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Illustrating the development of fair tests of treatments in health care

Armitage P (2003). Some recollections of the early years of the Medical Research Council (MRC) Statistical Research Unit.

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Cite as: Armitage P (2003). Some recollections of the early years of the Medical Research Council (MRC) Statistical Research Unit. *JLL Bulletin: Commentaries on the history of treatment evaluation*

(<https://www.jameslindlibrary.org/articles/some-recollections-of-the-early-years-of-the-medical-research-council-mrc-statistical-research-unit/>)

Editorial note: The original text of Peter Armitage's lecture is reproduced here as it was delivered in a talk for the MRC Biostatistics Unit, Cambridge, UK, on 7 September 2003. Citations to relevant material in the James Lind Library and other references have been added editorially by Vern Farewell in October 2023 after consultation with Peter Armitage.

Thank you for the invitation to speak to you today, and for the singular honour of having my name connected with these named lectures. The association with the MRC Biostatistics Unit is one I particularly cherish. However, it has not escaped my attention that such honours are usually posthumous, and I conclude that the organizers thought, quite reasonably, that I had been dead for some time! On discovering their error, they no doubt felt too embarrassed to retrieve the situation, but I hope they don't regret their mistake. Anyhow, it's a particular pleasure that the first lecture is to be given by Ross Prentice, whom I have known and whose work I have admired for a long time. I'm looking forward to hearing his talk.

I thought it might be interesting to look back on events some 50 years ago, in the present Unit's predecessor, the MRC Statistical Research Unit, which I joined in 1947. I think the composition of the Unit at that time can best be understood by looking back to the pre-war period, and indeed to the start of the first World War, because in 1914 the newly established Medical Research Committee (later to become the MRC) appointed John Brownlee (1868-1927) (Farewell and Johnson, 2013) as the first Director of its Statistical Department. He had been a Scottish Medical Officer of Health and gained a reputation in epidemiology. His work at the National Institute of Medical Research at Hampstead included studies on mathematical epidemiology (periodicity of measles) and on the cohort representation of tuberculosis death rates.

The leading figure in pre-war medical statistics was Major Greenwood (1880-1949) ([Greenwood 1924](#); [Farewell and Johnson 2014](#); [2016a](#); [2016b](#)). Major was his first name rather than a title, perhaps the only characteristic he shared with Duke Ellington and Count Basie. He was medically qualified, working at first in physiology, rather than clinical medicine, under Sir Leonard Hill (Austin Bradford Hill's father). He came under the influence of Karl Pearson ([Pearson 1904](#)) and was appointed statistician to the Lister Institute in 1910. In 1919 he joined the new Ministry of Health, working at the NIMR and therefore close to MRC colleagues although not directly under Brownlee. Sir Harold Himsworth (Himsworth, 1982) wrote that 'according to tradition, Brownlee was an endearing but unworldly genius' and that 'Greenwood was the key that unlocked Brownlee's mind.' In fact, Greenwood gradually displaced Brownlee as the Council's chief statistical adviser, and he became the dominant figure in the MRC Statistical Committee which directed the Council's activities in medical statistics (Greenwood 1924). In 1927, Greenwood was appointed to the chair in Epidemiology and Vital Statistics at the newly formed London School of Hygiene and Tropical Medicine (LSHTM) but continued to work at Hampstead for two years while the School was being built. In his report for the

academic year 1927-28 he wrote ‘...it is neither possible nor desirable to attempt to distinguish between work which is wholly School work and investigations originally set on foot by the Ministry of Health or the Medical Research Council. The whole of the workers have shared in all the activities of the Division.’ As we shall see, this absence of demarcation between School and MRC continued to hold over the next 30 or so years.

The workers referred to in this report included Hilda Woods (Farewell, Johnson and Gear 2012) and William Russell, who in 1931 wrote *An Introduction to Medical Statistics* (Woods and Russell 1931; Farewell and Johnson 2010a, 2010b, 2010c), and later, PG Edge, of whom little seems to be known. The LSHTM history, *Prevention and Cure* by Lise Wilkinson and Anne Hardy, says he “seems to have had no statistical qualifications, and it is not clear what his background was. If one can rely on Bradford Hill’s late recollections, occasionally bordering on the frivolous, he was ‘probably another of Greenwood’s relations’”. Edge, who was sometimes known as ‘Major’ Edge (this being a military title), became a specialist in overseas surveys and censuses.

