# Resume: Professor Malcolm Macleod

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**Current Appointments:**

- Academic Lead for Research Improvement and Research Integrity, University of Edinburgh (2019 - )
- Professor of Neurology and Translational Neuroscience, University of Edinburgh (2012-)
- Honorary Consultant Neurologist, NHS Forth Valley (2007 -)

**Previous appointments:**

- Reader (2010 - 12), previously Senior Lecturer (2007-10) in Neurology, Centre for Clinical Brain Sciences, University of Edinburgh.
- Consultant Neurologist, NHS Forth Valley (2005 - 07)
- Specialist Registrar, Neurology (NHS Lothian) and post doctoral researcher, University of Edinburgh (2000 - 05)
- Clinical Research Fellow, National Stroke Research Institute, Melbourne, Australia (2003 - 04)
- British Brain and Spine Foundation Postdoctoral researcher, University of Edinburgh (1998 - 2000)
- Medical Research Council Clinical Training Fellow (1995 - 98)
- Early career posts in medicine and surgery (1991 - 95)

**Memberships of professional bodies, national or international committees**

- Commissioner, UK MHRA Commission for Human Medicines (2014 - 22)
- Chair, MHRA Expert Advisory Group for Neurology, Psychiatry and Pain (since 2020; previously vice Chair (2016 -20), member (2013 – 16)
- Chair, Guarantors of EQIPD (2021 - )
- Member, Steering Group, UK Reproducibility Network (2018 -)
- Member, UK Home Office Animals in Science Committee (2013 - 18)
- Clinical Lead for Neurology, NHS Forth Valley (2005 – 20)
- Rector and Chairman of University Court, University of Edinburgh (1994 - 97)
- Fellowships of Royal Society of Biology (2016), Royal College of Physicians of Edinburgh (2006)

**Degrees awarded**

- B.Sc. First Class Honours in Medical Science (Pharmacology), University of Edinburgh (1988)
- M.B.Ch.B. University of Edinburgh (1991)
- M.R.C.P.(UK) (1994)
- Ph.D. “On the Neuroprotective Actions of FK506”, University of Edinburgh (2001)

**Selected research grants**

- MND SMART - Motor Neurone Disease Systematic Multi-Arm, Multi-Stage Adaptive Randomised Trial (Co-investigator, PI Chandran). MND Scotland £750k (2018 – 23)
- European Quality in Preclinical Data IMI (Co-ordinator; 28 partners) EU IMI €9.6m (2017 - 21)
- ivSyRMAF (In vivo Systematic Review and Meta-Analysis Resource) (PI) NC3Rs £495k (2013 - 18)
- European multicentre, randomised, phase III clinical trial of hypothermia plus best medical treatment versus best medical treatment alone for acute ischaemic stroke (EuroHYP 1) (co-Chief Investigator; 39 partners) EU FP7, €11.7m (2012 - 18).

**Awards**

- The Edinburgh CAMARADES group were delighted to receive the British Neuroscience Association Team Credibility Award (2021)
- Maria Sibylla Merian Fellowship, German Federal Institute for Risk Assessment, Berlin (2018 - 20)
- QUEST Visiting Fellowship, Berlin Institute of Health (2018-19)
- Visiting Professorship, Academic Medical Centre Amsterdam (2017)
- SGV Award for major contributions to the 3Rs (Switzerland) (2016)

**Contributions to the generation and flow of new ideas, hypotheses, tools and knowledge**

My research career is predominantly in the neurosciences, with early *in vitro* and *in vivo* research in the preclinical biology of neuronal death and stroke to post-doctoral level, followed by human clinical trials in stroke and in other neurological diseases, and then with increasing involvement in Research on Research. I led the application of systematic review and meta-analysis to the preclinical literature, initially as tool to inform drug selection for clinical trial. This approach also allowed evaluation of the prevalence and impact of reporting of measures to reduce risks of bias in preclinical research, and of publication bias.

In turn this led to the development of guidelines for the design, conduct, analysis and reporting of preclinical research, and to work with publishers and industry to increase the usefulness and value of research. I was an author in the Lancet Series on Research Waste, and have participated (as co-host (2015), invited speaker (2018), and program chair (2020)) in each of the REWARD-Equator meetings.

In recent years I have been concerned with developing a framework to provide evidence for research improvement, including initiating a randomised controlled trial of an editorial intervention (the IICARUS study), and – in my role as Academic Lead for Research Improvement and Research Integrity at the University of Edinburgh – leading a large-scale survey of institutional research culture, including an embedded randomised comparison of strategies to increase response rates. More recently, in this same role, I have been piloting the application of formal improvement strategies to research activity at the institutional level.

I have also led, since inception in 2013, the management of the NC3Rs funded Systematic Review Facility (SyRF), a freely available online platform hosting 800 projects and 1800 registered users. I have authored over 250 research outputs (publications, preprints and datasets), with examples given below. Since 2015, 93% of 151 outputs are openly available (source: ORCID mapped to Unpaywall).

