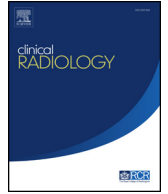




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Review

# Doug Altman, medical statistician par excellence: What can radiologists learn from his legacy?

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This narrative review describes our experience of working with Doug Altman, the most highly cited medical statistician in the world. Doug was particularly interested in diagnostics, and imaging studies in particular. We describe how his insights helped improve our own radiological research studies and we provide advice for other researchers hoping to improve their own research practice.

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## Introduction

2024 marks the sixth anniversary of Doug Altman's death. Doug was a medical statistician whose impact on clinical research remains immense. In 2019, his medical research was ranked second in the world.<sup>1</sup> Currently 284, his h-index continues to climb, with >885,000 citations. While readers will recognise the 'Bland-Altman' test of agreement<sup>2</sup> (the highest cited article ever published by the Lancet, currently 56,379), Doug's influence extends far further. Arguably, his greatest contribution was to promote reporting guidelines: He authored CONSORT for randomised controlled trials,<sup>3</sup> followed by several others, including PRISMA,<sup>4</sup> STARD,<sup>5</sup> STROBE,<sup>6</sup> QUADAS,<sup>7</sup> TRIPOD,<sup>8</sup> DAMOCLES.<sup>9</sup> Doug loved acronyms! He established EQUATOR (<https://www.equator-network.org>), a guideline

repository for medical researchers.<sup>10</sup> Doug's passion for reporting guidelines was driven by a belief that researchers must be completely transparent regarding what they have done, to whom, and how results were derived. Reporting guidelines expose and quantify research bias and deficiencies, helping readers assess generalisability, or even repeat the work themselves. Replicating research results is a cornerstone of scientific method.

In his seminal 1994 article, 'The scandal of poor medical research', Doug maintained it was effectively immoral to perform poor research.<sup>11</sup> Because clinicians often act on research publications, he argued patients could be harmed by inaccurate results and/or interpretation. He mandated researchers to consult with properly trained medical statisticians or equally able methodologists, to ensure good research design, analysis, and interpretation. Radiological

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training requires several years work, and medical statistics is no different. A radiologist cannot acquire sufficient statistical skills following a handful of lectures during a research course. Could a statistician become a competent radiologist after similarly brief training? By demanding that clinicians perform research for career progression, and admiring those who publish most ('publish or perish'), Doug argued the medical establishment was complicit. His BMJ obituary named his 1994 article the most important article published by the journal over the preceding 20 years, stating he did more than anyone to expose, 'shoddy research'.<sup>12</sup>

Doug was especially interested in diagnostics and we were fortunate to work with him on several radiological studies. Here we present personal accounts of the insights gained from working with such a talented individual. We hope our experience may benefit other imaging researchers.

### **Steve Halligan (professor of gastrointestinal radiology, UCL, London)**

In 2003, The European Society of Radiology awarded me a research grant, without remit. Systematic reviews of diagnostic tests were just becoming popular, so I suggested a meta-analysis of CT colonography (then a relatively new technique) to Wendy Atkin, a colorectal cancer epidemiologist. Saying I had little idea how to do this, she immediately suggested Doug Altman, who she knew well, and telephoned him straightaway. He accepted immediately. I learned later that Doug was always happy to help aspiring researchers. Very aware of his reputation, I was extremely intimidated: 'Practical Statistics for Medical Research'<sup>13</sup> was my favoured statistics textbook and I read his BMJ 'Statistics Notes' with Martin Bland, every week. Rising to greet me from a desk covered completely with articles and journals, which were also scattered all over the floor, he put me at ease immediately.