This was a pretty thin basis for a department of medical statistics, but the LSHTM staff was supplemented by the MRC staff from Hampstead, left stranded by Brownlee’s death, and so the MRC Unit was formed at the LSHTM. The pre-war MRC staff included Ethel Newbold (who worked with Greenwood on accident proneness), E Lewis-Faning (who researched the relationship between mortality and poverty), and several people who continued after the war, whom I shall mention in a moment. In particular, Austin Bradford Hill (1897-1991) transferred from the MRC staff to the LSHTM staff, to become Reader in Epidemiology and Vital Statistics in 1933. Before we leave the pre-war period I should add that one of the MRC workers with Brownlee at Hampstead had been HE Soper (1865-1930), a mathematician and electrical engineer who had studied under Karl Pearson in 1907, published in *Biometrika*, and wrote a book called *Frequency Arrays* on what we should now call probability generating functions.

This, then, was the position at the onset of war in 1939. The combined MRC/LSHTM group formed a secure base of postgraduate teaching and research in medical statistics and epidemiology. During the war the LSHTM concentrated on short courses on tropical public health for those going on overseas service. Many of the members of the statistics group were dispersed and normal activities were not resumed until 1945 when Greenwood retired and Hill became Professor of Medical Statistics, with the honorary directorship of the MRC Statistical Research Unit.

It is well known, I think, that Austin Bradford Hill had intended to follow his father into medicine but was prevented by a serious attack of tuberculosis incurred in the Aegean while serving in the Royal Navy Air Service, leading to two years in bed. He took a degree in economics at the London School of Economics, supplementing his statistics training by attending lectures by Karl Pearson, which he always said he barely understood but found greatly inspiring. He then joined Greenwood on an MRC grant for research on internal migration, and this led to MRC employment mainly on research in occupational health until he was appointed Reader in the LSHTM. His national renown at this time stemmed largely from the influential articles in *The Lancet*, which were the basis of his 1937 book *Principles of Medical Statistics* (Hill 1937; Farewell and Johnson 2011). Incidentally, he was always known to his friends and colleagues as ‘Tony’ rather than ‘Austin’. It was firmly asserted by his family that his parents were confidently expecting a girl, and when he was recognised as a male baby his father, Sir Leonard, was sent into the next room to look through a book of boys’ names. By the end of the A’s he had got fed-up, and he stopped at Austin.

In the immediate postwar period Hill had at his disposal several members of the prewar MRC staff, notably J Oscar Irwin, W J Martin and Eric Cheeseman. Irwin had an international reputation, having worked with Karl Pearson as a student during the first world war, then with Ronald Fisher at Rothamsted, before joining the MRC staff. During the period in the 1930s when both Ronald Fisher and Egon Pearson co-existed on different floors of University College, Irwin was said to be one of the very few people who was persona grata at tea parties in both departments. Fisher once told me that Irwin was the most competent mathematician of those with whom he had worked in the inter-war period. He had written on characteristic functions during the 1920s and was at home with Fisher’s theoretical work as well as with the computational aspects. He had performed a useful service to the statistical community by

producing annual reviews, in the RSS journal, of current developments in mathematical statistics. During the 1930s he became a leading authority in bioassay, and his interests tended to lean towards laboratory rather than clinical medicine.

Martin and Cheeseman had, I believe, joined Greenwood as non-graduates and taken first and second London University degrees during their employment. Martin was a highly specialist researcher on trends in vital statistics, which he wrote up regularly in the BMJ. Cheeseman had worked mainly as an assistant to Irwin. During the 1950s he was appointed to a new chair in medical statistics in Belfast. Irwin, Martin and Cheeseman were MRC staff, but they did a modest amount of teaching, Irwin in an annual short course that I shall refer to later, and the others mainly by demonstrating during practical classes for students on the various diploma courses. The LSHTM supported a new appointment in epidemiology, Donald D Reid (1950), a former squadron-leader who had been inspired by Hill during their wartime work in the RAF, and this later became a Readership and then a Chair. Another part-time appointment was John Fraser Roberts, an authority on medical genetics, who had links with Fisher and interests in the inheritance of intelligence, blood pressure etc.