**Selected Publications: ORCID id 0000-0001-9187-9839**

- Macleod MR, Collings AM, Graf C, et al. (2021) The MDAR (Materials Design Analysis Reporting) Framework for transparent reporting in the life sciences. Doi: 10.1073/pnas.2103238118
- Wang Q, Liao J, Lapata M et al. (2021) Risk of Bias Assessment in Preclinical Literature using Natural Language Processing. Doi: 10.1002/jrsm.1533
  *This work – the first author was a UK Reproducibility Network PhD student – describes the development and validation of a natural language processing tool to measure reporting of risks of bias in publications describing in vivo research, to be deployed in a project described at 10.31222/osf.io/cjxtf and with Stage 1 acceptance at PLOS Biology as a Registered Report.*
- Preprint: Macleod M, Hair K, Tanriver-Ayder E et al. (2021) Results of a randomised controlled trial comparing two different incentives to improve survey response rates. Doi: 10.31235/osf.io/sm36a
  *In which we show the feasibility of conducting randomised trials of approaches to improve the study of research cultures.*
- Dataset: Macleod M. (2021) Anonymised results from the 2020 UoE Research Culture Survey Doi: 10.17605/osf.io/82f4x
- Koroshetz W, Behrman S, Brame CJ et al. (2020) Research Culture: Framework for advancing rigorous research. Doi: 10.7554/eLife.55915
- Percie du Sert N, Hurst V, et al. (2020) The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. Doi: 10.1371/journal.pbio.3000410
- UK Reproducibility Network Steering Group (2020) Systematizing Effective Practice, Embedding It in Standard Practice. Doi: 10.1016/j.patter.2020.100151
- Hair, K., Macleod, M.R., Sena, E. et al. (2019) A randomised controlled trial of an Intervention to Improve Compliance with the ARRIVE guidelines (IICARus). Doi: 10.1186/s41073-019-0069-3
  *A randomised controlled study with blinding of authors, editors and outcome assessors in which we show that asking authors to complete an ARRIVE checklist (achieved in 88% of publications in the intervention group, and provided by 4% of control group publications) made no difference to reporting quality.*
- NPQIP Collaborative Group (2019) Did a change in Nature journals' editorial policy for life sciences research improve reporting? Doi: 10.1136/bmjos-2017-000035

- Macleod MR, Lawson McLean A, Kyriakopoulou A, et al. (2016) Risk of Bias in Reports of In Vivo Research: A Focus for Improvement. Doi: 10.1371/journal.pbio.1002273
  *An observational study in which we show low prevalence of reporting of measures to reduce risks of bias in* in vivo *research from leading UK institutions – with 68% of 1173 publications describing not one of the 4 items identified in Landis et al (below) as being of greatest importance.*
- Macleod MR, Michie S, Roberts I, et al. (2014) Biomedical research: increasing value, reducing waste. Doi: 10.1016/S0140-6736(13)62329-6
- Landis SC, Amara SG, Asadullah K, et al. (2012) A call for transparent reporting to optimize the predictive value of preclinical research. Doi: 10.1038/nature11556

**Contribution to research teams and the development of others**

In 2005 I co-founded (with Howells) the Collaborative Approach to Meta-analysis and Review of Animal Data from Experimental Studies (CAMARADES), which has grown to be an international community of largely early career researchers. One important purpose has been to provide methodological support and mentoring to those conducting such research, especially where this is not available to them in their own institutions. Our biennial meetings include formal mentoring sessions for ECRs, each with two senior colleagues usually comprising a PI from a different institution alongside a colleague from an external stakeholder, for example a publisher or a funder. This has been highly valued by ECRs. I also provide mentoring to several individuals at Edinburgh and elsewhere.

I am particularly grateful to have had the opportunity to mentor some excellent colleagues: Dr Emily Sena did her undergraduate student project with me in 2005; then a PhD jointly supervised by Howells and myself from which she accrued 18 publications; and has gone on to a Senior Lecturer role in our group; is editor in chief of BMJ Open Science; serves on several advisory boards including QUEST Berlin and CZI Open Science; and received a “Hidden Ref” award on behalf of the Edinburgh Race Equality Network.

Dr Alexandra Bannach-Brown did a joint PhD (also with Wegener, Aarhus) and went on to post doctoral positions with Paul Glasziou (Bond, Australia) and is now at Quest Centre Berlin. Emma Wilson came to us for an undergraduate student project as the first in her family to go to university; has worked with us as an RA for 2 years; including secondment to Munafò (Bristol) in the development of training programmes in open research; has won several awards for her own public engagement work; and has just started a PhD investigating research quality in the preclinical modelling of autism.

Our work is highly collaborative, and I have been involved in the creation and leadership of international consortia engaged in clinical trials (EuroHYP, PRECIOUS) and in research improvement (MultiPART, EQIPD). One important role has been in framing the tone of discussions about how improvement might best be achieved, seeking to recognise the pressures faced by researchers and to focus on improvement rather than judgement, while at the same time sustaining the justified passion of the meta-research community.

