FRAME Report 2021

A review of experimental design training provision for biosciences PhD students at UK Universities

Margarita Kalamara
PhD student, University of Dundee
Professional PhD Internship with FRAME

Fund for the Replacement of Animals in Medical Experiments
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Introduction

This report has been researched and written in winter/spring 2021 by Margarita Kalamara, a Molecular Microbiology PhD student at the University of Dundee.

Margarita completed a 3-month placement with FRAME (Fund for the Replacement of Animals in Medical Experiments) as part of the Professional Internship for PhD Students (PIPS) scheme ran by the East of England Bioscience (EASTBIO) Doctoral Training Partnership and funded by the Biotechnology and Biosciences Research Council (BBSRC).

FRAME's Education and Outreach Manager Amy Beale acted as project supervisor and supported Margarita during her placement.

We are very grateful to Margarita for her time, commitment and passion during her placement and in the completion of this project. We are also grateful to all the universities, institutions and other organisations that took the time to respond. This version of the report has been anonymised to protect these organisations.

Please contact FRAME to discuss this project, our other work, or other collaboration or volunteer opportunities with us. hello@frame.org.uk

FRAME

FRAME is an independent scientific charity dedicated to the development and promotion of alternative, non-animal research methods with the ultimate aim of replacing the need for laboratory animal use in medical and bioscience research and testing.

Whilst FRAME accepts that it is not possible to stop all animal testing immediately, it challenges the idea that all current animal research for human health, disease and safety testing is valuable and necessary. Where animal testing is still required the charity supports the 3Rs principles and believes that animal researchers should be doing everything possible to ensure that the research is robust, reproducible and reported accurately.

Margarita Kalamara

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Background

The Reproducibility Crisis

There is an increasing concern within the scientific community about the lack of reproducibility (the ability to replicate experiments and get the same results) among published research and a few studies have attempted to quantify this problem. Lack of reproducibility in preclinical research, which relies heavily on animal studies, is a particular concern due to the potential impact on society, in terms of the ethical implications of conducting animal research of little or no value and the high level of funding invested.

A survey conducted in 2016 to examine the views surrounding the reproducibility crisis among scientists showed that, of the 1,576 participants, 70% have failed to reproduce published experimental data and more than half of responders have failed to reproduce their own results (2). The findings of this survey mirror previous studies in which scientists from industry have tried to reproduce the results of "landmark" papers from academia. One such study by scientists at the biotechnology company Amgen, examining the reproducibility of preclinical cancer research findings, reported that they were only able to reproduce 11% of the published papers they examined (3). Another paper showed a reproducibility rate of 20–25% among preclinical studies in the fields of oncology, cardiovascular research and women's health (study conducted by a team at Bayer HealthCare)(4). This low level of reproducibility is very concerning.

Scientific progress is a collective process, where multiple researchers working in a field build on published information to increase the body of knowledge. This body of knowledge may be translated into medicines or other products, and influence policy that can help to address societal problems. Not being able to trust the reliability of the research data published in any given field is hugely problematic and it hinders scientific progress, whether this be hindering the development of new medicines or our understanding of disease. Additionally, the reproducibility crisis has been suggested to have negative impacts on the mental health of researchers (5) and has the potential to harm the reputation of biomedical research among members of the public. Importantly, lack of reproducibility can result in a huge waste of time, funding, resources and, in cases where animals or animal-derived reagents are used, animal lives. This poses great ethical concerns. Research involving animals is only approved on the basis that the harm caused to the animals is justified by the benefits of the expected research outcome. If the results of the research are not reproducible and are consequently not beneficial, the harm caused to the animals cannot be justified. Therefore, to avoid breaching ethical guidelines, especially when animals are used, it is important that research is carried out in a way that will yield reproducible results.

Background

Factors Affecting the Reproducibility Crisis

Multiple factors contribute to the reproducibility crisis, as this is a varied and complex problem. One of the major causes is believed to be systematic. Researchers in academia are under a lot of pressure to publish. Career progression and the ability to secure funding are dependent on a person's publication track record. Additionally, the most "publishable" research shows "positive" results; results that confirm all hypotheses and can be formulated into a neat and tidy story. This pressure to publish causes a partial shift of the focus of scientific research from "finding the truth and addressing problems" to "producing a story that can be published", and increases the bias of scientists, threatening the rigour and reliability of published data (6). The rigour of data can be compromised purposely by fabrication, which is thought to be a rare occurrence, or, more commonly, by carrying out questionable practices surrounding the production, interpretation and reporting of the data (6).

Other factors that have been shown to play a critical role in the lack of reproducibility include the reagents used in experimental work. For example, animal-derived antibodies, which are used to detect and bind to specific molecules in complex samples, are often variable and lack specificity, leading to major problems when trying to replicate experiments (7). Multiple research papers have shown poor specificity among antibodies (8, 9). This can be minimised with correct experimental design; for example, correct validation of reagents and inclusion of appropriate controls to ensure specificity (10).

Poor reporting is also believed to factor into the reproducibility crisis, as the ability to replicate experiments by another researcher is heavily reliant on the availability of sufficient detailed information about the methodology and raw data sets used. Problems in this area may arise from selective reporting, where researchers only show the results that prove their hypotheses (which of course is not correct practice), or providing insufficient details on the raw data, analysis carried out or methodology used. According to the Nature survey on the reproducibility crisis (2) many scientists believe that poor oversight and mentoring of early career researchers is also a major contributor to the reproducibility crisis. This is supported by a publication claiming that "a major factor in sloppy data generation, manipulation, and reporting would appear to be inadequate training and supervision of graduate students and postdoctoral fellows. To address this, principal investigators, institutions and promotions committees should place greater emphasis on training, mentoring, and supervising junior staff. There should be an explicit requirement that junior scientists will be thoroughly trained and supervised in experimental design and data interpretation" (11, p. 467).