My first lesson came minutes afterwards: Doug asked for my research protocol. I was shocked. I knew what I wanted to do, I considered myself a competent medical researcher, and systematic review synthesises research 'already done'. Why was a protocol necessary? Doug, patiently, explained that protocols benefit all research, irrespective of topic and scale. He described how putting plans 'to paper' forces researchers to consider the precise research question, the endpoint(s) required to answer that question, how to measure this, and how to analyse the data. Protocols explain your research to others and identify the roles and contribution of collaborators. When Doug asked me, 'what is your review question?', I couldn't answer precisely. 'How good is CT colonography?', doesn't define for what disease, in which patients, compared to what test? Despite many publications, I realised I was a novice and felt ashamed, especially given Doug's patient manner. So, I wrote a protocol, and we performed and published the meta-analysis.<sup>14</sup> Afterwards, I always wrote a protocol, even if brief. The benefits, in terms of clarifying and communicating the research plan, cannot be overestimated.

Doug taught me to focus on clinical benefit, especially how tests influence patient pathways. For example, studies of CT colonography used 'per-polyp' analyses, i.e. CT was performed first, and any polyps identified compared with subsequent colonoscopy. Doug asked what would happen if CT detected a significant polyp? 'The patient would have colonoscopy to remove it', I replied. He then asked how much of the colon would be examined by colonoscopy? 'All of it', I replied. Doug then said, 'So it's irrelevant if CT detects one or multiple polyps because patients have their entire colon endoscoped subsequently?' He concluded, 'These studies should be analysed per-patient, not per-polyp'. Our meta-analysis was the first to suggest this.<sup>14</sup> Doug explained that although researchers usually focus on the meta-analytic point estimate, the systematic review is far more useful because it unearths methodological issues, many of which are only apparent initially to statisticians. Ultimately, we were invited to contribute the chapter on systematic review and meta-analysis for an 'Evidence based practice in radiology' series, selected as a 'key article' for the American Board of Radiology.<sup>15</sup>

Working with Doug, I soon realised that attempting clinical research without statistical help was foolish. Statisticians are invaluable at all stages, from formulating the research question, right through to balanced interpretation of results without 'spin'.<sup>9,16</sup> A recent survey of UK trainee radiologists found that most would consult statisticians after data collection,<sup>17</sup> but this is unwise: Statisticians are needed when planning research, for proper design and powering. As a member of multiple grant-awarding panels, I have witnessed radiological research proposals fail repeatedly, not because the topic is unimportant, but because studies are poorly designed and inadequately powered, with no statistical co-applicant. I currently employ four medical statisticians. Good research is impossible without them.

### **Emma Helbren (consultant radiologist, Hull and East Yorkshire NHS Trust)**

Wishing to complete a postgraduate thesis during radiology training, I joined a project applying eye-tracking to CT colonography, hoping to explain why radiologists miss some polyps. While 2D eye-tracking was well-established, the 3D colonography video introduced multiple additional challenges. Notably, polyps were visible only intermittently and were also both moving and changing in size. We developed methods to eye-track moving images, collecting large amounts of data, but had no idea regarding analysis. Describing our dilemma to Doug, he asked, 'First, what is your primary research question?' We found this surprisingly difficult to answer. Doug always focussed on the clinical problem, insisting that collaborators could explain exactly what their aims were. Researchers frequently collect data without considering why, or how to analyse it.

To our dismay, Doug suggested we discard much of our data because it wouldn't be useful. Together with Sue Mallett, he proposed novel metrics to summarise

characteristics of observers interrogating moving images, describing analyses and novel graphs. 'Pursuit' (gaze following a moving polyp) could be related to polyp appearance onscreen, polyp size when first identified, and the proportion of screen time for which the polyp was followed.<sup>18,19</sup> Doug was expert at drawing out a simple, focussed hypothesis, and at reassuring and uniting investigators. Previously, I believed statisticians were best consulted following data collection, but this project demonstrated how early collaboration would have saved me considerable time and effort. I learned that clarity around the research question is fundamental, and that the very best statisticians develop novel approaches suited specifically to the task at hand where no solution exists already.

