

AUDIO INTERVIEW TRANSCRIPT

Nunn, Andrew: transcript of an audio interview (09-Aug-2016)

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Nunn, Andrew: transcript of an audio interview (09-Aug-2016)*

Biography: Professor Andrew Nunn (b. 1943) has been working in clinical trials and epidemiological research since 1966, when he joined the Medical Research Council (MRC) Tuberculosis & Chest Diseases Unit as a Statistician, becoming Senior Statistician in 1972. Until 1986 he was directly involved in the design, conduct and analysis of the programme of trials conducted under the leadership of Professors Wallace Fox and Denny Mitchison in East Africa, Hong Kong and Singapore, which led to the worldwide adoption of short-course chemotherapy for tuberculosis (TB). Following the closure of that Unit he joined the MRC's Uganda AIDS Programme which researched the dynamics of the human immunodeficiency virus (HIV) epidemic in a rural African environment. On his return to the UK, he became Head of the Division Without Portfolio within the newly formed MRC Clinical Trials Unit with responsibility for developing trials in neglected areas. He was Senior Statistician on the recently completed REMoxTB and RIFAQUIN trials. Currently, he is an Investigator and Senior Statistician on three international phase 3 trials of TB treatment, one of which, STREAM, he is Co-Chief Investigator, the first phase 3 trial in multidrug-resistant TB (MDR-TB).

TT: Tilli Tansey

AN: Andrew Nunn

TT: Andrew, could we start off by saying a little bit about your childhood, your schooling and how you got interested in statistics?

AN: Yes, well, I was born in Norfolk, in East Anglia. In fact, my parents both came from Suffolk, and the Nunn family, if you look at the distribution of surnames you still find a high concentration of them in that particular part of the world. We moved into Cambridgeshire when I was about seven, and then into Derbyshire when I was about 17, and from there I went to university. I was one of the very first students at the University of Sussex. The University had started in 1961 with an Arts course, but in 1962 they started onsite in Falmer down in Sussex. And I remember it was the day I was sitting my very first A level exam - the Deputy Head came along and said 'I don't know if any of you are interested, you've probably applied for university now, but the University of Sussex is looking for applicants if you're interested.' Now I had already got some provisional places at other universities, but I thought 'Well, that would be an interesting thing to do.' So I went down, had an interview, wasn't even on the university site, it was in Stanmer Park, right next door. And it just seemed an interesting challenge to be part of, because Sussex was one of the first new universities. And it really got off to a very good start, across all the Faculties, I think, it had some very good staff, both science and arts. The statistics staff were very good, and the maths staff. So I was very fortunate, I think, to be part of it. I did maths, a degree in maths and physics for my bachelor's degree, and I remember that the maths degree, the maths part of it had just a small module on statistics. And I found that interesting; I think I've always found numbers fascinating one way or another. I remember reading a book about number theory when I was younger, and I enjoyed observing frequencies and so on. And there was a little bit about clinical

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trials in that, but not very much, and I didn't really pick up on that at that stage. But I did feel I'd like to go on and do a master's in statistics. So I stayed on at Sussex and I did the master's in statistics alongside someone you'll know very well by name, and that was Virginia Wade - we were both doing the same master's - we didn't play tennis together, but we did do the statistics.

TT: I'd forgotten she was a physics graduate, wasn't she?

AN: That's right, and she went on to do the MSc in statistics and so we were part of that course together. I really wasn't at all sure what I wanted to do when I left. So I just looked at job adverts and I must say I didn't find anything terribly exciting. I did apply for a couple of jobs at the civil service, and got interviewed and got an offer for those. I thought about getting involved in agricultural research. The reason is that some of the basic concepts in statistics are in trials, in field trials in agriculture; and my grandparents on both sides had been in the farming areas, so it just seemed to be a logical connection of a kind. But the interesting thing, what happened was, I think it was around April/May in my final year in 1963, that would've been - hold on a second, 1966 - in 1966 I went along to see the careers people (they asked us all to go and see them), which I thought was very interesting, to discuss what our plans were. And I gave my rather unsatisfactory thoughts about what I was thinking about doing, and they said, out of the blue they said 'Have you thought about medical research?' And I said 'No, I didn't know there was any opening in medical research for statistics.' I mean even the concept of biostatistics wasn't something I was familiar with, even though I'd heard a little bit about clinical trials. They said 'Well, the person you ought to go and see is Richard Doll.' They actually suggested I go up to London to Gower Street, as it was then, to the MRC Statistics Services Unit, where Richard Doll was the Director, just to talk to him about what the opportunities were. And so I did that, and I don't really recall much of what was said on that occasion at all. But I do know that I came away and said 'This is what I'd like to do.' There was an opening which came up in that unit which I applied for. I wasn't successful in that one, but not long afterwards there was an opening at the MRC's TB and Chest Diseases Unit. I applied for that and that's where it all began really.

TT: That seems remarkably far sighted almost, of the careers advisor to say 'Go and see Richard Doll.'

AN: Absolutely. I owe them a huge debt really, I really do, because when I think of one or two other people, of my contemporaries who I bumped into in subsequent years, who sort of got off on one track and it didn't work out for them, or they didn't find it very interesting.

TT: It seems quite astonishing; in fact, it's almost as if there was a personal link, as if someone in Sussex knew Richard Doll.

AN: That's a very good point. I'd love to actually - that person is probably not around nowadays - but I'd love to know what it was that gave rise to that. And, indeed, I'd like to know what was said to other people as well and in which directions they pointed them.

TT: That is fascinating. Could I just ask you to say a little bit about your school, whether you had particularly influential teachers?

AN: The reason I moved was that my father was a Baptist minister, and as a consequence he was never very long in one place. So between five and ten years we'd move from one place to another. So I went to a Junior School in Norfolk. In Cambridgeshire I went to Soham Grammar School and that was, I suppose, for most of my secondary education. I did move just after I started my A levels, but when I was doing O levels (it was O levels in those days), and had to sort of think what I was going to do at A level. The subject I had found most interesting was actually history - I enjoyed history most, and I put that down; we had a really enthusiastic and dynamic history teacher. But the subject I had done best at was maths. And in those days, Soham Grammar School was not a particularly big school; it had two parallel stream forms - they weren't graded particularly, but there were two parallel forms, and you had to make a choice when it came to A levels, and it was a limited choice. You could either do the science route or you could go an arts route. I wanted to do history and maths, but it wasn't really an option. In some schools nowadays you can do both,

but it wasn't an option. I was given a rather wise bit of advice there, saying 'Well, yes, you may enjoy history, but you can go on reading history for the rest of your life, and you don't need a history teacher to do that. But if you want to do maths and the applications of that then it's best actually that you should study that.' And so I did maths, further maths, as it was called then, and physics as my A levels, which I started in Soham Grammar School, then in Long Eaton in Derbyshire where I went on to complete and get my A levels.

TT: And at that point you heard about this new university, and went to do maths and statistics?

AN: Well, the maths degree, I'd be pushed to tell you much about the content now, but there was a module, and it probably was not many lectures at all, about statistics. And just a little bit there which was part of it, and that's the bit that caught my fancy actually. I thought 'This is what I'd like to do,' and it wasn't in relation to medical statistics, although as I said there was just mention of it possibly at some point.

TT: Coming back, you've seen Richard Doll - which sounds to me absolutely amazing - you're sent to Richard Doll as a callow undergraduate, or a new graduate. And then you go to work for the MRC.

AN: That's right. In fact, as I said I'd already had some job interviews and some job offers within the civil service, but when I got the opportunity, as soon as I had got this interview, I had an interview in what was in those days in Holly Hill, Hampstead, because the TB Unit was there. It was the TB Unit which had been formed in 1948, and this was 18 years later in 1966, which was formed immediately following the streptomycin trial. I was interviewed by Wallace Fox, Denny Mitchison, and Ruth Tall. And I really do count it a tremendous privilege to have worked with them. Wallace Fox and Denny Mitchison are two of the key figures in the development of the treatment of TB over a long period of time really, and indeed had already been involved for quite a while before I even joined them.

TT: The Unit was based in Holly Hill?

AN: I was interviewed in Holly Hill, but in fact they were in the process of moving. But it was a temporary move, and when I joined in September 1966 we were in Linton House in Tavistock Square, but that was a temporary home while a purpose-built building was being put up in South Kensington. The Brompton seemed to be the right place because the Brompton initially had been a TB sanatorium, so clearly had strong links; it was a chest diseases work. After about 18 months or so we moved to the new building in the Brompton. One of the striking things I remember was that, in contrast to today, I suppose we had a staff of about 40 to 50, and there were two of us that were statisticians - Ruth Tall was the senior one and myself when I started. In contrast to what you find today, the Clinical Trials Unit, where I'm working now, we've got a staff of 200 where just over 40 are statisticians. The role of the statistician has changed considerably over the years.

TT: How big was the Unit?

AN: I suppose about 40 or 50 people, something like that. A lot of them were involved in data recording, and when I say data recording I mean there was a limited amount of data which we were putting onto computers at those stages. We were starting to use computers, and, interestingly, starting to use an electronic calculator. The very first electronic calculator I had was about something like four foot square. It was a huge thing sat on my desk, which couldn't do much - it had about four memories, and it could add, multiply, divide and do squares - and not much more than that. And it took up an awful lot of space. But most of what we recorded, most of what we did, even for patient studies of 1,000 patients, was recorded on what we called an analysis card, about six by four inches, where all the details of the patient's treatment were recorded very carefully in a sort of abbreviated form. All their bacteriological results, including their smears, cultures, sensitivity results for TB, and there was a place where you could indicate if the patient had died or if the treatment had changed. And you could look at that card and see immediately the state that the patient was in, which, in fact, the transition as years went on to when we started putting things on the computer, you then had to program the computer in such a way that it could pick up everything which could determine

the status of the patient - which in the analysis by hand you could see at a glance. But we were sorting things into piles in those days; that was how we did it.