Background

This brings us to the importance of correct experimental design and statistical analysis, the lack of which has been cited by many as a causal agent for the reproducibility crisis (2, 11, 12). When interviewing scientists involved with animal research, the authors of a paper report that "With few exceptions, interviewees involved in animal research expressed various levels of discomfort with the statistical aspects of experimental design and analysis" (12, p. 176). This is reflected in publications involving the use of animals. A study surveying the literature found that only 59% of the research papers examined stated the hypothesis or objective of the study and the number of animals that were used. Other issues included the lack of randomisation and blinding, in 87% and 86% of research papers examined respectively (13).

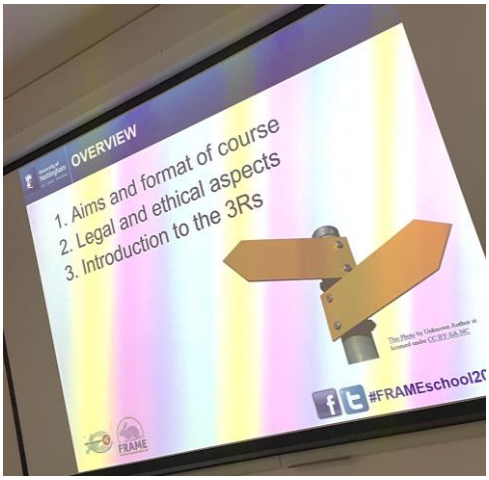
The factors mentioned above are by no means an exhaustive list of the causes of the reproducibility crisis, and it is evident that a lot needs to be done to address this problem and ensure published research is rigorous, useful and reproducible. Examples of areas for improvement include changing the research culture to not favour the publication of "positive results" which could decrease publication bias, introducing more strict guidelines for authors to ensure that all raw data and methods are reported, and providing training in experimental design and statistical analysis (and access to expert advice when necessary), especially to early career researchers. This would help ensure researchers are competent and experiments are designed and analysed appropriately to increase the reproducibility of the results.

Background

FRAME Training School

One such initiative to improve the quality of research is the training school in experimental design and statistical analysis run by the charity FRAME (Fund for the Replacement of Animals in Medical Experiments). Part of FRAME's mission is to support the implementation of the 3Rs — Replacement, Reduction and Refinement of the use of animals in research — particularly where animals are used for biomedical research and regulatory testing for the benefit of human health. One of the best ways to reduce and refine the experimental procedures performed on animals is good experimental design (14), which is also crucial for reproducibility.

FRAME's training school on experimental design and statistical analysis runs annually and aims to give researchers an understanding of the basic concepts of experimental design and statistical analysis, and the skills to more efficiently design their experiments. It also seeks to stimulate engagement with the 3Rs, particularly around refinement and reduction, as well as to encourage discussion between people that use animals in different fields (e.g. industry and academia). The training school has received FELASA (Federation of European Laboratory Animal Science Associations) accreditation and has been running for over 13 years, training participants from across Europe. The course is aimed at researchers from postgraduate student level and above. Feedback from previous training schools has been overwhelmingly positive and has indicated that many of the participants had never been exposed to such training before, suggesting that there may be a gap in the provision of basic experimental design and statistical analysis training among early career researchers.



Background

Sources of PhD Funding and Training

This UK-based project focusses on the training that biosciences PhD students receive on experimental design and statistical analysis. It is therefore important to take into account the major sources of training accessible to PhD students. It is apparent that the training courses that PhD students can attend vary greatly and are impacted by multiple factors. Sources of "generic skills" training include courses provided by the universities themselves, some of which may be specific to a school or faculty (for example, through PhD induction programmes for new students joining the school or faculty). Often, universities have structures in place, such as Organisational and Professional Development (OPD) and doctoral academies, providing courses on a range of subjects.

For some students, another major source of generic skills training will be provided by their funding body structure. For example, students funded through research councils and some charities are likely to be part of a studentship cohort, such as a Doctoral Training Partnership (DTP) or similar structure (other examples include Doctoral Training Centres (DTCs), Collaborative Training Partnerships (CTPs) and CASE studentships). DTPs are blocks of funding that are awarded either to individual organisations or cross-institutional consortia. They usually have a specific set of training requirements that their students are expected to fulfil, in addition to the training provided by their own universities.

A report by the Wellcome Trust, published in 2018, collated statistics acquired from the Higher Education Statistics Agency and estimated that almost half of PhD students in biological and biomedical sciences disciplines were either self-funded (27.6%) or are funded internally by their institution (20.6%) (1)(Fig. 1). Therefore, as any training that may be provided by funders is only applicable to a subset of the student population, the primary focus of this project was on training provided by the universities themselves, as this was deemed as a more representative source of training is accessible to the entire student population.