This was the ambience to which I was introduced in 1947. I had been appointed, after wartime experience in industrial sampling inspection, and the completion of an interrupted degree course, primarily to be an assistant to Oscar Irwin. Irwin was a deeply sensitive man, somewhat gauche in his relations with others. In some ways I am reminded of Himsforth's characterization of Brownlee: 'an endearing but unworldly genius'. Oscar was the epitome of an absent-minded professor. One day he passed, in the corridor outside his room, a young lady who had been in the Department for several years, saying to her 'Haven't we met somewhere before?'. He was erudite and (like Greenwood) particularly well-versed in the classics and in history. To a Greek visitor he said 'Now, I've just forgotten what happened in Greece during the war.' When the visitor started to explain about the German incursion Oscar interrupted: 'No, no, not that war. I mean the Peloponnesian War in the 5th century B.C.' But he had a keen sense of humour. In a discussion after a paper at a scientific meeting, he complimented the speaker on some point and remarked that he wished he had thought of it. He then recalled the remark of GK Chesterton when Oscar Wilde had said the same thing: 'You will, Oscar, you will'.

Irwin admired Bradford Hill's work and I think envied his easy rapport with members of the medical profession. He once remarked that no-one in the mid-1930s would have predicted that Hill would achieve the eminence he had in the 1950s. They had very different temperaments and were, I think, never soul-mates. Hill was charming and generous in his social contacts, but there was perhaps an element of reserve and certainly an awareness that his grasp of statistical theory was not deep. He succeeded in his research by virtue of superb ability in planning and execution, a remarkably strong intuitive ability to interpret numerical information, and an ability to spot snags and fallacies. Added to this was a deep knowledge of medicine and superb powers of exposition, in both writing and speaking. He was a most congenial head of department, introducing even the most junior members as 'my colleagues'.

My activities were partly determined by Oscar Irwin's interests, which led to my own involvement with bioassay, and partly by my position as a younger person with a theoretical background and perhaps more approachable than Oscar who was thought by some to be an ivory-tower dweller. Hill would from time to time ask me to do things, and his involvement with clinical trials encouraged me to work on sequential methods and to forge my own links with various clinicians. I was quite free to work with other members of the School staff and in fact probably collaborated much more with University staff than on MRC projects. One incident sticks in my mind. I was collaborating with a medical research team on a trial of vitamin E in the treatment of intermittent claudication. When I returned to the office one day one of the young female assistants said: 'Dr so-and-so rang up, and he would like to speak to you about intermittent fornication'. I have never been able to decide what she really thought I was up to.

The projects handled by the Unit were to some extent determined by the needs of MRC Committees or other bodies on which members of the Unit sat. This would apply, for instance, to a major study of the medical effects of ionizing radiation by Richard Doll and Court Brown, and to much collaborative work in clinical trials or chronic disease epidemiology. But there was ample opportunity for us to follow lines of research that interested us. I, for instance, spent a good deal of time on projects in microbiology, working with School staff rather than other MRC workers.

It was, I suppose, a feature of the Unit and Department, perhaps characteristic of the period, that individuals got on with their own thing without much discussion with colleagues. There were no regular meetings apart from the daily tea-parties, the conversation at which was more gossipy than academic in tone. I remember only two specially arranged departmental meetings: one to hear the plans for the lung cancer case-control study, and one to hear a talk by Archie Cochrane (1941), recently returned from the USA. For the first year or so I found the tea parties rather formidable, as they were dominated by Major Greenwood, who had a room in the Department until his death in 1949, and several of his prewar cronies who had similar emeritus status in other departments but seemed to like our tea room. Younger people were not readily drawn into the conversation. Greenwood was a rather austere figure, who probably found it difficult to converse with new acquaintances. At that time, of course, people behaved more formally and more deferentially than nowadays. I addressed Bradford Hill as 'Sir' for many years before he became 'Prof' and eventually 'Tony'.

