were used to re-engage respondents with the study and its follow-up survey that launched in March 2019. In addition, class talks were given to the same full-(two-term) classes in the winter semester by the same presenters. The same social media and messaging channels were used with information specific to the follow-up survey. Reminder emails were also sent to baseline respondents to inform them of on campus events such as the booths with redeemable lunch and branded items. In all messaging, the incentive of a chance to win one of ten iPads and ‘a call to action’ was emphasised to increase student interest.

<table>
<thead>
<tr>
<th>Survey section</th>
<th>Measure/item</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Section I—personal factors</strong></td>
<td>Date of birth</td>
</tr>
<tr>
<td></td>
<td>Sex/gender</td>
</tr>
<tr>
<td></td>
<td>Self-reported height and weight</td>
</tr>
<tr>
<td></td>
<td>Varsity athlete; entrance scholarship; domestic/foreign student</td>
</tr>
<tr>
<td></td>
<td>Ethnicity</td>
</tr>
<tr>
<td></td>
<td>Physical and mental health self-rating</td>
</tr>
<tr>
<td></td>
<td>Mental health lifetime diagnosis/treatment history</td>
</tr>
<tr>
<td></td>
<td>Rosenberg Self-Esteem Scale</td>
</tr>
<tr>
<td><strong>Section II—family factors</strong></td>
<td>Family history of mental illness</td>
</tr>
<tr>
<td></td>
<td>Parental highest level of education</td>
</tr>
<tr>
<td></td>
<td>Parent country of birth</td>
</tr>
<tr>
<td></td>
<td>Family intactness during childhood</td>
</tr>
<tr>
<td><strong>Section III—environmental factors</strong></td>
<td>Resilience Scale for Adolescence (peer relations, social identity)</td>
</tr>
<tr>
<td></td>
<td>Perceived Stress Scale</td>
</tr>
<tr>
<td></td>
<td>Childhood physical and sexual abuse</td>
</tr>
<tr>
<td><strong>Section IV—psychological and emotional health</strong></td>
<td>Locus of Control Scale (expectancy beliefs)</td>
</tr>
<tr>
<td></td>
<td>Motivation for Learning Scale (value appraisal and self-regulated learning)</td>
</tr>
<tr>
<td></td>
<td>Lifetime Columbia Lifetime Suicidal Behavior-screening</td>
</tr>
<tr>
<td></td>
<td>Generalised Anxiety Disorder Scale (GADS-7)</td>
</tr>
<tr>
<td></td>
<td>Patient Health Questionnaire (PHQ-9)</td>
</tr>
<tr>
<td><strong>Section V—lifestyle, habits and behaviour</strong></td>
<td>Frequency of alcohol, caffeine consumption and exercise</td>
</tr>
<tr>
<td></td>
<td>Sleep condition indicator (insomnia)</td>
</tr>
<tr>
<td></td>
<td>Seeking of university support services/help-seeking</td>
</tr>
</tbody>
</table>

**Survey measures**

**Background literature**

Measures included in the baseline and follow-up survey targeted the assessment of factors hypothesised to contribute to student mental health and academic outcomes. Specifically, measures were chosen on the basis of: (1) the available evidence; (2) their relevance to post-secondary student populations; (3) good psychometric properties (Supp. table 1) and (4) acceptability as judged from PHE and student feedback.

**Survey content**

The baseline survey (table 1) included factors from five domains: personal factors (eg, socio-demographic, self-esteem28) family factors (eg, family intactness (parental marital status) and parental warmth29) environmental factors (eg, peer-relations30 and early adversity31) psychological and emotional health (eg, anxiety,32 depressive symptoms,33 suicide-related behaviour34 and expectancy beliefs35) and motivations for learning36 and lifestyle habits and behaviour (eg, frequency of alcohol, caffeine consumption and exercise and sleep37) (see table 1 for measure information).