Background

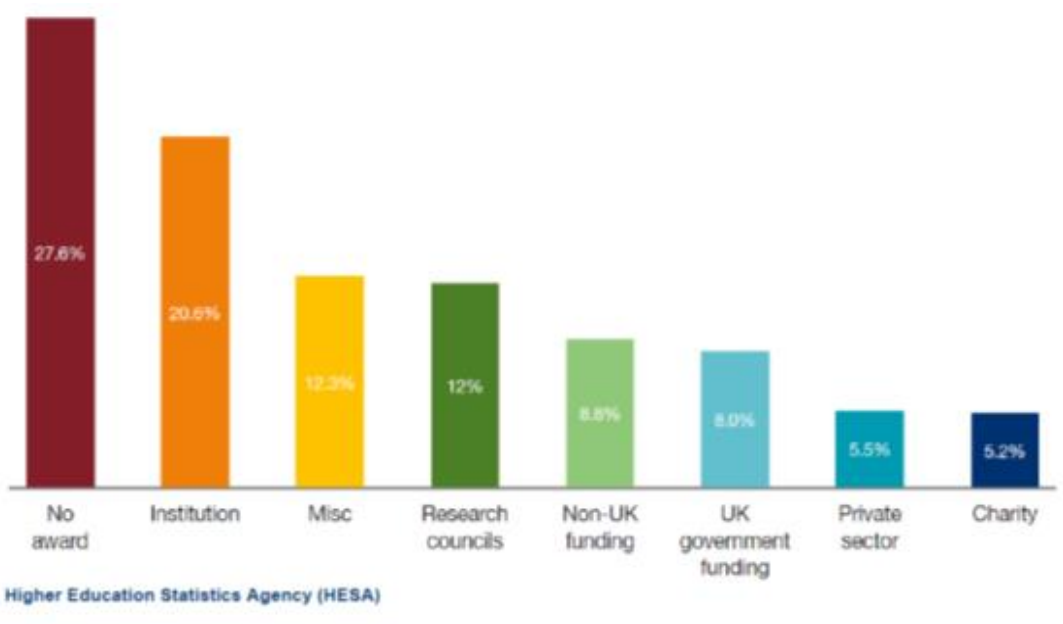


Figure 1: Funding sources of PhD students in biological and biomedical sciences in the UK (1).

Aim

The aim of this project was to help understand to what extent PhD students in biosciences subjects are provided with mandatory training in experimental design and statistical analysis as part of their generic skills training. PhD students are the focus of this research, as they are early career researchers who receive formal training and are likely to be the next generation of researchers and leaders in the field of bioscience research.

Methods

Selection of Organisations to be Contacted

Universities and medical schools accounted for more than half of the procedures performed on animals in 2019 (15). Therefore, this study focused on PhD students in academia. Universities were contacted by email, as it is expected that some generic skills training will be available to all PhD students affiliated with each organisation.

The emails described the mission of FRAME – to promote the 3Rs principles, to help ensure research involving animals was performed to the highest standards – and provided information about the FRAME training school. In addition, the emails explained the scope of this project: to help understand whether there is a need for experimental design training among PhD students.

Organisations were asked to provide an outline of any mandatory training related to experimental design and statistical analysis that PhD students were expected to attend. The primary focuses of this study was on mandatory training, as it was reasoned that optional courses are less likely to be taken up by all, or most, students.

Universities and Research Institutes Contacted

One of the aims of FRAME is to ensure that research involving animals is carried out correctly, to avoid wasting animal lives. Therefore, organisations were chosen based on the numbers of scientific procedures they had performed on animals. Some research organisations have signed the "concordat on openness on animal research in the UK" (16), committing to being open about the use of animals in research. There is a requirement that signatories of this concordat publish the numbers of scientific procedures they performed on animals. These organisations were therefore examined (15) and those that had performed 10,000 or more procedures on animals in the last year for which information was available were selected. This criterion generated a reasonable number of institutions that could be contacted about the provision of experimental design training within the available time frame. In cases where multiple faculties, colleges or schools within an organisation appeared to conduct research likely to involve the use of animals, they were all contacted. The names of the organisations are not included in this report to preserve anonymity.

Methods

Participating Universities and Research Institutes

Information about experimental design and statistical analysis was acquired from twelve of the twenty-six research organisations (ROs) identified and approached for information. Table 2 provides a summary of the sources of information. For some of the organisations contacted, when responses were not received by email, freedom of information (FOI) requests were submitted.

Table 2: List of research organisations (ROs) for which information regarding the provision of experimental design and statistical analysis training was acquired.

Research organisation	Faculty/School	Source of information
RO-1	N/A	Responded to email
RO-2	Not specified	Response to FOI request
RO-3	All identified relevant faculties/schools	Responded to email
RO-4	All identified relevant faculties/schools	Responded to email
RO-5	All identified relevant faculties/schools	Internal information from FRAME trustee
RO-6	Part of the identified relevant faculties/schools	Internal information
RO-7	Part of the identified relevant faculties/schools	Response to email
RO-8	Part of the identified relevant faculties/schools	Response to email
RO-9	Information received about all PhD students	Response to email
RO-10	Information received about all relevant PhD students	Response to FOI request
RO-11	Information received about all relevant PhD students	Response to FOI request
RO-12	Part of the identified relevant faculties/schools	Response to email

Methods

Funding Bodies and Doctoral Training Partnerships Contacted

Although the primary focus of this project was on training provided to students by universities, some funders of biological and biomedical sciences PhDs were also contacted to help understand their role in determining, or encouraging, the provision of experimental design training.

Some of the major funders have published statements surrounding their requirements for the provision of training on experimental design and statistical analysis. Specifically, in a joint report, the Medical Research Council (MRC), the Biotechnology and Biological Sciences Research Council (BBSRC), the Wellcome Trust and the Academy of Medical Sciences claim that *"…we require that PhD 'students should receive training in experimental design and statistics appropriate to their disciplines, and in the importance of ensuring research results are robust and reproducible* (17, p. 6).

Therefore, to help understand if this requirement is implemented, four major funders of biological and biomedical sciences PhDs were contacted. In addition, seven individual DTPs were contacted, focusing on DTPs associated with the top ten universities for animal research.