### **David Burling (consultant radiologist, St. Mark's Hospital, London)**

Undertaking a research degree during radiology training, I coordinated a multi-centre study comparing diagnostic accuracy of CT colonography for different reader groups; experienced subspecialist gastrointestinal radiologists, less-experienced radiologists, and radiographic technicians. Participants interpreted 40 scans and identified polyps.<sup>20</sup> Analysis appeared straightforward to me: Simply determine per-polyp sensitivity for each reader (and per-patient specificity for patients without polyps), average each group, and then compare groups. However, Doug immediately explained this was incorrect: Because readers assessed the same patients and polyps, the data were correlated. Patients with multiple polyps may exert a disproportionate effect if clustering is ignored (multiple polyps in a particularly well-prepared colon will inflate per-polyp sensitivity and vice-versa). Doug explained that bootstrap analysis was necessary, deciding to draw 1999 random samples from the original sample, with replacement and analysis of each resultant dataset. Results were calculated for each bootstrap sample and their distribution used to calculate a bootstrap confidence interval. A probability value was then calculated by considering how many of the values were further from zero than the observed values. This was a very complex analysis and I realised that by not seeking advice, an inexperienced researcher would perform a simple analysis that was inappropriate. I would have published an article with incorrect and probably misleading results.

Given that multiple observers measured the same polyps, I decided to compare measurement accuracy for the different groups. Again, this appeared simple to me but Doug explained that 'true' polyp diameter could never be known, since all measurements have errors, whether radiological, endoscopic, or histological. Indeed, Doug said that practically nothing can be measured with absolute accuracy. The 'Bland-Altman' analysis of agreement, states that where a 'true' measurement is unknown, the mean of two measurements (frequently by different observers) will likely provide the most accurate estimate.<sup>2</sup> Using this

approach, we compared polyp measurements by radiologists and colonoscopists.<sup>21</sup> I learned why correlation cannot assess 'agreement' between measurements.<sup>2</sup> Before my thesis viva, I was concerned about statistical questions, but it transpired I knew more about measurement error than my examiners. I realised that statistical understanding is generally poor, even amongst experienced radiologist researchers. Without statistical advice, I would have performed inappropriate analyses and published incorrect results. Doug was also welcoming and never intimidating, despite my limited statistical knowledge. He was always happy when clinicians sought statistical advice.

### **Darren Boone (consultant radiologist, University College Hospital, London)**

I first met Doug when researching eye-tracking of CT colonography. Learning the Bland-Altman method as an undergraduate, I knew that Doug was very eminent but I was surprised that we consulted him when designing my study, since I assumed statisticians were only required to analyse data. I learnt rapidly that statistical help is invaluable when designing experiments, to avoid bias and to ensure enough subjects are recruited for meaningful results (i.e. adequate power). We discussed 'recall bias', specifically that observations of the same images (often under different viewing conditions) are usually temporally separated so that the reader does not remember their prior diagnosis. Doug asked what separation was typical and I replied, 'around two to four weeks'. He then said, 'What is the evidence for that?' I responded, 'It's just what people do'. Doug hypothesised that a very unusual image would probably be remembered for years, even for life, whereas a routine image might be forgotten in minutes. Our discussion soon extended to other radiological study designs that modify the normal clinical environment, for example by increasing the prevalence of abnormality or by concealing clinical information, collectively known as the 'laboratory effect'. Doug soon suggested we do a systematic review. At the time I had little idea what that meant, but now appreciate systematic reviews gather and assess available evidence on a topic, in an unbiased fashion.