TT: What was the main work of the Unit?

AN: The main work of the Unit was TB. The name of the Unit changed over time. It was originally called the TRU, the Tuberculosis Research Unit. When I joined it became the Tuberculosis & Chest Diseases Unit around about that time, particularly with the move to the Brompton. But still the bulk of the work, I would say 75%, was around TB, and the other 25% was sort of working with the chest physicians at the Brompton in terms of various areas of medicine, including cystic fibrosis, asthma, allergic rhinitis and so on. And most of the TB work was done in the developing world, particularly in East and Central Africa, Hong Kong and Singapore. There were some other studies, well, Czechoslovakia was another area where we did quite a bit of work. But, by and large, it was actually outside of the UK. We did some surveys in the UK, we did one or two treatment studies in the UK, but mainly it was outside.

TT: And did the statisticians would work just within the Brompton with calculators, or did you go out to where the field studies were?

AN: By and large we didn't go, no. In fact, I think I can remember the first time I ever went anywhere apart from going to a conference in Turkey; it was in the early 1970s, mid 1970s. And that was a bit of a one-off; we were working with a group in Algeria, helping them to set up trials. There was a very enthusiastic chest physician by the name of Pierre Chaulet, who in fact had done a certain amount of research himself, and he wanted to work with us, and we did a couple of studies. One was particularly interesting; it was called the "Sahara Study", which we did amongst the nomads and also settled residents in the Sahara. That was after the studies in short-course treatment in TB had started, and this was a particularly interesting one in terms of the outcome and the results, and, indeed, just in the experience of going over there and helping them to set up a research work.

TT: You mentioned that study briefly in the Witness Seminar we had. We will come back and talk about that, but this idea of trying to monitor nomads and how you arranged for them to pick up their drugs; could you say something more about that study?

AN: Yes. The earliest studies in short-course chemotherapy were all done in very controlled settings, not because it was necessary, but because it had already been demonstrated in a study in Madras many years previously that patients could be treated as well out of hospital if they got TB as in hospital (the Home Sanatorium Study which Wallace Fox was involved in). But we kept them in hospital to be absolutely sure that they got all their treatment. Because it was really a proof-of-concept in those days: can you give treatment for a much shorter period of time than had been the standard treatment? The Algerian study was a break from that in a way, because it was really investigating what happened when we go into field conditions where things are very different, where in some instances you can't even depend that the patients will be around in the same area, they may be mobile patients in the sense that they're going, like the nomads who moved from one place to another depending on the season, with their goats and their sheep and whatever, and also picking dates as well, because that was part of what they were doing. So we had to have an arrangement whereby sometimes they would collect their drugs in one place and be told, well, next time if they're not here, the next place they can pick them up is some distance away, if that's the area that they were going to be working in. There was no Directly Observed Treatment (DOT) in the sense of directly observed treatment by an independent person of any kind. Possibly the head of the tent took some responsibility for the patient, but in fact it was absolutely fascinating because the results in that study were just as good in that nomad population as they were in the settled members of the population who were living in one or two of these sub-Saharan towns, which suggests one of two things: either they were extremely assiduous in taking their treatment or possibly that they could actually take it and afford to miss some from time to time and still get good results. Whichever way it was, the results were remarkably good and it was a fascinating study. And I did have the opportunity to go to various hospitals, and indeed go and see some of the conditions under which the nomads were living.

TT: Could I just now go back to you starting at the Brompton. Who was Director of the Unit?

AN: Wallace Fox was the Director. Wallace Fox had joined the MRC's Tuberculosis Research Unit in 1952, and he subsequently succeeded the previous Director, who I think I'm right in saying was Marc Daniels, who died rather prematurely in 1953. In 1956 Wallace Fox was seconded by the WHO (World Health Organization) to go and set up a Tuberculosis Research Centre in Madras, as it was then - Chennai today. The centre is still there; in fact, I was out there just the year before last when they were putting up a memorial plaque to Professor Fox, for the work that had been done. There were two studies which in fact had very interesting results. One was called the Home Sanatorium Study, asking the question 'If you treat patients in hospital or at home do you get better results keeping them in hospital, or can they do just as well at home?' And, surprisingly, well perhaps to some people surprisingly, the results in people treated at home were just as good as the ones treated at hospital. The other interesting thing was in relation to the contacts; there didn't appear to be any greater risks if the patients were at home to if they were at hospital. Now I think that's probably down to the fact that once you start on a treatment regimen with a drug like isoniazid, which has a very dramatic effect on the bacteria load, the infectiousness of the patient drops quite dramatically. So, in fact, after a very short time, even a week, patients were much less infectious than they were before starting treatment. And that may be the reason why it didn't matter whether they were in hospital or at home; they weren't going to infect many people. Wallace Fox was in India for five years, but then he came back to the UK and headed up the TB and Chest Diseases Unit, which I joined in 1966.

TT: And this was a completely MRC Unit?

AN: This was a completely MRC Unit. The MRC had quite a number of Units across the UK doing various things; in fact there were two MRC TB Units potentially. One was Wallace Fox's Tuberculosis & Chest Diseases Unit, and the other was under Denny Mitchison, who was a bacteriologist who headed up the Unit, which became the MRC Unit for Laboratory Studies in Tuberculosis. The two Units worked very closely together, and when new trials, new investigations were being designed, we always met with Denny Mitchison. He'd come across to the Unit at the Brompton, he met with Wallace Fox and other members of the scientific staff, discussing the next direction we should be moving in in terms of studies.

TT: When you joined as a statistician, were you directed to support ongoing studies, or did you have input into the organization of studies?

AN: It would be nice to think right at the beginning I had input, but I think my input at the beginning would have been very little. For two reasons: I was the Junior Statistician and Ruth Tall was the Senior one who had been working there for six years already. But having said that, Wallace Fox had a philosophy which I think is an excellent one. It wasn't always followed, it certainly wasn't in those days, and I don't think it always is today, that in fact this is a team work, and so everybody should be involved, right from the outset. So I went to meetings where I didn't understand the concepts that were being discussed. But Wallace Fox did feel it was important that I was there. He felt the statistician shouldn't just be somebody who was called upon at just certain points in time, when we need to know 'How many patients we need?', 'Ok, well you can go away until we're ready to, we've got some data for you to analyse.' It wasn't like that at all; we were involved so that we were part of the discussion of what's going on, in terms of planning a study, in the running of the study, in terms of the quality of the data and so on. Obviously there are interim analyses from time to time, the main analysis which is often seen as what really matters, but it's not the be-all and end-all, and then the writing up of the report and the interpretation of the results. So it was the whole way through; I think it's a very good philosophy, and it's one I think that has been adopted more as time's gone on. But it certainly used not to be the case, often because you used to get people very often come to us at the Brompton; they'd just got a problem and they wanted us to give them an answer to that problem, and then they'd just go away. It wasn't very satisfying.

TT: I've heard that, talking to statisticians previously. They're regarded as the people who crunch numbers right at the end of a study almost.

AN: I'm afraid so.

TT: That's very frustrating. You were employed as the Junior Statistician? Was it a new position?

AN: Yes it was, because I think they recognized the work was expanding. Clearly one statistician in these days in a Unit of 40 or 50 people I think is very isolating to just have one person on their own. In fact, as time went on we did have one or two others who joined as well. So it was a learning process to begin with, but then clearly I had responsibilities as new trials were being developed which I took on responsibility for, whereas Ruth Tall was working in other areas.

TT: As new trials were developed, what was the mechanism for that? You mentioned already WHO. What was the relationship, how were new trials decided upon?

AN: It was really on the basis of where we were at this point in time. In fact, a lot of the emphasis was on looking for new treatments - we're talking about the mid-1960s - at which point in time the standard treatment for the UK had been pretty well established based on PAS [para-aminosalicylic acid] and isoniazid, with recognition that it needed to be given for 18 months. To give it for less you were going to be running into problems of failure. So that was the treatment that worked well, but that had been established round about 1962 in a trial that was referred to as the chronic trial. There was a recognition that PAS was too expensive a drug to actually use in the developing world. I remember what minimal amounts, very little money, they had to spend on drugs for treatment in those days, in countries in East Africa, for example. It's amazing to look back and see; I was looking at a journal article which was published in 1964, before I started work, where in fact it said that one of the WHO recommendations even then was isoniazid alone for treating TB, which is surprising in some ways because the lessons of streptomycin were that if you give one drug on its own you've got the problem of resistance developing - although with isoniazid on its own I think you got better results than with streptomycin on its own. On the other hand, you definitely ran the risk of patients developing resistance. But you could cure a substantial proportion with isoniazid alone, which was interesting, but it wasn't ideal. There was a drug that had been around for a few years called "thiacetazone", an inexpensive drug, produced by Smith & Nephew Pharmaceuticals as it happened. And some early studies were being done that had started in East Africa looking at thiacetazone. And it was a question of finding out what was the optimum use of this drug, what was the correct dose to be using, what should it be supplemented with if you gave it with isoniazid, should you supplement it with streptomycin? And those early trials in the late 1960s addressed that particular question. There was also a very large side effects study called the "Thiacetazone Side Effects Investigation". It was the second of two investigations - this one involved over 4,000 patients - and I was responsible for that particular study. It was just getting under way when I started work, and it was conducted in countries in Asia, Africa, Europe and in the West Indies as well - just addressing the question of the side effects associated with thiacetazone, whether there were ways in which they could be prevented. It had been suggested that giving a vitamin supplement with thiacetazone might be helpful, and the study I was involved in had part of it where patients were given a thiacetazone tablet with a core in it that was a vitamin core, in the hope of being able to reduce side effects which were problematic in certain populations. There was a lot of care-taking in that study, because they had a dummy core in some of the tablets so that you couldn't tell which pack contained the vitamin core. So for this large study that I was involved in supervising the labelling of the drug study, I had to go up to Hull on a regular basis for that purpose. This big study of 4,000 patients was analysed largely by hand actually - 4,000 cards to analyse. So that's where the main emphasis was at that point in time. It was all going to change because in the mid-1960s came the advent of rifampicin, and in fact that started a whole new era beginning with that first short-course study in 1970.