Responses were received from two of the funders contacted.

Results

Experimental design training provision by different organisations

Research organisation 1

The first research organisation is an independent institute focusing on biomedical discovery. The relevant training that is **mandatory for all** PhD students is outlined below.

Workshop in responsible animal research (two-half day workshop):
This workshop covers the principles of animal welfare, implementation of the 3Rs, PREPARE guidelines, experimental design, research methods and models, research reporting standards and public engagement, all in the context of the local research framework.

The workshop is intended to provide participants with:
— An awareness of the expectations of UK research councils and major charitable funding bodies regarding the responsible conduct of bioscience research involving animal use.
— Knowledge about initiatives seeking to improve research practices and freely available resources to help support researchers to meet expectations, including tools to improve experimental design and planning, research reporting standards and open science/data sharing.
— Recognition that when conducting research involving animals, implementation of the 3Rs and good animal welfare are essential components of research integrity and responsible research conduct.
— Understanding that the implementation of good animal welfare and the 3Rs principles of humane experimental technique is a requirement for animal-derived data to be reproducible and translatable.

Introduction to statistics for biologists:
This workshop gives an overview of statistics, and explores the general principles of data analysis that students will be able to absorb and reapply to their own research. The course covers:
— Why statistical methods are important
— Confidence intervals
— Descriptive statistics
— Inferential statistics
— P values, hypothesis testing and multiple testing
— Simple comparison concepts
— Introductory statistical modelling

Results

Experimental Design Training Provision by Different Organisations

Research organisation 2

The second research organisation for which information about experimental design and statistical analysis provision was acquired is a large university that has multiple faculties which do research on topics where animal use is common. Their response was that, as the organisation is so big, there is **no centrally mandated training** on experimental design and statistical analysis. The training that students will be offered will be dependent on their funding source and the departments, centres or faculties in which they are based. Students do have access to optional courses on statistics and research methods.

Optional courses that are of relevance for experimental design and statistical analysis are:

Experimental design and statistical methods:
This two half-day course will show students how to design high quality experiments using rigorous but easily accessible statistical thinking, and consists of lecture sessions and a written exercise.

Introduction to statistics for researchers:
This course is for doctoral researchers and research staff who wish to learn more about statistical methods and apply statistical techniques in practice.

Statistical analysis with R:
This course will allow students to connect the concepts behind statistical tests and their implementation. Participants will use R scripts to analyse data and learn the basics of conducting reproducible research.

Results

Experimental Design Training Provision by Different Organisations

Research organisation 3

There are a number of mandatory courses that PhD students at this organisation are expected to attend. These include, among others, Equality and Diversity Essentials, Research Integrity and Introduction to research data management.

There are **no mandatory courses on experimental design and statistical analysis.** The organisation does however operate on a points-based system, where PhD students are required to complete a certain number of training points by choosing from a wide range of available training courses. Some of the courses that students have access to and can take to complete their training points that are related to experimental design and statistical analysis include the following:

Applied statistics for postgraduate students:
This course consists of three, three-hour sessions that build on any statistical background students have from their undergraduate courses. The three sessions cover:
— Session 1: designing your experiment, what factors do you need to consider?
— Session 2: Introduction to statistical modelling, including linear models; and
— Session 3: More advanced statistical modelling.

More advanced use of R:
The aim of the session is to explore some of the more advanced aspects of R as a statistical computing environment. Participants will be invited to express interest in particular topics and this will have an influence on those chosen as the focus of the session. Possibilities include random effect models, flexible regression models, spatial analysis and the use of R as a programming environment. There may be an opportunity for participants to bring their own data, depending on the size of the group.

Methods

Research Organisation 3 Cont.

Design and analysis of comparative experiments:
Comparative experiments are at the heart of hypothesis-driven research and yet they are surprisingly difficult to design and to analyse. Often it is only during write-up that design flaws become apparent, making it difficult to draw meaningful conclusions. This course explores the challenges of designing and analysing comparative experiments, and their practical solutions. In four half-day sessions we will address the following issues:
— How to formulate questions and hypotheses
— How to design meaningful controls
— How to identify and evaluate sources of variation
— How to choose the appropriate statistical analysis methods
Each day will comprise a lecture followed by facilitated group work. The students will have the opportunity to apply the knowledge gained to their own research project and to discuss specific problems with peers and staff. Note that this is not a statistics course, although considerations of how the data can and should be analysed will be an important part.

T-tests and ANOVA for the analysis of laboratory data:
Students doing laboratory-based projects often have to analyse their data using t-tests and ANOVA. This course will introduce how to:
— decide when t-tests and ANOVA should be considered
— check these methods' assumptions
— analyse and interpret data with these methods (using Minitab)
It will also briefly consider alternatives to t-tests and ANOVA. Whilst the course is aimed primarily at those doing laboratory-based projects, it is open to anyone who is likely to need to use t-tests or ANOVA.

Methods

Research Organisation 3 Cont.

Statistics — Linear regression:
This course introduces the methods of correlation and multiple linear regression for use in medical, veterinary and life sciences research. The focus is on detailing when these methods are appropriate and interpreting SPSS and R output (correlation coefficients, linear regression coefficients, confidence intervals, p-values).

Statistics — Logistic regression:
This course introduces the method of multiple logistic regression for use in medical, veterinary and life sciences research. The focus is on detailing when this method is appropriate and interpreting SPSS and R output (odds ratios, confidence intervals, p-values, Hosmer-Leme show test, c-statistic).