This was not easy. Typically, radiological systematic reviews investigate a specific disease and technique, e.g. studies of 'prostate MRI' will be easy to find. However, my task was to identify any study that incorporated a potential 'laboratory effect', and investigated its effect on outcome (if any), irrespective of imaging modality or pathology. I learnt a tremendous amount about how to search literature. I read 11,247 abstracts to unearth just 12 relevant studies. Our published review concluded there was no evidence that recall bias existed, nor that studies required 'washout' between interpretations.<sup>22</sup> I learned that several sources of bias potentially affecting radiological studies were poorly researched, for example prevalence expectation, and concluded it would be more profitable researching these instead of another potential biomarker. While I did not want to appear stupid in front of someone who was so obviously

held in the very highest regard by researchers, at no point did Doug ever make me feel out of my depth, ignorant, or likely to fail. Instead, he included me in all discussions and listened to my opinions. I never had any interaction with Doug that wasn't positive and looked forward to our meetings with great pleasure.

### **Sue Mallett (professor of diagnostic and prognostic statistics, Centre for Medical Imaging, UCL, London)**

While working as an immunologist/virologist, I decided that I would have more impact by retraining as a medical statistician. I approached Doug, who appreciated immediately that a laboratory background was particularly suitable for a career in diagnostic statistics. He asked me to help with a study seeking US FDA (United States Food and Drug Administration) licensing of computer assisted detection (CAD) for CT colonography. The FDA insisted we use the area under the receiver operating characteristic curve (ROC AUC) as the primary outcome, and Doug asked me to determine how many radiologists our study needed. Using data from previous studies, I examined the additional proportion of patients with polyps that were classified correctly when radiologists used CAD, and tried to relate this to a change in ROC AUC, so as to calculate sample size. Surprisingly, ROC AUC appeared unrelated to the proportion of correct diagnoses. I explained this to Doug, who was intrigued. Between us we ultimately concluded that ROC AUC suffered from several problems, especially when considering lesion detection (versus characterisation) because while ROC curves are constructed from confidence scales, lesion detection tends to be binary, i.e. present/absent.<sup>23,24</sup> Speaking to clinicians, we realised that both they and their patients found ROC AUC hard to understand because results are not expressed in terms of effects on individual patients.<sup>25</sup>

Publishing our work was difficult as it challenged accepted statistical thinking for imaging studies. Doug taught me that measures like ROC AUC must report additional statistical outcomes, like sensitivity and specificity at clinically relevant thresholds, so that effects of diagnostic tests on clinical decision making are illustrated clearly to doctors and their patients.<sup>25</sup> His prime concern was always how test results impact on patients. He taught me that statisticians should design studies that focus on an important clinical question, and to always be alert for bias when collecting and analysing data, and when reporting study results, so that research findings are as close to the 'truth' as possible. Encapsulating our ROC AUC work in a 2018 email, Doug said, 'We did interesting and important work, and had a lot of fun on the way. That's how I like to work'.

### **Andrew Plumb (consultant radiologist, University College Hospital, London)**

I first met Doug at a meeting to consider alternatives to ROC AUC, where Sue Mallett described problems with

ROC AUC as a summary measure for diagnostic tests. I was a keen but junior radiologist, just starting a PhD, and didn't understand most of the discussion. However, Doug anticipated this and explained several points in a manner which was his hallmark – with absolute clarity and using simple language. I was so inspired I subsequently read all of his BMJ Statistics Notes series with Martin Bland, commencing in 1994.<sup>26</sup> Ultimately, I worked with Doug on two other articles, both of which were offshoots from the main collaboration between our statistical and radiological teams. Despite these being relatively small and unimportant topics for Doug, as an inexperienced researcher, they were important and educational for me. My over-riding memory of Doug was how kind he was, and generous with his time. While his reputation was tremendously intimidating, in person or in correspondence, he was never daunting. Indeed, he always went out of his way to be encouraging and inclusive, to even the most junior researcher. No matter how seemingly trivial the topic (certainly when compared to his major research collaborations), his behaviour, comments, edits, and corrections were always phrased with immense sensitivity and respect. From Doug I learned that good research pivots on sound statistical advice but, equally, he also taught me how to treat junior researchers later in my career. It is far easier to build a successful research collaboration when all team members are treated with respect. His ability to assist collaborators across disparate specialties and disciplines, and to get the very best from them, was exceptional.