TT: When you said you went up to Hull, this was to Smith & Nephew? Was that a routine thing that you got involved with the drug companies at that level?

AN: Well, Smith & Nephew were providing the drug for this particular study, and they were producing the placebos. The drugs had to be labelled before they were dispatched out to the different countries around

the world, so my job was to make sure that the labelling was being done appropriately. Now, interestingly, today that whole thing would be done differently; that sort of thing would be done by some sort of independent group. We labelled drugs on a number of occasions for different studies, but that's something which nowadays is done in a different way.

TT: It seems quite interesting that the statistician was doing that - was integrated into the whole study.

AN: It is interesting in the way you're thinking about it. In fact, the structure of the staff in the clinical trials set up has changed over time in the sense that we now have different categories of staff, like data managers, trial managers, clinical project managers. And those are the sort of staff who would do that sort of thing today. Interestingly, looking back, there weren't many statisticians either, so there was just a little bit broader remit than perhaps we might have today. We might be responsible for producing the randomization lists, but not actually overseeing the labelling of the drugs.

TT: I'm fascinated by the roles and responsibilities of the MRC and WHO, and the countries in which you were working. What were the relationships? Was this in any sense, because there's so many conflicts and we're aware of so many tensions nowadays, western medicine being imposed?

AN: I don't really know how some of these arrangements were initiated. I know that in East Africa, for example, particularly in Uganda, the MRC had been working since the 1950s, not necessarily in TB originally, but in Mulago Hospital in Kampala, in various areas. I think there was a recognition of a responsibility to assist in these Commonwealth countries, although they weren't even necessarily Commonwealth countries at that stage. Some of them were, before they achieved independence. There was an East African community in those days which was made up of Uganda, Tanzania and Kenya; we had staff working in all three - we had a Senior Technician, a Laboratory Technician based in the lab at each of those three countries, the main lab. We also had field staff in fact who were based in the country. Dr Pierce Kent was one such person who was based in Nairobi overseeing the trials because many of the trials that we did were in lots of centres. You could have between 30 and 40 centres in one study. So the patients enrolled in the study might not be at one particular centre, and centres would perhaps enrol no more than 20-25 patients in some cases while a larger centre such as in Nairobi would enrol 50 patients. So that was the setup was in East Africa. Hong Kong was slightly different, although there were centres in Hong Kong also. In Singapore we didn't do as much, but those were the main areas - how they came to be chosen, I'm sorry, I'm not exactly sure.

TT: There may be historical reasons for previous connections. When you say you had staff in East Africa, these would be MRC staff?

AN: Yes, they were all paid for by the MRC. Laboratory staff were members of Denny Mitchison's Unit; he had a Senior Technician based in each of these countries.

TT: And these would be native staff?

AN: No, they weren't. These were people who went from the UK to set up the laboratory, to oversee it, to train local staff at the same time. But they were based there for a long period of time, in Nairobi, in Kampala and in Dar Es Salaam. A bit later we expanded to Zambia, Lusaka, because we had to get out of Uganda when Idi Amin started misbehaving. We had the staff in the UK; there was a doctor, Joan Heffernan, for example, who had responsibilities initially for those studies in East Africa, who would go and visit for a period of about six weeks at a time, and would go round all of the sites to oversee what was happening. What didn't happen was the statistician going - that's something that we didn't do. I mentioned about involvement in Algeria - that was exceptional. I never got anywhere near East Africa in those days. That was really left to clinical officers who had that responsibility.

TT: So you were a part of the MRC Tuberculosis & Chest Diseases Unit for many years, what were the changes over that period?

AN: Twenty years, 1966-1986, yes. One change, I touched on this briefly, was that we got our first electronic calculator. Another one, we started putting the data not just onto the analysis cards, but we started to use a computer. We used the London University Atlas computer, which was based in Gordon Square. That was fine when we were based in Tavistock Square next door, because that is the adjacent square. We used paper tape, often from the Creed machines, as they were called in those days. Or we did a certain amount on IBM punch cards. And you would take the programs round to Gordon Square and they would run the job, and then you'd go back a bit later and look at the output. When we moved to the Brompton Hospital it might have only been about two or three miles away, but in fact we were relying on a van service that came and picked up the program to be run, and then delivered the results of the program which had been run the previous time. Now the problem is if you've made one mistake anywhere in the program, you had to wait and rerun it again the next day. It took a long time to get a program running properly, because it wasn't like we can do today; you can have multiple goes very rapidly until you get it working properly. So that was very frustrating, and in some ways the advantages were not that great as we were doing just as well doing a lot of the analysis by hand, because in fact we were looking basically often at a binary outcome, to say 'Has this patient had a successful outcome at the end of treatment?' 'If they had then, subsequently did they relapse, and when did they relapse, and if they relapsed did they have acquired resistance?' and so on. These could be analysed in a reasonably straightforward way by setting cards out. Yes, they could be done on a computer, but we got very skilled at using the card-sorting approach. It was a very gradual transition to using computers. And it took the best part of 20 years before we were using computers more than using cards.

TT: You talked about patients relapsing, so these studies were really quite long-term?

AN: They were, yes. When we did the short course studies the key metric in terms of outcome was whether patients had a relapse-free cure. In other words, they were treated satisfactorily and then they were followed, usually for another 24 months. We even in some cases followed them right up to five years to see whether there was any chance that they were going to relapse in that period.

TT: And what was the definition of relapse?

AN: Well, it was a recurrence, a bacteriological recurrence. We were not able in those days to distinguish between relapse and reinfection. That technology wasn't available at those stages. So all we could say was the patient had a recurrence. They were actually called "relapses", but some may have been reinfections, so in fact nothing to do with their original infection.

TT: During that period was there any particular trial you were especially proud of, or involved in?

AN: Yes, undoubtedly the one that stands out is the very first short-course study. As I mentioned earlier, rifampicin was the drug which became available in the mid-1960s. There had been no new drugs for TB for a while, but rifampicin stood out as the drug, which, along with isoniazid, looked to be a really powerful combination. And there had been some studies in the laboratory and in mice in the USA, which had suggested that in fact it both had a bactericidal effect in having an immediate effect in reducing TB bacilli, but also a sterilizing effect in terms of wiping up the persisting bacilli. Denny Mitchison and Wallace Fox suggested this could revolutionize the treatment of TB. Now it's fascinating to look back because this is a discussion which goes on today in a way, saying 'If you get a new drug, should that new drug, if there's not a lot to choose from, should that be reserved for treating difficult or resistant cases, or should it be used for the regular treatment of TB?' And it was felt that it was appropriate that we should look at this as a way of potentially shortening treatment. It had been established in the early 1960s that in fact you had to treat patients for 18 months or more. In the early days they just had no idea how long to treat; they started with three or four months - that didn't work very well; even 12 months wasn't enough. Some of the studies, before I joined, had established that you needed to be treated for 18 months or more. The trouble is 18 months is a long period of time in whatever populations you're dealing with, whether in the developed world or the developing world. Often patients would not collect their treatment, and many of them relapsed and failed their treatment, simply because they weren't taking it properly. So we had a meeting, in late 1969 or the beginning of 1970, in which we actually planned to do this study looking at a regimen which was only

six months in duration. We took the opportunity to study a number of regimens, all based on streptomycin and isoniazid; four regimens in total, one with rifampicin added, one with pyrazinamide added, one with thiacetazone added, and one with nothing added. It became very clear that the last two of these regimens were completely ineffective; the relapse rates were high, and they were stopped early, because they were inadequate in terms of the drugs that were being given. But the one with rifampicin gave remarkably good results, and that was what was really very exciting, to see the results of that, because the relapse rates were only of the order of three per cent. It was very consistent with the results that we were getting from the 18 months under very controlled conditions, where you made sure the patients were getting their treatment all the time, and excluding those who were missing treatment and not getting it. You were getting as good results with the six-month regimen as with 18 months of standard treatment. So that particular study stands out as being, I think, it was the biggest landmark since the streptomycin trial in 1948. We published our early findings for that in 1972, and confirmed it in subsequent analyses by following the patients for a longer period of time.

TT: Who manufactured rifampicin?

AN: There were two companies; they were Ciba-Geigy and Lepetit. One was Swiss-based and the other was Italian-based. As time went on, the companies were both bought up by others, and ultimately were acquired by Sanofi-Aventis.

TT: When you were conducting these trials, what was your relationship with the drug companies?

AN: We had some meetings with them when planning the trials, and obviously they recognized that if we, an independent group, were to conduct this trial, it would carry much more weight at the end of the day, and be more convincing, than if it had been just the drug trial initiated by the pharmaceutical company. But essentially, we didn't have many meetings of that kind because most of the planning - all of the preparation for the trial and the development of protocols and so on - was actually done within the TB Unit.

TT: At the beginning of this period, legislation in this country was rather different, before the Medicines Act of 1968. Were you always governed by the legislation in this country? Or did you have to consider legislation in the countries where the trials were carried out?