Statistics — Survival analysis:
This course introduces the methods of Kaplan-Meier and Cox regression for use in medical, veterinary and life sciences research. The focus is on detailing when these methods are appropriate and interpreting SPSS and R output (Kaplan-Meier survival estimates, logrank test, Hazard Ratios, confidence intervals, p-values).

Statistics — Diagnostic testing and comparing methods of measurement:
The session will cover:
— Sensitivity and specificity, positive predictive values, negative predictive values, prevalence and ROC curves
— Bland-Altman plots and 95% limits of agreement
It will also briefly mention inter-rater agreement methods but will not cover these in detail.

Methods

Experimental Design Training Provision by Different Organisations

Research organisation 4

This organisation responded to the enquiry through a freedom of information request. The only compulsory training that all doctoral students are required to undertake is a course on plagiarism awareness. In addition, students are required to accumulate a certain amount of "training points" throughout their PhDs by selecting and attending a range of training sessions. The themes of these **optional** training sessions are: research communication, personal effectiveness, industry and enterprise, research impact, professional progression, graduate teaching assistants, research computing and data science, professional business skills, and research integrity.

Looking into the themes that appear to be the most relevant, which are research computing and data science and research integrity, the following workshops are of interest to experimental design and/or statistical analysis training:

Basic statistics:
Students that complete this workshop are expected to be able to:
— Understand the need for statistics in scientific studies
— Interpret graphical representations of sampled data
— Calculate descriptive statistics for sampled data
— Apply the normal distribution to answer questions about a population
— Identify potential sources of bias in a scientific study

Methods

Research Organisation 4 Cont.

Data science: Introduction to sampling & hypothesis testing:
This course provides an introduction to the statistical theory of sampling, parameter estimation and hypothesis testing. There is some overlap with the class on Basic Statistics, but the concepts are explored in greater detail.

The class is taught either with Python or R examples (see the course information for details). This covers the concepts of prerequisites review (mean, median, mode, variance, standard deviation, random variables and distributions, normal distributions), properties and standardisation, skewed distributions, sampling, central limit theorem, sampling distribution, sampling variability and standard error, standard deviation versus standard error, statistical inference, confidence intervals, hypothesis testing, test statistics, type I and II errors, and steps in the hypothesis testing process.

Data science: Further hypothesis testing:
Building on the material covered by Introduction to Sampling and Hypothesis Testing, this workshop will explore the application of hypothesis testing to data sets that may deviate from theoretical distributions. This covers the concepts of the t-test and its variations, comparing variances, ANOVA, testing for normality, non-parametric testing, goodness of fit, multiple testing corrections, and choosing appropriate statistical methods.

Methods

Experimental Design Training Provision by Different Organisations

Research Organisation 5

This organisation responded via a freedom of information request. Their response was that there is **no mandatory training** on experimental design or statistical analysis that PhD students in biological and biomedical sciences disciplines are required to attend. They indicated that students have access to optional courses but did not provide any further details.

Research Organisation 6

The person contacted was the development coordinator for research students at the relevant faculty. The response was that there are **no mandatory training elements on experimental design**. They do have several optional training and support elements, including one to one statistical advice. Some of the **optional** sessions that may be of relevance to the understanding of experimental design and statistical analysis are the following:

Research ethics:
A theoretical backdrop for the consideration of ethics in bioscience research is presented. There are opportunities to discuss the concept of bioethics and its implications for the individual, society and professionals working in bioscience, medicine and health sciences.

Statistical support**:**
One-to-one advice and one-to-one statistical support sessions are provided throughout the year. These sessions are intended to help students with specific issues in the design and analysis of their quantitative research. Participants are required to provide details of their query on application.

Basic statistics:
A succinct tour of contemporary statistical tools and techniques commonly used in medical and bioscience research. Topics include summary statistics, confidence intervals, hypothesis testing, ANOVA, correlation and regression.

Methods

Experimental Design Training Provision by Different Organisations

Research Organisation 7

Information about training provided was collated and is outlined below. There is a **mandatory training** session on statistical analysis that all students are expected to attend in their first year of study.

Introduction to research statistics for bioscience:
This two-day course introduces statistical analysis using the program R and its associated graphical user interface RStudio. The following topics will be covered in the order given:

— The use of RStudio to import data from Excel, and to explore its properties using graphics
— Using descriptive statistics to understand data structures
— The use of keyboard shortcuts
— Checking assumptions (normality & constant variance)
— t-test & analysis of variance (function aov); model simplification & model checking
— Transforming the response variable
— Multiple comparisons in analysis of variance
— Correlation; first & second order partial correlation
— Regression using lm (linear model); the independence of significance & explanatory power
— Analysis of covariance; the blending of analysis of variance and regression
— Model specification & model simplification (the minimal adequate model)

Methods

Research Organisation 7 Cont.

Other optional courses include:

An introduction to statistical analysis using R:
This workshop will introduce modern statistical modelling of data using the open-source language R and its associated graphical user interface R Studio. The following topics will be covered in the order given:

— The use of RStudio to import data from Excel, and to explore its properties using graphics.
— Using descriptive statistics to understand data structures
— The use of keyboard shortcuts in R
— Checking assumptions (normality & constancy of variance in model residuals)
— Analysis of variance (function aov), and regression (function lm), model simplification, model checking and final model selection.

Intermediate research statistics for research staff and postgraduate researcher:
This course extends the introductory course, by broadening the treatment of core topics such as analysis of variance and regression, and introducing new material based on the implementation of generalised linear models with binomial and Poisson error structures.