The follow-up survey (table 2) included measures of mental health such as symptom rating scales of anxiety,32
depression, student life satisfaction and emotional well-being. Academic success was defined both in terms of self-reported average grade percentage, any occurrence of expected academic probation or suspension, and retention (ie, plans to return to university the next year). For those students providing informed consent, actual course grades will be provided through linking survey student numbers to the university academic database (eg, grade point average (GPA) for term 1, term 2 and cumulative). Students' help-seeking and use of university health and wellness services was measured by asking students to indicate from a defined list which campus mental health services they accessed over the year. Students attempting to access services also completed measures on perceived barriers to care while timing, frequency and satisfaction of service utilisation was assessed through items from the service utilisation section of the Canadian Community Health Survey–Mental Health. Students also offered the opportunity to explain in free text any barriers they encountered in accessing indicated university services, how helpful they found these services, and for suggestions as to any additional services they feel should be provided that are not (see table 2 for measure information).

Data linkage
The survey response records were linked to administrative and academic data through the unique student numbers allowing us the novel opportunity to examine the association between perceived and actual academic performance. Academic outcome data in this study include: course grades, overall grade percentage, rate of failed courses and any instance of academic probation or suspension. Authorised university administrators through the Office of Research and Institutional Planning provide the research team with the pre-specified outcome variables (as per Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (HSREB) approved protocol) in encrypted files for analysis. Procedures in compliance with the Queen’s University HSREB guidelines were in place to ensure data security and protection (ie, https://www.queensu.ca/secretariat/policies/senate/electronic-information-security-policy-framework/electronic-information-security).

Analytic plan
Different mixed effects regression-based models will be used to determine the contribution of candidate risk and protective factors to well-being and academic success while accounting for clustering where appropriate. Primary outcomes include clinically significant mental health symptoms at follow-up as measured by clinical rating scales (ie, GADS-7, PHQ-9, suicide-related thoughts and behaviours) and academic grades. Secondary outcomes include life satisfaction and well-being at follow-up and any new or recurrent mental health diagnosis between baseline and follow-up. Specifically, we will examine whether different domains (personal, environmental of family) at baseline predict a change in mental health symptoms from baseline to end of first-year follow-up, predict the new onset or recurrence of a mental health condition between baseline and follow-up, predict level of life satisfaction and well-being at follow-up and academic grades. Self-reported outcome data on wellbeing and academic success at follow-up will be quantified as continuous total scores and binary outcomes where mental health diagnoses are used, and when using clinical cut-off scores of clinical symptom scales (eg, GADS-7, PHQ-9).

Administrative data on academic outcomes (eg, GPA) will be treated as continuous. Because of clustering of students within school programme, we will use generalised linear mixed models, which can be used for continuous or categorical outcomes. Potential confounders (eg, age) have been identified a priori from the literature and included in the survey. From this set of pre-identified
variables, we will test for confounding through estimating
dissociations of these factors with both the exposure and
outcome and will adjust for in multivariable models where
appropriate. Missing responses on survey questions will
be dealt with through multiple imputation where only
one item is missing. If more than one item is missing,
complete case series analyses will be used. Characteristics
of item study non-participation and item non-response
will be explored to test for potential selection biases to
determine the influence on effect estimates of primary
associations. Access to basic socio-demographic data is
available through Queen’s University allowing the testing
of selection biases associated with non-response. Sensi-
tivity analyses will be conducted to determine whether
non-response is associated with key factors associated
with the outcome. Factors identified will be statistically
adjusted for in multivariable models where appropriate.

We outline sample size requirements for a binary
and continuous outcome. Binary response, sample size
depends on the probability of success with larger sample
sizes required for probabilities closer to 0 or 1. As an
example of a binary outcome (eg, past year prevalence
of suicide attempts), in order to detect a difference (eg,
between men and women) as small as 0.2 and an alpha
level of 0.05 we would have >90% power with our total
sample size at follow-up (n=1984). Similarly, for a con-
tinuous outcome (eg, mean PHQ-9 score) and 66% of the
sample being female, we will be able to detect a mean
difference as small as 0.2 between females and males
on the PHQ-9 with >90% statistical power with our total
com/Menu/OE_Menu.htm).