AN: I think a lot of things were in many ways much easier in those days. Committee structures or getting permissions of various kinds, and indeed even patient consent and so on, were not given anything like the same sort of attention in those days as they are now. And as it rightly is now. And Medical Officers of Health in the other countries - I wasn't involved in the process because, as I said, we didn't get to go and visit those countries - but I think there was some communication with them and discussion as to whether they were willing to have the particular trial conducted, and it was left to us to get on and do it.

TT: Would you like to say something about ethical changes?

AN: It's interesting, if you go back even before I started, to the streptomycin trial. Sir John Crofton noted that the patients were not told they were in a trial, and they kept those who were on streptomycin in a different ward from the ones who were not on streptomycin, so they didn't know what was actually going on. So it has changed a lot. I think in a way it could be argued in some sense that the pendulum may have swung too far in some cases, because the patient information sheets which now have to be given to the patients often run - and depending on who's producing them and what the study is - to many many pages, and it's hard to imagine many patients really reading or even being able to take it in, even if it is written in a language which is meant to be understood by a 12-year-old. One can understand why it's important to do this. But on the other hand it's also been demonstrated - not just in trials in the developing world, but also in trials in this country - that if you go to a patient who's been in a study for a little while, despite all the effort that has gone into making the patient, you think, understand what the study's about, you can ask them questions and in many cases they haven't necessarily got a good grasp of what it is at that stage. I'm not sure how we can do better than we're doing. I think it's certainly an area where there's room for improvement, because,

currently, the process of getting a patient's consent is an important one, but whether we're doing it in the best possible way, I'm not entirely convinced. But I think there's more work to be done on that.

TT: Can we go back to your career, and moving into the 1980s, and 1986 in particular, which was when Wallace Fox retired. The standard MRC procedure on the retirement of a Director was closure of the Unit. Was there any discussion about continuing the Unit?

AN: Yes, indeed. Wallace Fox did perhaps a rather strange thing, in that the Unit was the Tuberculosis & Chest Diseases Unit. And, in fact, that had worked extremely well, and we had produced some important publications outside of the area of TB. But when it came to putting in his final report he put the emphasis on thinking, trying to look forward in terms of persuading the MRC what should be done with this Unit - he put the emphasis totally on TB. Now in many ways one can understand that, but on the other hand you can also, from the MRC's perspective, understand why, when they looked at the situation, they might have said 'You have developed short-course chemotherapy,' and it wasn't just that first study, we had done a lot of following studies in terms of looking at ways to improve or to simplify the regimen. And the question was 'What other major questions need to be addressed at this stage? Or is it really a question of people getting on and doing treatment?' We had incidentally tried shortening treatment to four months without success, we got a successful regimen of six months, and that seemed to work well. Unfortunately, we were not aware of the effect of HIV in the developing world, particularly in Africa at this stage. We had no idea of the impact just at the time in the mid-1980s - the rates of TB were just beginning to go up in many African countries; for example, in Zambia they went up fivefold, from being around 100 cases per 100,000 in the population to 500 per 100,000 in the population. And Zambia was typical of many other countries at that time. If we'd known that HIV was going to have such an effect on TB, I think we could have made a strong case for saying 'It is really important, that this Unit continues to look at TB, and in conjunction with HIV as well.' There would have been another opportunity, and hindsight's a wonderful thing, and that is that there were no such things really in those days as Clinical Trials Units, and for the Unit to have become a Clinical Trials Unit, not saying we'll just focus on TB, or even just TB and HIV, but actually open up to doing trials in other areas. The Unit had incidentally been doing some work in cancer, but that had been moved on to Cambridge at that point in time. So, in fact, the cancer element was no longer there, but, that could have been the ideal time to form a Clinical Trials Unit, which could have actually looked at other disease areas as well. It was a missed opportunity, I think.

TT: Another couple of years it would have been much clearer.

AN: It would have been much clearer, I think, that's true.

TT: So, where did that leave you and your situation?

AN: Well, this is interesting. There were four members of staff who were senior staff at that stage, who had been working on TB and in the Unit for some time, who were all tenured staff, so the MRC had a responsibility to find a job for us. What they could easily have done is scattered us to the four winds; we could have all gone in different directions. But we said that we would like to be able to stay together at least for a short period of time to see what could be developed in the course of that. So the MRC agreed to that, and they formed not a Unit but an external scientific group called the "Cardiothoracic Epidemiology Group". It was called that because it was based at the Brompton Hospital. It was a slightly odd name to give it, but in fact it was headed up by Professor Corbett McDonald, who came from the London Hospital, he was also working at the London School of Hygiene & Tropical Medicine. And what was fascinating was we hadn't been in existence for more than a year when the AIDS Committee of the MRC decided that the time had come to do research, clinical trial research, in AIDS. This was immediately following a very successful trial conducted in the USA with zidovudine or AZT (azidothymidine), in which they had seen a dramatic reduction in the time to death in patients with AIDS who were given AZT in a placebo-controlled trial. The next question really was 'If we gave AZT or zidovudine to asymptomatic patients who were infected with HIV, could we actually delay the whole process of their developing AIDS?'; in other words, delay the developing of symptoms and increase their lifespan as a consequence. So the MRC, together with the French

equivalent, which is INSERM [Institut National de la Santé et de la Recherche Médicale] proposed the trial in which patients who were asymptomatic but infected with HIV should actually be randomized to receive AZT or a placebo. And, in fact, one of the four members of our group (the group of these four researchers Janet Darbyshire, David Girling, Peter Fayers and myself), David Girling, put forward the proposition that we should do it in our group, in this group of external staff, that we should actually take this on. The MRC agreed to that and so the “Concorde Study”, as it was called, was born; an Anglo-French study (which is why it was called “Concorde”). It enrolled about 1,800 patients, half of them in France and half of them in the UK. And that was the start of a whole programme of HIV trials, and that group evolved into an HIV Clinical Trial Centre, not a Unit, still external staff, but to all intents and purposes it was actually a Unit; it was a Unit in a way which was researching HIV, cures, well, a treatment for HIV. I was involved in the planning and the initiation of the study. It started in 1988: the idea was proposed in 1987, the study started in 1988, but in early 1989 I heard about an opportunity in Uganda, and so I jumped ship as it were.

TT: Can we just go back to the Concorde trial, because of course at that time, 1986, 1987, 1988, this whole thing is really blowing up. Were you involved with Burroughs Wellcome on their trials of AZT?

AN: Yes, well, obviously Burroughs Wellcome were making AZT (also known as zidovudine or Retrovir), and in fact they provided the drug that we used, and, indeed, a matching placebo. I think we had to have a rerun of matching placebo to get a decent match. There was a concern at one stage as to whether there would be drug-sharing, and people would know what drug they were on. It's one of the things, because many of the HIV-infected patients were very astute in terms of actually knowing what was going on. There was fear that they would be able to work out which drug they were on, and then they would start sharing drugs, but there wasn't any major evidence of that. What happened after I'd left, because when it got to the stage of there being results in the study Burroughs Wellcome were unhappy about the way that we'd analysed the study; they didn't like the intention-to-treat approach, they said 'There are many patients who hadn't had their treatment properly, and therefore they should be excluded from the analysis, and we should analyse the data another way.' A whole year went by from the point at which the trial should have been published to the time it actually did get published. Another interesting feature was that the Americans were running a parallel study at the same time called “019”, and they stopped their study very early. The early results suggested that giving AZT improved the outcome for the patients who were getting it, and so their Data Monitoring Committee [DMC] decided to terminate the study. Our DMC which included Peter Armitage as one of the members, and a top-level French statistician as well, said 'This is much too soon to stop, we should not stop at this stage.' Incidentally, they were not particularly knowledgeable about HIV; this was the first study of its kind, so they didn't know an awful lot about it, as it had happened. But they did make a very wise decision that in fact it would be premature to stop it on the basis of an early suggestion of benefit. And so the Anglo-French study went on for much longer before they reached a point where they said 'No, there is no benefit, and we're stopping it not because there's benefit, but in fact there was an excess of deaths in those receiving AZT.' So there were two things: one was that Burroughs Wellcome did not like the outcome and did not want to see the results published, but we made it very very clear that in fact we weren't going to compromise on those results, that they had to be published; and the second thing was in relation to stopping the study early, because there wasn't a case for stopping it early; it was a question of waiting to see what was happening. It did become clear that the AZT on its own, just like streptomycin on its own in the TB setting, was not sufficient.

TT: It's interesting you talking about the idea of all the external staff coming together, all four of you being funded by the MRC.

AN: I don't know the extent to which it happens today, but certainly historically there have been external MRC staff who have been working on a particular area who have sometimes been attached to a university department, or a hospital, or sometimes even attached to a Unit doing something else. We had one such person who in Wallace Fox's days was attached to his unit, called Donald Mitchell, who was doing work on sarcoidosis. He wasn't part of the Unit, he wasn't doing any trials or involved in trials in TB, but he was

working on sarcoidosis. He was an external scientific staff member, which was a flexible approach, I think, and had certain benefits.

TT: And then you mentioned the Concorde study.