Methods

Experimental Design Training Provision by Different Organisations

Research Organisation 8

There are two faculties at this organisation that host research topics likely to involve the use of animals and information was received about one of them. The response stated that, although the training postgraduates are given varies by department, as the faculty covers a broad range of subjects, for the relevant laboratory-based students the only mandatory required training is a literature review unit and a research training module. The aim of the latter is to provide students with a broad understanding of the general research skills that are considered necessary in the research environment of students, and to provide postgraduates with the skills required during and after completion of their PhD studies such as safety training, upkeep and precise dating of research conducted, training needs analyses/learning plans and the preparation and delivery of an oral presentation. There is an additional **optional** relevant course titled "Statistics for Scientists".

Research Organisation 9

This research organisation stated that they currently have **no specific training course for PhD students related to experimental design**. The response explained that each principal investigator (group leader) is expected to provide their research students with the necessary training and oversight in relation to animal use and ethics and applying for the relevant approvals. When asked specifically about optional courses available, the response was that there are **no formal courses in experimental design and/or statistical** analysis to which research students have access.

Methods

Experimental Design Training Provision by Different Organisations

Research Organisation 10

The response to the request for information received was that students are not required to take any mandatory training courses (they can choose the modules they need based on their personal development plan). Mandatory training in experimental design and statistics is only provided to the subset of students that are funded via a doctoral training partnership. When asked about optional training courses accessible to the students, they explained that their schools offer many courses involving experimental design/statistical analysis that students can undertake if they wish.

Research Organisation 11

Information about the training provided to biological and biomedical sciences PhD students at this organisation was acquired through a freedom of information response. The training provided is highly varied as multiple departments offer PhDs in these subjects. The information provided is detailed below by division.

Division 1:
There are currently no compulsory statistical courses offered by this division. The only mandatory courses for their students 'Research integrity' and 'Avoiding plagiarism'. Within the division, an institute makes the course "Experimental design and statistics in pre-clinical research: the good, the bad and the ugly" compulsory for their first-year doctoral students as part of their induction in the first term. Notably, the institute partnership between the research organisation and an external funding body and many of the students affiliated with the institute are also funded through a studentship.

Division 2:
Within the Doctoral Training Centre, courses relevant to experimental design and statistics are offered. In particular the course "Statistics and Data Management" is compulsory, but only for students funded through an externally funded DTP.
In the one of their departments, optional statistics training is offered. There is no mandatory training in experimental design for students in that division.

Methods

Experimental Design Training Provision by Different Organisations

Research Organisation 12

Two faculties were contacted at this organisation. A response was received from the Graduate Administration Manager at one of the faculties stating that they do not require their PhD students to complete any mandatory training in statistical analysis / experimental design, other than what is required for Procedure Individual Licence (PIL) and Procedure Project Licence (PPL) holders by the home office. No information was received about optional training courses in experimental design and statistical analysis available to PhD students.

Methods

Collated Information

Table 3: List of mandatory and optional experimental design and statistical analysis training available to PhD students by organisation.

Organisation	Mandatory experimental design training	Mandatory statistics training	Optional courses available
RO-1	✓	✓	
RO-2			✓
RO-3			✓
RO-4			✓
RO-5			✓
RO-6			✓
RO-7		✓	
RO-8			✓
RO-9			
RO-10			✓
RO-11	For some students	For some students	✓

Funding bodies

Two of the funding bodies responded to the request for information. The response from the first one was that they **do not mandate** or have specific training requirements in place for their students centrally, as the DTPs should provide appropriate training for their cohort (from basic, general training such as research integrity and statistical analysis to more tailored and complex training relating to the strategic priorities of the DTP). They therefore advised us to reach out to the DTPs directly.

A similar response was received from the second funding body, which stated that the students on their studentships "belong" to the universities they are enrolled at. They **do not provide training** of any sort, so they suggested that we get in contact with the universities directly.

Discussion

The aim of this project was to gain an understanding of the training related to experimental design and statistical analysis that PhD students in biosciences subjects are exposed to, focusing on some of the research organisations that are the top users of animals. Information has been collated about the training mandated, or available, to PhD students in twelve research organisations and two funding bodies. While it is noted that this is a small sample and does not allow for an in-depth examination of the training experienced by the average PhD student, it suggests that provision of mandatory experimental design training is severely lacking and/or inconsistent within and across organisations.

Of the organisations contacted, only one provides a mandatory comprehensive course for all students that covers the principles of experimental design, which is a workshop on responsible animal research. Notably, this organisation is different to all other organisations contacted as it focuses solely on research of human diseases such as cancer, heart disease, stroke, infections and neurodegenerative diseases. This focused approach to biomedical research is reflected in the high numbers of procedures involving animals and is perhaps the reason for the comprehensive training provided to PhD students.

Courses on statistical analysis appear to be a bit more widespread. Only two organisations provide mandatory training in statistical analysis. Nearly all universities do, however, offer optional courses on statistical analysis and some also provide optional training related to experimental design.

The way in which generic skills training is regulated varies between organisations. Many organisations have specific mandatory training that they require their students to undertake and additional courses available for students that are interested in participating. Others do not have any mandatory training, allowing the students to only take courses if they are of interest.

Two of the research organisations examined operate on a credits-based system, ensuring the students get some level of generic skills training but allowing them to choose the courses that are most relevant to their subjects. While this does not guarantee that students will receive adequate (or any) training on experimental design and statistics, it does allow some flexibility which could be beneficial.

Discussion

Biological and biomedical sciences disciplines encompass many fields, ranging from bioinformatics to medical subjects and, therefore, finding a "one fits all" approach is perhaps not the most beneficial. FRAME and others do nonetheless support the notion that it is important for researchers to have a basic understanding of the principles of experimental design and statistical analysis, as this would help ensure the production of better and more reproducible data (11, 18).