The great technical difference between then and now, in the practice of statistics, is of course the absence then of the computer. Before the war the group would have used Brunsviga mechanical calculating machines, and Oscar Irwin never used anything else throughout his career (which ended in the early 1960s). I remember visiting the Statistical Laboratory at Ames, Iowa, where Snedecor had worked before the war. In a cupboard I found a manual for a Brunsviga, published in the 1920s, which contained a statement to the effect that 'such was the perfection of this machine that it was impossible to imagine any future improvement in the art of computation'. On a Brunsviga one did long division by subtracting the divisor at each stage until the residual became negative, at which point a bell rang, and you turned the handle once in the opposite direction (the bell ringing again) before moving the carriage on to the next position. Thus the statistics corridor resounded with ringing bells. I had worked during the war with electric calculators and continued to use one at the LSHTM, and gradually the hand-operated Brunsvigas for class use were replaced by electric machines. Since computation was slow, all the academic staff members were helped by computing assistants. Similarly, the typing, which nowadays most academic workers do themselves on their PCs, was done by secretarial staff. There was therefore a considerable group of non-academic staff, all women. Electronic computing was not an option until the 1960s, after the period I am describing. Survey data were recorded on punch cards and sorted and tabulated on Hollerith or Power-Samas machines — a very slow process, especially as repeated passes through the machines tended to fray the cards.

I need to say more about my other colleagues during this time. Richard Doll joined the MRC Unit at about the same time as me, retaining for many years a clinical appointment at the Central Middlesex Hospital (Doll 1959). Donald Reid (Reid 1950) led the teaching in epidemiology and had his own programme of research in cardiovascular epidemiology with funding from various sources including the MRC. Richard and Donald were highly congenial colleagues, and I worked in various ways with both of them. A year or so later, Ian Sutherland joined the MRC Unit and started his long period of association with the Tuberculosis Research Unit (Sutherland 1958); later, of course, he followed Doll in the Directorship of the Statistical Research Unit, supervising the move to Cambridge and the transition from 'Statistical Research' to 'Biostatistics'. Several workers, too numerous to mention, were attached for periods of a few years to the Department or the Unit. Among these were John Knowelden, later to become Lecturer in Epidemiology before moving to Sheffield, John Colley, who moved to Bristol, and Walter Holland, who moved to St Thomas's.

The visitor with whom I had the closest association was H Oliver Lancaster, a remarkable polymath from Australia ([Lancaster 1951](#)), who, on his first day of arrival in 1948, immediately set off to watch the Australian cricket team at Lords. He possessed doctorates in medicine, mathematics and science and had developed an interest in medical statistics while serving as a pathologist in the Australian armed forces in New Guinea. He came with some partially written up research papers, some of which Oscar Irwin helped him to revise for publication. Later he would hold chairs successively in medical statistics and mathematical statistics in Sydney, and became an authority on aspects of multivariate analysis, Australian vital statistics, the history of medical statistics, and statistical bibliographies. He made two interesting epidemiological discoveries, the first an excess of deaf infants in Australia born in 1898 and 1899 relating to a previous rubella outbreak ([Lancaster 1951](#)); and the second showing that the incidence of malignant melanoma in Australia varied with latitude which affected the intensity of sunlight. Lancaster died in 2001 at the age of 88. One of the topics that intrigued him in 1948 was the stability of the sex ratio at birth. He maintained that a large data set collected by Geissler in the 19th century provided no evidence against the hypothesis that the sex ratio was constant, in contrast to those who thought that abnormal ratios ran in families. At that time he had four sons and no daughters, so he might have been thought to have a vested interest in the outcome of his research. He returned home to produce another child – a fifth son!

I have not said much about teaching, because that was a School rather than MRC responsibility, although we all took part in various ways. I ought, though, to mention the short course in statistical methods attended for a month or two each year by some 20 or so part-time students, many of whom were or became distinguished medical research workers. It had been inaugurated in the mid-1930s by Oscar Irwin and was rooted firmly in Fisherian methods such as analysis of variance, although of course not in the theory. It continued after the war, and I believe survives in spirit in courses currently given at the LSHTM. It provided the backbone for my own book on statistical methods published in 1971 ([Armitage 1971](#)).

It is difficult in retrospect to separate the School and MRC activities, and I suspect that the dual sponsorship of the combined group gave it an unusual breadth of outlook which helped to make it such a stimulating experience – one which I have never ceased to value and which has been the dominant influence in the whole of my career. Tony Bradford Hill controlled the whole operation with a very light touch but considerable skill and tact, without which it might have disintegrated. On his retirement in 1961, I moved to the chair in Medical Statistics, Donald Reid assumed direction of the Department (now Epidemiology and Medical Statistics), and Richard Doll took over the MRC Unit, remaining in the LSHTM for one year and then moving it to UCH Medical School. The rest, as they say, is history.

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