**Contribution to the wider research and innovation community**

I am a member of several editorial boards including PLoS Biology (Meta-Research section), the PLoS Data Advisory Board, and the Registered Reports section of Scientific Reports. I am a member of the Independent Statistical Standing Committee of the CHDI Foundation and chair the Guarantors of EQIPD. I have served on grant review panels for HRB (Ireland), BMBF (Germany, chair) and ANR (France, co-chair). Since 2019 I have been University of Edinburgh academic lead for research improvement and research integrity. In this role I led our 2020 Research Culture Survey (1490 responses, 12.4% response rate), discussed the findings with diverse groups within the University community, and wrote the first draft of the University’s action plan to improve research cultures. I was vice convener of our Research Metrics working group, charged with making recommendations for changes in promotion and appointment criteria following our becoming a signatory to DORA; and I led the University’s response to the UK Parliament Science and Technology Committee on Reproducibility in Research. I was a member of the External Advisory Groups for the development of the NC3Rs Experimental Design Assistant and for the Vitae Research Integrity Landscape study, and am a member of the Steering Group of the UK Reproducibility Network. I give around one invited presentation per month, most recently a keynote presentation to the World Congress on Alternatives

and Animal Use in the Life Sciences on approaches to improving research quality (available at https://vimeo.com/593173630). As routine, I make all slides available CC-BY at the Open Science Framework (https://osf.io/de6qh/).

## Exploitation and Impact of our research

I firmly believe that research findings are of greatest value when they are used to inform changes in practice. A major goal has been to improve the reproducibility and quality of preclinical research through informing and improving standards and processes at institutions, publishers, funders and pharmaceutical companies. We followed our early work on reporting of risks of bias in the in vivo stroke literature with Good Laboratory Practice guidelines, which were adopted by the three leading journals in the field. Later I was involved with the extension of this approach to in vivo research (the Landis guidelines, ARRIVE) and to life sciences research in general (the MDAR Framework). Working with industry in the EQIPD Innovative Medicines Initiative project we systematically reviewed guidelines for the design, conduct and analysis of in vivo research, and I then used this to inform the curriculum for our Edinburgh Research Optimisation Course. We have made this freely available to all researchers (https://edin.ac/2SZvY4U), and it has been accessed by 417 users since launch in June 2021.

Encouraging behaviour change in researchers can be challenging, and I led an observational study of the impact of a change in editorial policy at Nature on reporting quality. I also initiated a randomised trial of an intervention to improve compliance with the ARRIVE guidelines. Importantly, while the intervention - that Journals “require” ARRIVE checklist completion – was a considered a key element of ARRIVE implementation, this was in fact without effect. This demonstrates the necessity for us to show that our proposed interventions in research improvement actually work.

The impact of our work is described in a University of Edinburgh submission to REF2021.

**Impact on publishing:** In response to the growing concern around reproducibility of biomedical research, in April 2013 Nature Publishing Group (NPG) introduced editorial measures to improve the consistency and quality of reporting in its articles. This abolished space restrictions in method sections to allow authors to describe their methods in as much detail as necessary, and provided a checklist to prompt authors to disclose technical and statistical information in their submissions. The Director of Author and Reviewer Services for NPG at the time (Veronique Kiermer) has written

> *“Not only were the reporting criteria based on the essential indicators of validity identified in Macleod and Sena’s research, but the impetus for the policy change was strongly driven by their demonstration of the poor reproducibility and under-reporting of risks of bias seen in preclinical research studies. In particular, their finding that under-reporting of steps taken to minimise bias is associated with overstated estimates of efficacy precipitated the need for a policy that requires these steps to be reported.”*

The observational study described above showed that this change in editorial policy had resulted in substantially improved reporting quality.

**Impact on pharmaceutical industry**: Our work is influencing policy and practice in the pharmaceutical industry through the European Quality in Preclinical Data (EQIPD) Consortium (which I lead). Thomas Steckler, Associate Director at Janssen Pharmaceutical, has said:

> *“As a direct result of our engaging with this research, we have changed our internal research procedures at Janssen and put increasing emphasis on research rigor and experimental design of our preclinical studies, including more focus on randomization, blinding, upfront specification of exclusion criteria and sample size calculation, and early involvement of our biostatisticians, both as integral part of our ethics approval processes for internal projects and procedures involving animals and during experimental planning. It was the CAMARADES research […] that alerted us to the issues and informed us how best to address them.”*

Similarly Glenn Begley, as CEO of BioCurate, an Australian not-for-profit company aiming to generate high-quality preclinical candidates from academic research for the bio-pharmaceutical industry, said:

> *“Research from the CAMARADES group was pivotal in establishing a quantitative approach to identify research reports that are at risk of bias. In addition, they have provided important insights as to how these issues can be improved.”*