The importance of providing biosciences PhD students with experimental design training has also been identified by some of the major funders. Responding to concerns surrounding the reproducibility crisis, a symposium was held in 2015 in which members of the BBSRC, the MRC, the Wellcome Trust and the Academy of Medical Sciences discussed the issue and possible solutions for the reproducibility crisis. A report was published in 2016 with an update of the progress that funders are making around addressing the issues identified at the symposium. The report states that "improving experimental design and the completeness of reporting is critical to reproducibility and the scientific validity of the results"(17, p. 4). When discussing the role of education and training, the report highlights that "it is a condition of our funding that research organisations provide researchers with appropriate training.

Continuing education and training for individuals at all career levels is one way to improve experimental design, research methods, and statistical expertise" as well as that "…we require that PhD 'students should receive training in experimental design and statistics appropriate to their disciplines, and in the importance of ensuring research results are robust and reproducible", as mentioned above (17, p. 6).

In addition, a blog posted on the MRC website in 2016 states that "all PhD students we fund now need to have training in experimental design and statistics. They will also need to understand the importance of ensuring robust and reproducible results" (19).

Discussion

The results of this project suggest that, while there may be the expectation that all research organisations provide researchers with training related to experimental design, when looking at PhD training provision at universities at least, this expectation is not always met. There is the possibility that DTPs will provide some training to their specific cohorts of PhD students, but it has not been possible to examine this further, as none of the DTPs contacted have responded to the request for information. When contacting the funders directly, both responses received stated that there is no centrally mandated training on experimental design and statistical analysis and that this is arranged by the individual DTPs or universities.

One of the initiatives that was put in place as a result of the identification of this gap in training was the funding of an award by BBSRC which would be used to develop a five-day annual training course around robust research approaches. The proposed training course would be designed to include 30 students over three years, the feedback of which was aimed to be used to develop online teaching materials (17). The progress of this initiative is currently unknown, but it is nonetheless important that the lack of widespread experimental design training is being addressed.

Part of the problem when examining and, presumably delivering, generic skills training could be a “too many cooks” situation. The training received by students, even based in the same laboratory at the same university, has the potential to vary greatly based on whether the students are part of an externally funded studentship cohort, the training provided by their specific studentship and the importance that each individual student, and their supervisor, places on generic skills training. While the specific training needs of each individual should be taken into account, allowing students to access the courses that are most relevant to them, the basic principles of experimental design are important for all researchers, and the findings of this review suggest there is currently room for improvement.

Discussion

Suggestions for Improvement

1) As mentioned previously, some of the main funders of biosciences PhD students have reported that they are committed to the provision of experimental design and statistical analysis training and have published statements claiming that they require experimental design and statistical analysis training to be provided to the PhD students they fund. A sensible improvement to the current system would be a baseline level of experimental design training implemented and applied to *all* bioscience PhD students, regardless of their source of funding.

It would be beneficial to ensure that this experimental design and statistical analysis training is provided by the universities themselves and not through external structures such as DTPs. Funders are undeniably crucial in driving change within organisations. It would be hugely beneficial if the major funders could take that first step, building on the report published in 2016 (7), by agreeing a set of training criteria for core experimental design and statistics skills to be covered for all their funded students. Any guidelines or expectations produced would be provided to DTPs and universities to direct training for relevant PhD students and set out the minimal mandatory training expectations covering topics such as bias, blinding and research ethics.

2) The implementation of experimental design and statistical analysis training is complex, especially for large research organisations that have multiple faculties, schools, colleges and institutes covering subjects related to the biosciences. A way to implement general experimental design training could be through the development and provision of online resources. Such resources could be delivered to all laboratory-based students through online university platforms. For example, one of the research organisations examined delivers training on research integrity in this manner and requires that students complete the modules online before transferring from MSc to PhD status (a process known as PhD transfer which is usually completed after 9 months of enrolment into a PhD programme).

Some online resources for guiding experimental design already exist, for example the Experimental Design Assistant (EDA) developed by NC3Rs (20) which could be adapted and used alongside teaching materials to the appropriate level for PhD students to use. Individual universities could develop internal training materials and programmes, particularly if suggested or mandatory guidelines were set out by funding bodies. There are also opportunities for collaboration with other PhD providers, or through the identification of existing resources that could be signposted to training providers.

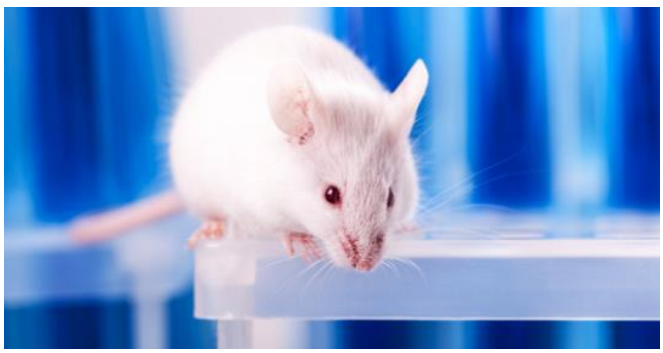
Discussion

Suggestions for Improvement (Cont.)

3) The level of experimental design training that will be useful for students depends on the subject of their PhD research. For example, the basic principles of experimental design should be taught to every laboratory-based bioscience student to help ensure experimental work is planned, carried out and analysed correctly.

Students working with animals could benefit from additional experimental design training. Prior to working with animals, early career researchers need to gain a personal licence to work under a licensed project. The training provided to people applying for a personal licence does not cover the principles of experimental design. The responsibility for correct experimental design is placed on the project licence holder (most commonly the group leader who will be supervising the student).