Ethics and dissemination
Participants were provided with a Letter of Information at
the beginning of the electronic survey sent via students’
emails. Students provided implicit digital consent having
read the letter of intent and then completed the survey.
Students were encouraged by PHEs during engagement
events to ask any questions they might have. The consent
form details that any information provided in the survey
will be kept confidential. To help ensure confidentiality,
the participants are made aware that their responses will
be de-identified and given a unique alphanumerical study
identifier for analysis. Participants are asked to consent
to having their survey data linked to their university held
administrative and academic data and were assured these
data will be kept strictly confidential by the research team.
The Qualtrics survey platform ensures that responses are
secure sockets layer encrypted and access to Qualtrics
survey accounts by authorised research team personnel
are single sign-on/password protected. Some of the
survey items are of a sensitive nature (eg, suicide-related
behaviour). Students are informed of this at the begin-
nning of the survey in the letter of intent and are provided
with a list of university support services contacts (eg, crisis
line).

We will mount a national and international effort to
fast-track the dissemination and translation of research
findings through Editorials and Opinion pieces in newspa-
papers, presenting at national and international confer-
ences and generating peer-reviewed publications. An
important part of the knowledge translation effort will
both target and involve students through the inclusion
of our PHEs in these activities. Findings will be shared
with students and other stakeholders through student-
driven support and advocacy groups (Jack.org), newslet-
ters and social media. Findings will also be shared with
Best Practices in Canadian Higher Education (https://
bp-net.ca/).

DISCUSSION
More young people are entering university and the ratio
of foreign to domestic students is increasing. This trans-
lates into a sizeable population of emergent adult students
from different backgrounds and with highly variable risk
profiles and mental health needs. There is limited data
to inform universities about how best to support this
growing and diverse student population. The anticipated
impact from this study is to inform the development of
evidence-based targeted mental health prevention
and early intervention initiatives for the undergraduate
student population. The long-term goal of this longitudi-
ナル survey is to form the basis of a national and inter-
national multidisciplinary programme of student mental
health research to continue development and improve
outcomes for students moving forward. Specifically, these
data will enable us to characterise both risk and resilien-
try pathways and accurately estimate mental health needs of
university students. Future research stems from this
work will include the mapping of transitions to student
mental health services and the development of infor-
mative quality of care indicators. A model of proactive
student mental healthcare across the spectrum of need
with embedded standardised metrics for evaluation and
further development will then be possible.

Author affiliations
1Psychiatry, University of Oxford, Oxford, UK
2Queens University, Kingston, Ontario, Canada
3Public Health Sciences, Queen’s University, Kingston, Ontario, Canada
4Psychology, Queen’s University, Kingston, Ontario, Canada
5Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada
6Mathematics and Statistics, Guelph, Ontario, Canada
7University of Ottawa, Ottawa, Ontario, Canada
8University of Oxford, Oxford, UK
9Psychiatry, Queen’s University, Kingston, Ontario, Canada

Acknowledgements We would like to thank the students and faculty who
participated in the engagement campaign of the U-Flourish survey contributing to
a very successful response rate. We would also like to thank Riz Murphy for her
help with graphics and the students for their participation in this research. Anne
Duffy is a Visiting Fellow at All Souls College, University of Oxford for the 2019-2020
academic year supporting the launch of the U-Flourish research at the University of
Oxford.

Contributors AD is the principal investigator leading the U-Flourish research and
collaboration with all authors (SMG, DR, HF, NK, MM, CDGK-S, JH, ET, CRB, WP, KH,
REFERENCES


BMJ Open first published as 10.1136/bmjopen-2019-029854 on 26 August 2019. Downloaded from http://bmjopen.bmj.com/ on October 1, 2023 by guest. Protected by copyright.