AN: Oh yes, well, what was fascinating was that this was in January 1989 and the MRC got in touch with David Girling and myself. David and I were the two who were responsible for setting up the Concorde study. The MRC thought it would be good if we could meet a certain Dan Mulder, a Dutch epidemiologist who had been appointed to head up a programme to look at the dynamics of HIV infection in a rural population in Uganda. He was in London, so we went to meet him in London, just so that we could learn about what he was doing, and he could learn about what we were doing. And he described that he was hoping to start this study later that year, round about September, in Uganda. But he'd had a frustrating time in finding a statistician; he had got other staff in place, I won't go into it; basically it wasn't going to be a large expatriate staff - there were going to be four people, that's all. He wanted a laboratory person, an epidemiologist, a social scientist and a statistician. And he said 'He hadn't been able to find a statistician.' Well, that lit a light as far as I was concerned; this is what I'd absolutely love to do. And the reason why it was possible was because we'd just reached the stage when PCs were becoming routine. You weren't dependent on mainframe computers, where you had to send a job to a computer, but you could have a desktop computer. And the Ugandan Government was very keen on the project, but they made very clear that the data all had to be analysed in the country unless there was a very good reason that it could not be done in-country: that included all the laboratory work and all the data analyses. In other words, they were very much against the parachute form of research, whereby researchers would come in, collect data, take it away and analyse it outside the country without involving researchers in the country at all. So the MRC agreed to that approach, and therefore as a consequence they needed a statistician to be based in Uganda on the job. And so I got in touch with Dan Mulder after the meeting and said I'd be interested, and I got the job. Later that year I left the Concorde study and went to Uganda and spent six years working on that project.

TT: Were you already familiar with the setup in Kampala and in Uganda?

AN: I knew absolutely nothing about it really, I knew about the TB studies we'd done, but within the six-year period I was there we didn't really have many TB connections, although there is this strong connection between TB and HIV. We were not actually addressing that particular interaction as it happened, and so we were based at the Virus Research Institute in Entebbe, which had done landmark work in the past on diseases like yellow fever. It was, it so happens, in a pretty ropery state prior to HIV coming along. HIV brought new life to the Institute. And that's where we had our offices; we did our field work in a rural area in south-west Uganda, a bit further out from there.

TT: And this was again completely funded by the MRC?

AN: It was MRC-funded, yes. It was from the Department of International Development, funded through the MRC.

TT: It's now very common to expect that work is done in-country, and there's a lot going on about distribution of funds, like the Wellcome Trust is doing now for example. Making sure that it's in-country, the money's kept there. Was that unusual at the time?

AN: It was unusual because it wasn't very much earlier that the PC, the desktop PC, had been developed. Otherwise it wouldn't have been possible, not if you were going to use computers. You could have done work without a computer. As far as the work that I'd been involved in, most of the TB work, as I said, we did use computers to some extent, but not a great deal. A lot was done by hand analysis. So it was a break point; it was quite an important transition point.

TT: I hadn't thought about the availability of PCs.

AN: It did make a big difference. I was the only statistician. My responsibility was for the statistics and also the computing; the database side as well. After I'd been there a year I said to Dan Mulder 'We should be appointing Ugandan statisticians,' so from then on, each year we appointed another Ugandan statistician, so we had one start in 1990, another in 1991, another one in 1992, and so on. We were building up a core group of Ugandan statisticians.

TT: Did you help train them?

AN: Yes. We trained them on the job, because their experience, their training, was that they had done a Master's in economics and statistics at Makerere University in Kampala. They didn't know any biostatistics, and there were some fairly basic tests they were not very familiar with, because they were just not applicable in their area. But with one or two exceptions, it worked very well. We had one or two that didn't work out quite so well as others, but in fact it was an interesting experience. Some of those went on to get Masters and PhDs elsewhere, which was good.

TT: And then they came back?

AN: Yes.

TT: It was very interesting, one of the people I've interviewed is Eldryd Parry, and he talks very enthusiastically that his job was to replace himself with native personnel.

AN: Well, I'm glad to say that the Ugandan Unit has gone a long way down that road, in the sense that the Director of the Unit and the Deputy Director are both Ugandans now, as are a number of other top senior posts. Unfortunately, they really struggled to get a Senior Statistician to head up the Unit. In fact, I've been involved in the recruitment process with them of late. They had a South African who was there for five or six years, and he left about 18 months ago, and we've still not been able to get a replacement; we've interviewed internationally three times without success. Incidentally, we'd like to get a Ugandan, but, it's interesting, of course to actually head up a group like that, you haven't just got to have a good ability with statistics, you've also got to manage people, and sometimes you get people who are good in one area but not in the other. We've not been able to find somebody who we really felt we could take that on at the moment, so we're still trying.

TT: Perhaps it's one of those instances where it's easier to be an outsider.

AN: I think so, unfortunately. Having said that, the Director of the Unit now is Pontiano Kaleebu, who is doing a great job. And the Deputy, who's actually just left, was somebody who'd been there since 1989, Anatoli Kamali, a Rwandese as it happened. They were working together extremely well as a team.

TT: So when you got there this was a rather different kind of job to what you'd been doing before?

AN: It was. The responsibilities were considerably more. After I'd been there for a while I was asked to become Deputy Director of the group. It became a unit eventually. It wasn't called a "Unit" to begin with, but I became Deputy to Dan Mulder. There were considerable responsibilities over the data entry staff, the Junior Statisticians and working with the senior scientific team. It was a tremendous six years; I enjoyed that very much.

TT: Were you involved at all in the data collection? Going out and collecting?

AN: Going back to the days in the TB Unit, I'd been very much involved in the design of the case record forms for collecting data, and it was the same also in the Ugandan setting. I used to go regularly - if it wasn't once a week it was at least once a fortnight - to visit the field station area where we were doing our collection. I used to drive down; it was about 130-140 km away. I'd go down for the day, sometimes in fact we'd stay

overnight, but sometimes just for the day, to observe what was going on and to have discussions with the field staff who were collecting the data.

TT: And what was the main focus of this research?

AN: The main focus at that stage was to understand the dynamics of the HIV epidemic in a rural African setting. You have to bear in mind how much was known, or how little was known, about HIV in those days. This was 1989, September. There had been, outside the knowledge of HIV in the western world, case reports and data coming out of some hospital settings and so on in Africa. But, by and large, this was limited; not a great deal. There were no cohort studies, and what this was, actually, was a cohort study. It followed a whole population, in the first instance to see what proportion of the population were infected, and the demographics, of those infected. And then, looking forward, who gets infected, and how does the course of the disease manifest itself over time. And this was really fascinating, because there were assumptions that were made, which were actually found to be completely wrong, as it happened. They thought, for example, that the transmission might be as a result of many things other than sexual transmission. But basically it was heterosexual transmission with mother-to-child transmission as well. There was a thought that some local practices such as circumcision might actually have a negative effect. Subsequently it's been found to be positive; it actually reduced the chances of HIV infection. What often happened in practice was that a whole load of young boys would all be lined up and circumcised at the same time, using the same instrument to do the circumcisions; well, that would be a way that you could easily be transmitting from one to another. Also there was a feeling that some of the scarification that was done, might facilitate transmission. Regarding blood transfusions; Uganda was in such a bad way that there were very few people who got transfusions - the proportion who got HIV through blood transfusions was absolutely negligible. But we established that of all the children who had got infected, either their mother was already infected, or their mother had died of AIDS-like illness. Or there were one or two exceptional cases where there was evidence of child abuse, or a child who had had multiple injections because of asthma or something of that kind. But by far and away for large numbers of them, it was their mother who had actually been the cause of their disease.

There were also misconceptions that mosquitos might be transmitting HIV. But if you looked at the age profile it was very clearly associated with sexual activity, with the young girls, teenage girls, having higher rates than the teenage boys. And then the boys catching up in their 20s to 30s, and so on, and all dropping off when you got to the age of 55 or more. So that was very clear. One of the other interesting things was the life expectancy from the time of HIV infection. We thought that in an African context, where people obviously were immune-compromised for a number of reasons, and they have other morbidities, subsequent life expectancy might be different from what we find in the West. But it was, interestingly, very similar to what it was in the West in the days before the advent of antiretroviral drugs; it wasn't strikingly different. I think the most interesting of the publications that came out of there in the first year or two was the one that looked at the attributable mortality of HIV in the population. What proportion of deaths could be attributed to HIV? The adult sero-prevalence rate was 8%; high, but it wasn't enormous, although Uganda had a name for having a very high HIV infection rate. The reason we reckoned it was the worst place anywhere for HIV was probably largely because the Government was extremely open about their HIV, which virtually no other African country was. Everyone else was trying to suppress the fact that they'd got problems with HIV. Anyway, there was an 8% sero-prevalence rate amongst the adults, but then, when we looked at the deaths - one year later when we did our first repeat survey, and then looked to see which patients had died - we found that in fact 45% of the deaths that had occurred in that last year were attributable to HIV, coming from only 8% of the population. That was the overall figure, but if you looked at deaths in the 25 to 34 or the 35 to 44 year age groups nearly 80% of the deaths were caused by HIV. So clearly it was having a huge effect on the population. We looked at a reduction in life expectancy, did calculations on how life expectancy had been brought down dramatically by comparing life expectancy in HIV infected persons compared to the non-infected. Clearly the HIV epidemic in that setting was having a very dramatic effect on those in the population.

TT: This is very different work from your clinical trials days.

AN: Absolutely, and there were no clinical trials; well we did start a preventive clinical trial while I was there; basically the work was more epidemiological, yes.

TT: And a cohort study, how big a cohort?

AN: The population we started with came from 15 villages in south-west Uganda, with a population of 10,000 people - we surveyed adults and children. That cohort got expanded a number of years later to 15,000, so it wasn't an enormously big one, but it was of a sufficient size to be able to give us very helpful information. In fact, from within it we had sub-cohorts of patients, for example, a sample of those who were infected with HIV, and some controls to just see what was the course of their disease. They were looked at clinically on a more regular basis than the annual surveys.

TT: Were there other groups in Uganda?