The level of involvement of PhD supervisors with students is variable and, from a training point of view, students and other early career researchers should be gaining these skills as they are likely to be the future leaders in their field. It would be beneficial to provide specific training to early career researchers that are applying for personal licences to introduce experimental design concepts related to animal work such as the PREPARE (Planning Research and Experimental Procedures on Animals: Recommendations for Excellence) and ARRIVE (Animal Research: Reporting of In Vivo Experiments) guidelines. There are opportunities here for guidelines and resource signposting that will help improve the provision of this training which could be implemented in some capacity at university level.



Conclusion

FRAME has a strong interest in promoting the 3Rs principles and ensuring that research, especially when animals are involved, is done to the highest standard. As such, the FRAME Training school in experimental design and statistical analysis was born to provide training to those wishing to improve their knowledge of animal study design. These courses have consistently proven popular and have indicated that, in some cases, attendees had not attended similar training. As correct experimental design is crucial both for reducing the number of animals used in research and for improving the reproducibility of data, this study set out to examine the level of training in experimental design and statistics that biosciences PhD students are exposed to. Information was collated about the mandatory, and in some cases optional, training provided by twelve research organisations.

The results suggest that provision of such training is very limited, with only one organisation offering compulsory training in both experimental design and statistical analysis to all of their students. While it is noted that most organisations offered some optional courses in these subjects, in light of the impact of poor experimental design on the validity of research, scientific progress and reproducibility, this seems insufficient. Several institutions and organisations, including FRAME, consider experimental design a core skill for laboratory-based students.

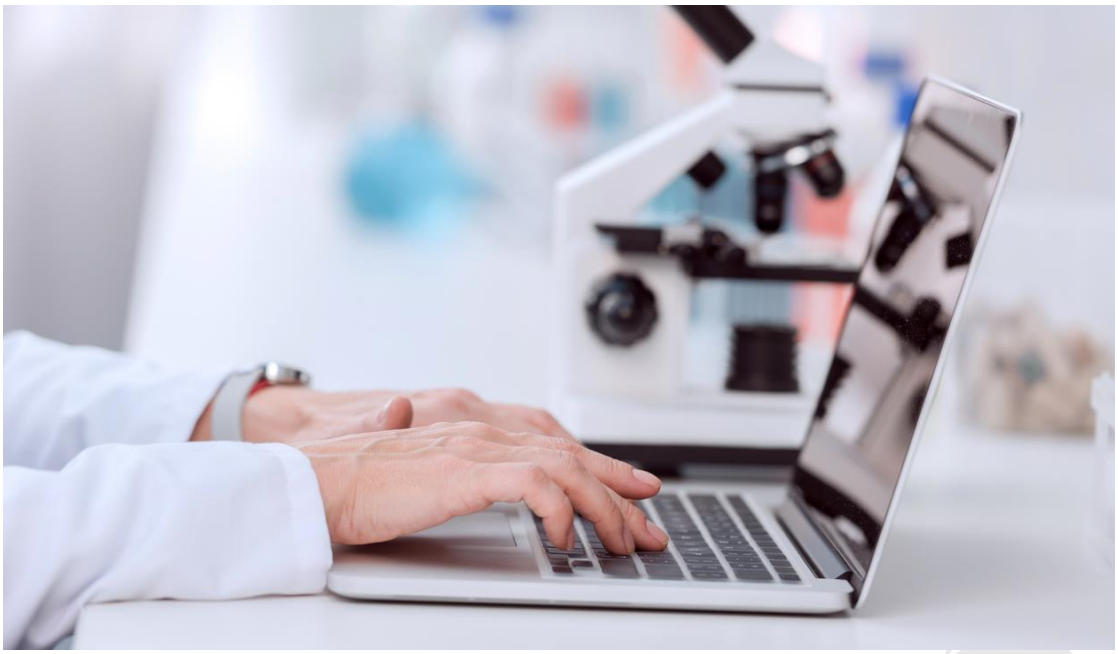
To improve the provision of experimental design training, a possible solution would be to invite some of the major PhD funders to create a set of training guidelines that could be implemented by all PhD providers, including universities. Best practice could be shared with the ultimate aim of producing a standard level of training across the UK. In the future, the content of such courses could be validated and perhaps even made available outside of the UK.

This can be made more manageable by developing online training courses that can be delivered through university platforms. FRAME also believes that, while all laboratory-based biosciences students should undertake basic experimental design courses, additional more specific and in-depth training specifically covering guidelines for animal work, should be provided to students that are preparing to work on animals.

Conclusion

Future research that could help understand the current state surrounding the provision of experimental design and statistical analysis training might involve a bigger sample of universities and/or students as one of the limitations of this research is the small sample size, making it hard to accurately determine the actual level of training the most PhD students receive. Collating information about a large number of DTPs would also be helpful.

Even though it is noted that DTPs and similar structures only apply to a certain subgroup of the PhD student population, the training provided by such partnerships is reflective of the level of emphasis that funders place on experimental design and statistical analysis training, something that would be interesting to explore in a more practical way, rather than relying on official statements around their commitment to this issue. Finally, it would be helpful to explore whether other organisations are as keen as FRAME to identify and/or address this issue. Collaborations between interested stakeholders could help to make the provision of experimental design and statistical analysis training more widespread across UK universities and research institutions.



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FRAME Fund for the Replacement of Animals in Medical Experiments

Cawley House, 149-155 Canal Street, Nottingham NG1 7HR

email: hello@frame.org.uk telephone: +44 (0) 300 030 1016

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