### **Summary**

This narrative review has described our experience of working with Doug Altman on radiological research projects. [Table 1](#) summarises key learning points. Most obviously, the methodological quality of our research benefitted immensely. In contrast, it is unfortunate that most radiological research appears to happen without statistical input. A recent UK survey found that while trainee radiologists were expected to participate in research, only 3% had allocated research time and access to statistical support was exceedingly poor.<sup>17</sup> Exacerbating this, funding bodies appear more concerned with supporting specific clinical research areas rather than the infrastructure that underpins good design and analysis. This is probably injudicious since a well-trained statistician can support multiple studies across a wide range of different clinical disciplines. At their final lunch together in 2018, the first author was astonished when Doug described his difficulties obtaining support for EQUATOR, despite its obvious attractions; in 2015 EQUATOR attracted 22,000 visitors monthly.<sup>27</sup>

In conclusion, we return to Doug's seminal 1994 article,<sup>11</sup> that argued patients could be harmed by inaccurate research results and/or interpretation. We must ensure our research is designed, analysed, and interpreted properly. We also argue that personal fulfilment is enhanced greatly

**Table 1**

Key learning points and their elaboration.

Key learning points	Elaboration
Ask yourself, 'What is the clinical question'?	Good clinical research answers an important question relevant to patients and clinicians. Unimportant questions do not need an answer, meaning the research findings are irrelevant.
Always write a protocol	A research protocol, even if brief, helps focus and define the research question, explains how it will be answered, defines the endpoints necessary to do this, how they will be analysed, and identifies collaborators and their roles.
Seek statistical advice	Discounting statistical support risks biased study design and inappropriate analyses, so that findings may be inaccurate. Patients may be harmed if incorrect results are published.
Seek advice early	Statisticians help design unbiased studies that can answer the research question with adequate power. Delaying consultation until after data collection risks wasting time and resource in the long term.
Interpret your results properly	Statisticians will help you interpret results in an unbiased fashion, avoiding 'spin' and inappropriate conclusions.
Consult the appropriate reporting guideline	There are generally accepted reporting guidelines for most study designs. Adhere to these when writing up your research. Also consult guidelines at the study design stage, to help identify all important components of the research.
Consider a systematic review first	A systematic review will help identify similar research, in an unbiased fashion. A review will facilitate decisions around whether your research is worthwhile and will also help identify areas where evidence is lacking. Research funders increasingly require a systematic review before allocating funding.
Treat colleagues with respect and courtesy	Research is best performed when all collaborators, irrespective of profession or rank, are made to feel part of a team.

**Footnote:** The links below are to YouTube videos of Doug speaking about various aspects of research design:

- An interview with Doug Altman: [https://www.youtube.com/watch?v=gzW2FQ\\_gbB0](https://www.youtube.com/watch?v=gzW2FQ_gbB0)
- Is statistics good for your health? <https://www.youtube.com/watch?v=TkqtlgxTwhk>
- Improving reporting standards: <https://www.youtube.com/watch?v=MUMBM-2coUo>
- The EQUATOR network: <https://www.youtube.com/watch?v=jBjN8sYots>
- Publishing raw data: <https://www.youtube.com/watch?v=8SrYAv56jtE>.

by knowledge that our research maintains the highest methodological standards. The footnote to Table 1 provides links to YouTube videos of Doug speaking about various aspects of research design, and are tremendously inspiring.

## Ethical

Our institution does not require ethical permission for narrative reviews.

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## Author contributions

Guarantor of integrity of the entire study: SH Study concepts and design: SH, SM Literature research: SH Clinical studies: N/A Experimental studies/data analysis: N/A Statistical analysis: N/A Manuscript preparation: All authors. Manuscript editing: All authors.

## Conflict of interest

The authors declare that there are no conflicts of interest.

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