AN: Yes there were. There was a group working in Rakai from Colombia University in the USA. In fact, also based in the Virus Research Institute in Entebbe in Rakai a neighbouring district to Kyamulibwa - not exactly a neighbouring district, but a neighbouring part of Uganda. So we didn't interact, we didn't overlap or anything, there was quite a bit of space between us. But they were doing a similar sort of work.

TT: What impact did this work have? Did it have any immediate effect in terms of Government?

AN: I think the Government in Uganda in those days had a very enlightened approach to HIV; there's a lovely anecdote, a lovely story. There was a non-aligned summit in the mid-1980s where Yoweri Museveni, the President of Uganda, was attending, and he met up with Fidel Castro. Fidel Castro said 'You've got soldiers from Uganda training in Cuba. Did you realise that one-third of those soldiers are infected with HIV?' This is in the mid-1980s. Museveni's response was 'that's not possible, it's a western disease.' 'Well,' Castro said, 'It's true.' So Museveni went back to Uganda and asked the Ministry of Health how many ELISA [enzyme-linked immunosorbent assay] machines they'd got for testing for HIV, and was told 'In the country there were only two, one in a Government hospital and one in a mission hospital.' And he said 'Well, we must start testing. We must find out what the extent of this problem is.' And he invited researchers to come in, including the British and the Americans. Indeed, Uganda was at the forefront of what went on in terms of acknowledging the problems, and there were big posters showing lots of people saying 'Can you tell which one's got HIV.' They had this ABC approach: abstinence, behaviour change, and using a condom. This sort of approach, had two consequences. One is that people felt that Uganda must have got the worst problem of anywhere because of the way that people were hearing about it. But on the other hand it was the one country that did see a dramatic effect on dropping the prevalence. The prevalence of HIV in antenatal clinics in Kampala when we started, and we weren't working in Kampala, was about one-third; 30% of women attending antenatal clinics. Over the course of the years that followed that dropped to 10%, and we saw a drop also in our rural population in terms of the incidence rates and in prevalence, particularly in the young men. I think there were multiple things going on, so it would be hard to dissect the effect our group had. The findings on the high attributable mortality were very interesting and we submitted the paper to *The Lancet*. Now, *The Lancet* had been publishing lots of papers on HIV. Every week there was an article on HIV, for several years. We were now into the early 1990s, and I think they may have been getting to the point of thinking 'We've published enough on HIV,' and they turned the paper down. We went back twice and said 'This is a very important paper, and you're making a big mistake in not publishing it,' and we got some other people to back us up, including Professor Peter Smith from the London School [of Hygiene & Tropical Medicine]. They eventually did publish it, and they put a leading article in from two people, Dondero and Curran from the CDC [Centers for Disease Control and Prevention], who in their leading article said this should put a nail in the coffin of these people who said that HIV doesn't cause AIDS. There was this American molecular biologist called Peter Duesburg, who was going around saying that. And he influenced, unfortunately, the South African Government. At the time when we were in Uganda, the South Africans had very little HIV. They had an explosion of HIV across the 1990s when rates went up in antenatal clinic attenders in some parts of KwaZulu-Natal, from 5% to 40% over the course of 10 years. It was

terrible; the message didn't get through. Our *Lancet* paper that was probably the most important publication that came out from our research group at that time.

TT: During this period, were you married, did you have family? Did they come with you?

AN: I was married in 1969, so when we went out in 1989, 20 years later, we'd got children, one of whom was just leaving school. We've got four children, one of whom was just going to music college at the time, one of whom was just about to do his A levels, and then two younger ones. And we took the two younger ones out with us. The older of those two, who was 13, did correspondence school for a while, but found it tough going, so he went back to the UK and boarded as his older brother had done for his A levels. My wife home-schooled the youngest one, who was only 4 years old when we went out, so she was in Uganda with us for 6 years.

TT: Did you and they enjoy being in Uganda?

AN: Yes. Having said that, it was a mixed picture in the sense that, for example, in our second year there we had an armed raid, and people broke into the house, saying they didn't want to steal anything, they just wanted to kill us. The trouble is, if you are there as an expatriate you were an obvious target for thieves. They didn't lay a finger on us, they just wanted to scare us obviously, but they saw us as people who were well off, and were in a good place.

TT: Did you live in a compound?

AN: No. We were in individual compounds, and when we were first there, 1989, we didn't have too much trouble the first year. We didn't even have a guard or a dog or anything. The second year we had a dog, but the dog got poisoned by these people who came in, and then after that the MRC recognized that we should have a guard. This was a mixed thing; the guards weren't great. The expats obtained a CB [citizens band] radio so we could contact the local police. Not that that worked very well; they used to turn up very late after we'd called them sometimes. It was a lovely place, it was lovely living out there, but security was an issue. Our youngest son, who was there at the time of the armed raid, went back to school in England soon after. He said 'I like Uganda in the daytime, but not at night,' because there was always the feeling of what might happen. When the rain came - very heavily, a tropical storm - you could hear absolutely nothing outside, and the power would often go off as well. So you didn't know what was going on. And so it was, we moved; the house we lived in for the last four years had a compound which was more secure, and we ended up with a decent guard, who we told his main job was to make sure the dogs didn't get poisoned. Because would be thieves would throw poisoned meat over the fence to poison the dogs so as to be able to get in. I said to the guard 'If you can stop the dogs getting poisoned, then people are unlikely to break in.'

TT: What were your relationships with the MRC back in London? Did you have to come back fairly frequently?

AN: Not particularly, no. We were just left to get on with it, really. Clearly there was a scientific advisory group, although I'm not sure even in those early days whether we had a lot of contact with them. But that group, yes, they did come out, they did visit us. I remember Professor Peter Smith was part of that scientific advisory group; they did come out from time to time. But otherwise we didn't have much contact. Interestingly the MRC in London didn't seem to have much of a clue what it was like for people to live in the developing world. They didn't tell us anything about what we had to do healthwise, anything like that. They didn't give us any advice about malaria, anything whatsoever; we just had to find that out for ourselves. They had, of course, got the Unit in the Gambia which had been going for many years, and they'd had another one in the West Indies at one point in time too. So really they were rather unhelpful in that respect. But we survived.

TT: Did you ever feel cut off and abandoned by the MRC or were you just grateful that you were allowed to get on with things?

AN: I don't think we felt abandoned. My wife did have a nasty attack of malaria, but the MRC couldn't have done anything about that - these things happen. We didn't feel abandoned, just felt 'This is how it is.' I don't know if we were expecting anything more, just in hindsight there was no preparation whatsoever for going out there, no indication at all what it would be like. We were clueless. I mean, when I expressed an interest in going, and I met up with Peter Smith and Richard Hayes at the London School of Hygiene [& Tropical Medicine], actually I didn't even have an interview - they just said 'Would you like the job?' And when I went for what I thought was an interview, they just wanted to know what I wanted to know, what questions I could ask. So I asked my questions and then the MRC said 'Would I like to go out to Uganda for a week to have a look round to make a decision?' Nowadays the spouse would go out with the person as well, have the opportunity to as well, but in fact I went out for a week and came back, and persuaded my wife this would be something worth doing.

TT: You were there for six years. There would have been a quinquennial review? An MRC review?

AN: Yes, I'm trying to think. I think there was a programme for an initial period, and I'm not quite sure exactly how long that period was. Dan Mulder was out there for a year, just setting up, making all the contacts, deciding where, what field, what work, where the work would be done, in what part of the country we would do the work, finding somewhere which we could get to, where the roads would be such that it was passable. He was there a year before we started, and then I went in September 1989, which is exactly when the fieldwork started. I'm not sure at what point exactly we then started planning what to do next, which was partly planning an intervention study, to look to see whether there were ways in which the population could be better informed to try to reduce the incidence. Sorry, I haven't properly answered your question because I don't particularly recall it as a quinquennial review in quite that sort of way.

TT: Well, perhaps if there was a period of setting up, you probably left before there was one.

AN: Probably, although in fact what happened was that Dan Mulder left a year before I did, and I was stand-in Director then until Jimmy Whitworth came, who was the second Director. And after that Heiner Grosskurth was the third one. And then the fourth one was the Ugandan, Pontiano Kaleebu, who is there now.

TT: What made you decide to leave?

AN: Well, basically I was given a four-year contract in the first instance, which was unusual in a way, because most people get two years. After a further two years, my wife and I discussed the fact that I would like to continue for another two. It was really family reasons, children getting to a particular age and so on and feeling, that my wife's experience wasn't quite so rosy as mine, in the sense that obviously I'd got a job which was extremely fulfilling. She wasn't able to do anything employment-wise; she was teaching my daughter. We did take a piano out with us - we left it out there, we sold it to somebody while we were out there - and in fact she actually did a piano tuning course before she went out. She's a pianist, she teaches piano. Since we'd been there a music school was setup in Kampala, Kampala Music School, which in fact was developed by the wife of another expatriate; there was a programme about it on the World Service of BBC, about it a year or so ago. That would've been something that would've been very fulfilling if she could've been involved in that. So there was a bit of frustration on her side; she also wasn't entirely happy about the security situation, and also the family growing up, so it seemed to be the right time to come back. In some ways I felt I could've just gone on and on.

TT: One can understand the pressures. So you came back. Did the MRC reassign you?

AN: Yes, this is interesting. David Girling and I had started the HIV Trials Centre effectively through the Concorde study. I had left to go on to Uganda; David had left to go on to Cambridge and joined the Cancer Trials Office at Addenbrooke's Hospital, the MRC Cancer Trials Office, and Janet Darbyshire took on the HIV Trial Centre at that point. When my time came to go back, I think I naively thought that I would automatically go back there. It wasn't automatic, but Janet made it possible that I could re-join the HIV

Trial Centre, which had by then moved from the Brompton Hospital, because it was not quite its natural home now; it was HIV-orientated, to Mortimer Market at UCLH [University College London Hospital]. And so I re-joined and got involved in HIV trials, and particularly microbicide trials for protection and prevention of HIV in women, including one very large phase 3 trial of over 9,000 women, conducted in a number of countries.

TT: You were coming back into clinical trial work, with the HIV experience in which you'd done cohort studies.

AN: Yes, but it was picking up my trials experience, not forgetting that just before I'd been to Uganda I was doing the Concorde Trial, so it was really getting involved in trials again, but now in treatment and, particularly, in HIV prevention at Mortimer Market.

TT: And that was very much UK-based?

AN: Yes. Well, some of the trials were in treatment, but the treatment trials were UK-based. In fact, the microbicide work which became the largest component as far as I was concerned was actually Africa-based. Uganda was one of our sites, we included South Africa as well, and Tanzania, they were the main sites, and Zambia - they were the four main countries.

TT: Were you collaborating again with your former colleagues in Uganda?

AN: Yes I was, actually, but also with a group in Mwanza in Tanzania, and in Lusaka in Zambia. At the same time I did start to get involved in TB again, in parallel to this HIV work.

TT: Is this because of co-morbidity?

AN: No, it wasn't actually. I don't know if you've come across the *Mycobacterium vaccae* story, and John Stanford. Well, *M. vaccae* is a mycobacterium which is found in the soil, which I think was first discovered in Uganda as it so happened, but all sorts of claims have been made for this being a way of treating (using injections of *M. vaccae*) TB and, indeed, allergies and even cancers and things. A meeting had been held at the London School of Hygiene [& Tropical Medicine] in which the promoters of this, John Stanford and Graham Rook, said 'Look, this is a fantastic drug, and really we should be doing more with it.' They'd published some rather unsatisfactory studies, where they even ignored the randomization schedule at various times - there were things they hadn't done properly and so on. And this meeting held at the London School was promoting it; I'm not sure if Janet was chairing that meeting, I think she may have been. No, somebody else was chairing, and said 'Is there anybody who doubts whether this drug does work?', and I think Janet Darbyshire doubted it, and somebody else as well. So straightway afterwards someone, Ali Zumla (he works at UCL), said 'Well, we should do a trial to really answer this question properly.' And it was going to be done in Zambia and Malawi. Janet rang me up, knowing I'd just come back from Uganda (I hadn't actually gone into the office at this point), knowing that I'd had African experience, and she asked if I would be interested in running this trial? And I said I'd be very interested, because I was already feeling, coming back from Africa, I was going to miss it, not being there. So in parallel to the HIV work, I was involved in running this *M. vaccae* study in Zambia and Malawi, which actually didn't show any benefit whatsoever, as it happened. But it did manage to start the TB work again; it was the first of a number of studies.

TT: So were you principally involved in HIV studies?

AN: Principally in HIV and principally in microbicide studies.

TT: Had that already been started or was it something you initiated when you came back?

AN: I'm just trying to think about the early work, where the early work in microbicides came from. I was involved in some of the early studies, and fairly early, because there were some early phase studies, phase 2 studies,

which I was involved in. The concept was one which had been around for a little while in terms of a woman-controlled product, which could be used by women, because there was always a feeling, often in African settings, that you couldn't persuade the men to use condoms, and if you couldn't persuade the men to use condoms then if the woman could apply a gel of some kind, it could be a major step forward in terms of helping to reduce the chances of women being infected, and all that went with that as well. So the concept wasn't entirely new, but it was in the early days of developing anything by way of phase 3 trials. There had been one unsuccessful trial, rather seriously unsuccessful insofar as, in fact, the product caused more HIV infection than the placebo in that case, because it caused ulceration, and therefore an entry for HIV infection, which was not a good thing at all. So this was going on - we're talking about between 1995 and 1998, time-wise. It was around about 1997, that Janet Darbyshire was asked if she would head up the Cancer Trials Office in Cambridge, and she said 'No'; she wasn't interested in that. They couldn't find anybody else so they said 'Supposing we brought the Cancer Trials Office back to London...' - because it had been a part of Wallace Fox's Unit - '... and then form a Clinical Trials Unit, would you be interested?' She talked to me and Abdel Babiker, who was a Senior Statistician who had been in the HIV work after I'd left, saying would we be interested, and we thought it was an interesting idea. So we were very supportive. So Janet agreed to that and the Unit was formed with three Divisions: there was an HIV Division, which Abdel Babiker, the statistician, headed up; there was the Cancer Division, which the Senior Statistician from Cambridge headed up; and then there was the division without the portfolio that I mentioned before, which in fact I headed up. Because the MRC said 'We don't want you just to be doing work in HIV and cancer, we think there's a need to be developing clinical trials in other areas,' which in fact just hadn't had the same sort of attention with respect to clinical trials. We know that TB has had a really long history going right back to the streptomycin trial. Cancer also had been doing quality trials for a long period of time, but there were areas of medicine such as musculoskeletal medicine where trials had been done but the quality of the trials had not been good, or transfusion medicine where there hadn't been any trials, or dermatology, and, indeed, one of the areas that had been neglected was respiratory medicine. The BTS [British Thoracic Society] historically had done some quite important studies. They had done their own short course TB studies, and some other studies as well, but all of that had fallen by the wayside. There's a group in Oxford at the Churchill Hospital who were very interested in getting respiratory medicine trials going in this country. Interestingly, when people were aware that the Unit had been set up they came to us and said 'We'd like to set up a Clinical Trials Unit in musculoskeletal medicine, or dermatology, or whatever.' We said 'That's not going to work very well, because you'll have a small group of staff; you'll have one statistician who'll be isolated, and you may struggle to do it that way.' So what we asked them to do was to provide funding whereby a Senior Statistician could work with me to help to develop trials in that particular area, but be based within the Clinical Trials Unit. So we had one who was working in each of the different areas.

TT: Funded by the different organisations?

AN: Yes, funded by the different organizations. The very first one, I think, was in musculoskeletal medicine, the Arthritis Research Campaign and then the National Blood Transfusion Service. There was an Arthritis Research committee which came up with the ideas for studies and funded them along with the statistician based in my group, for example, the British Society for Rheumatology. They were the ones who were doing studies, and interested in studies, and interested in doing things better. Interestingly, there were some links with an MRC Unit in Southampton, but basically we helped to develop trials in these and other areas; from 1998 to about 2008 or so, about the time when Janet Darbyshire retired as Director. When she retired the MRC did a re-evaluation of the Unit's programme. The Unit appointed a new Director for the Clinical Trials Unit, in which they then effectively said 'Look, you've been fairly successful in getting these other groups to set up, and they can go off on their own.' For example, there is now a Respiratory Trials Unit in Oxford, which was formed from the group that started with us. Dermatology is slightly different, but they've got things working well, and two of us (myself and an epidemiologist) are on the Research Committee - we meet regularly with them and are helping in the design of trials in dermatology.

TT: This is the British Association of Dermatology?

AN: That's right. Their office is in Fitzroy Square; it's called "BAD House". So I go every few months there, to a meeting of the scientific committee to discuss new ideas for trials. It's linked, interestingly, with the Nottingham Clinical Trials Unit and Professor Hywel Williams - I don't know if you know Hywel Williams, he is a dermatologist who now heads up the NIHR HTA [National Institute for Health Research Health Technology Assessment] Programme. What also happened, though, if you go back, as I said there were very few Clinical Trials Units around at all until relatively recently. Now there are at least 50 Clinical Trials Units in the UK. So things have changed totally in the sense that the MRC now has to have a very strong justification for doing clinical trials, because almost every university has got one or more than one.

TT: Are there too many, do you think?

AN: Arguably I think there could be too many, because I think some are not such good quality as others. So now we have focused back on two main areas, which are infections and cancer. I say infections because it's not just HIV; there's a recognition that HIV has had a huge amount of input into it. To begin with it was quite a bit of ring fenced money for HIV, and the new Director who was actually the one who is heading up the cancer group, Max Parmar, he said that he wants the focus on infections to move a bit away from HIV to other areas such as to do more work in TB, so we're getting back to TB, and other areas such as hepatitis. So, now, we're really back in doing quite a lot of work in TB again. The area that I'm particularly working on is MDR-TB, and the STREAM, which is pretty well the first phase 3 multicentre clinical trial there's ever really been in MDR-TB.

TT: And is this completely funded by the MRC?

AN: This is not funded by the MRC at all. No, that's not correct! For the first part of what's called the STREAM Trial, the main funder is USAID [United States Agency for International Development] with the MRC (we went for some supplementary funding from the MRC); they've provided about a million pounds of funding towards that. The background to that trial is very interesting because, in contrast to drug-sensitive disease, which has got a very good evidence base, built up over many many years (Archie Cochrane spoke very highly of the MRC, of the evidence base for TB), drug-resistant disease has been a seriously neglected area, and there's a growing problem. MDR-TB is a slight misnomer, because it doesn't just mean two drugs or more, it means resistance to isoniazid and rifampicin, the two key drugs. If you've got resistance to those two drugs, then your outlook is pretty poor. The evidence for treatment is based on expert opinion, not on clinical trials; it's from cohort data and expert opinion. There are about half a million new cases of MDR-TB every year. Only about one-fifth of them ever get treated and, of those that do get treated, the WHO data shows that only 50 per cent have a good outcome.

TT: This is global health.

AN: This is global health. This is quoting the very latest data from the 2015 report from WHO, which said there were 480,000 cases, I think, of which of those that had been treated in a cohort starting a couple of years earlier, only 50% had a successful outcome; the rest either died or packed up treatment and just gave up on it. Now during the 2000s, a Belgian doctor by the name of Armand Van Deun, working with a charitable group called the "Damien Foundation", was fully aware that the treatment is very unsatisfactory for the MDR disease, and not cheap as well, because the second line drugs that are available are of a poor quality, very toxic, and expensive as well. So the treatment could run into thousands of pounds. And yet you were getting very poor outcomes. So he looked to see if there were ways of improving the treatment using existing drugs, but combining them in different ways to what had been done previously. He did this in a very unusual way; he actually looked at cohorts of patients - well, an unusual way, not very unusual. He looked at cohorts treated with what was his first choice of regimen, and then he would tweak the cohort by taking one drug out and putting another drug in, then look at another cohort, and he'd sort of move on like that. Now the sixth cohort, there were 206 patients in the cohort, and the results were really very good. They hit about an 85 per cent success rate. Questions were raised about how selected the patients were, but everybody sat up and took some notice of this, and there were two responses. One response was 'Well, everybody should be treated like this, clearly it's the way forward.' Other people were much more sceptical and said 'We don't

really know, it wasn't a clinical trial, we don't know how he selected his cases, what would happen if we compared that with what WHO were recommending?', and so on. And at this point in time the International Union against Tuberculosis and Lung Disease came to me and said 'Would you be prepared to do a trial?' Well, they said a trial, but instead it looked as though it might be more another set of cohort studies trying to see whether these results could be replicated in other settings. Basically they had got funding from USAID in a competitive bid, as it happened, to do a trial, but the trial that was designed was too expensive; there wasn't enough money for it. They asked me what they might do and I said 'Well, DFID [Department for International Development] might give you additional money,' but DFID weren't interested. So they came back to me and said 'How about if we did four cohorts in four different countries, each with 100 patients, one in South Africa where there's a lot of HIV as well, one perhaps in a country like India, and two other countries?' We designed a study but always had a nagging feeling that in fact it would be so much better if it could be randomized, and then thought 'There is a way we could do this,' and designed it as a non-inferiority trial. I'm not sure if you've heard about non-inferiority trials. Incidentally, this regimen in Bangladesh is only given for nine months with these highly successful results, it could be extended for a couple of months for people who had a slow response, but was very different from the WHO regimen which was given for 24 months, so it was a big step forward, and it cost quite a lot less too. And I said 'Well, supposing we could show that the treatment with this nine-month regimen, which looks to be better than the WHO regimen, if we make the assumption that it is slightly better, but we want to demonstrate that it's not inferior?' This is the idea behind a non-inferiority design. Most trials are superiority, but non-inferiority is when you're really trying to show that something is not worse than another treatment. 'If we succeed in showing it's better that's good, but let's do it that way.' And so I did the calculations again and found that, yes, with 400 or so patients we could do that. We couldn't demonstrate superiority, because I made assumptions that it wasn't going to be a lot better, in which case you wouldn't need a lot more patients. I assumed that results in Bangladesh might not be as good when done in other places, and also assumed that WHO results would be better in a controlled setting, when they were being done in a randomized control setting, and, indeed, in countries which you selected it to do in. So I made the assumption that the WHO regimen would be 70% successful, rather than 50%, and the Bangladesh regimen would be 75% successful rather than 85% or 88%. In other words, there would be a marginal benefit, but one that we couldn't show - we hadn't got enough numbers to show it significantly better - but we could show that it could be regarded within confidence limits as being equivalent in efficacy. So that's how the STREAM Trial was born. And we have recruited to the first stage of that study; we've recruited 424 patients from four countries: South Africa, Ethiopia, Vietnam and Mongolia. And we completed enrolment to that a year ago. We won't get results of that first stage until the beginning of 2018, because we have to wait until the patients have completed 24 months on the long regimen, the WHO regimen, and then see, go a bit longer than that to see if any of those relapse. But in the meantime USAID came back to us again and said 'Would you be interested in extending the study to include some new regimens?', because there was a new drug that had been provisionally licensed for TB, a drug called "bedaquiline", from Janssen Pharmaceuticals which had received provisional licensing from the FDA [Food and Drug Administration] in December 2012, and would we be interested in adding on a regimen? We said 'Yes, we would,' and it would be possible providing any comparisons were made of one's patients who were admitted at the same time; we wouldn't make a historical comparison, it would have to be concurrent. So we started to design a study to do that. They did, incidentally, say 'What would be the main questions you would want to answer?' and we talked to a number of colleagues, as well as within our own group, about this, and we said 'Well, if there was any one study that we could do, the question that seems to be the most burning question is, is there a way to get rid of the injectable drug in the nine-month regimen?' Because sadly quite a lot of patients actually developed profound deafness as a consequence of this drug. It's in the same sort of family of drugs as streptomycin, which also had this problem. The deafness can be irreversible, so the last thing you want to do is give people irreversible deafness at the same time as possibly curing their TB. So we said 'That's what we'd really like to be able to do, to replace the injectable drug with an oral drug.' If we could include a second new regimen we'd like to ask 'is it possible to even shorten treatment from nine months to six months? Why should we not be able to possibly do this, with this potentially very good new drug added to the regimen?' And we looked for ways of finding additional funding, apart from that from USAID. We weren't very successful. Then we were approached by Janssen Pharmaceuticals, and they said 'Look, we've still not done our definitive phase 3 trial for definitive licensing with the FDA. Could we become part of this next phase, next

stage of the STREAM study?’ And we agreed to that, and so they agreed to fund half of the study themselves as well, and we have just started a few months ago the next stage of the study, with two new regimens. One is the fully oral regimen and the other is the six-month regimen, for which we’re going to need to enrol 1,100 patients.

TT: Still in the same four sites?

AN: No, we’re expanding now to ten countries. There were seven sites in four countries, but we’re now expanding to ten countries, including, we hope, India and China, and other countries in Africa, and two countries in Eastern Europe, Moldova and Georgia. So the whole thing has grown a lot. We’ve just had our investigators’ meeting in New York, who are at the offices of the International Union Against Tuberculosis, and it’s really quite exciting that we’re just moving into this next stage of what will be an incredibly important study, because patients with MDR-TB are just not being treated satisfactorily. There are other studies which are hoping to start later this year, but we’re a bit ahead of the game at the moment, so it’s quite exciting to be on this one.

TT: That’s really brought your career up to date; it’s almost gone full circle.

AN: Absolutely, it’s great to be back with TB. I’m also involved with some other TB studies, but I’m Chief Investigator on this study, which I’ve never been before, because that’s always been a clinician. I was asked if I’d be Chief Investigator, and I asked a clinical colleague if they would be Co-Chief Investigator with me.

TT: Can I just ask you one final thing? When you spoke about the creation of the Clinical Trials Unit how did the MRC spearhead that? Was it from the office, was it a Member of Council?

AN: Just to go back, Janet Darbyshire was asked would she head up the cancer group in Cambridge, and she said ‘No.’ Then she was asked again from head office. I don’t know the individual who asked her, no. But they had the foresight to think, when I say foresight it was as though they were trying to say they were committed to the HIV trials group, she was happy working there, heading that up. They were sort of saying ‘Would you be happy to take on the cancer as well?’ They were saying an easy answer would be to take the cancer on. When she said ‘Yes’ to that, the thinking was ‘Ok, we’ll call it a “Clinical Trials Unit”, but we won’t just do cancer and HIV, we’ll actually expand to other disease areas as well.’ So it was a sort of step process. ‘You turned down the cancer, would you be prepared to take the two together?’ And then saying ‘Ok, let’s turn it into a Unit.’

TT: I think at that point we’ve got to stop this part of the interview. Thank you very much Andrew.

[END OF TRANSCRIPT]

Further related resources:

1. Christie D A, Tansey E M (eds) (2005) *Short-Course Chemotherapy for Tuberculosis*. Wellcome Witnesses to Twentieth Century Medicine, vol. 24. London: Wellcome Trust Centre for the History of Medicine at UCL.
2. Overy C, Tansey E M (eds) (2017) *Historical Perspectives on Rural Medicine. The Proceedings of Two Witness Seminars*. Wellcome Witnesses to Contemporary Medicine, vol. 61. London: Queen Mary University of London.
3. Reynolds L A, Tansey E M (eds) (2001) *British Contributions to Medical Research and Education in Africa after the Second World War*. Wellcome Witnesses to Twentieth Century Medicine, vol. 10. London: Wellcome Trust Centre for the History of Medicine at UCL.
4. Tansey E M (intvr); Tansey E M, Beanland S (eds) (2016) *Moore-Gillon, John: transcript of an audio interview (29-Apr-2016)*. History of Modern Biomedicine Interviews (Digital Collection), item e2016126. London: Queen Mary University of London.

5. Tansey E M (intvr); Tansey E M, Beanland S (eds) (2016) *Moore-Gillon, John: transcript of a video interview (29-Apr-2016)*. History of Modern Biomedicine Interviews (Digital Collection), item e2016127. London: Queen Mary University of London.
6. Tansey E M (intvr); Tansey E M, Beanland S (eds) (2017) *Nunn, Andrew: transcript of a video interview (09-Aug-2016)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017057. London: Queen Mary University of London.
7. Tansey E M (intvr); Tansey E M, Yabsley A (eds) (2017) *Parry, Eldryd: transcript of an audio interview (12-Jul-2016)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017067. London: Queen Mary University of London.
8. Tansey E M (intvr); Tansey E M, Yabsley A (eds) (2017) *Parry, Eldryd: transcript of a video interview (12-Jul-2016)*. History of Modern Biomedicine Interviews (Digital Collection), item e2017068. London: Queen Mary University of London.