Scottish Covid-19 Inquiry

Day 1

July 26, 2023

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(10.00 am)

LORD BRAILSFORD: Good morning, everyone, and, first of all, thank you for attending this presentation, which is the first public gathering of the Scottish COVID-19 Inquiry.

The purpose of today's presentation is to hear a report prepared by Dr Ashley Croft on the epidemiology of COVID-19.

It is a presentation -- I use that word deliberately -- and it is not a hearing where there will be opportunity for anyone else apart from Dr Croft to participate.

Be well aware, however, that you will all or certainly core participants will get the opportunity to participate at later hearings, I imagine on more than one occasion, in relation to epidemiology and any other matters, because the Inquiry will be hearing evidence from a number of other sources in relation to the epidemiology of COVID-19 on a number of occasions throughout the coming months.

I should also indicate at this stage that the first public hearing at which core participants will be offered the opportunity to participate will be a preliminary hearing to be held at Meadowbank[sic] Stadium in Edinburgh for two days -- we've deliberately

allowed two days, because we appreciate people may have a lot they wish to contribute -- on 28 and 29 August. For core participants, I can inform you that you will receive a letter very shortly, at the beginning of next week, which will outline the format of that hearing and will also give you more details in relation to the conduct of it.

So, with that very brief introduction, I should indicate that the other participants today will obviously be Dr Croft, the author of the report, and lead counsel on this part of the Inquiry, Stuart Gale KC.

The hearing or the presentation has been set down to -- or we have available two days, and I understand from Mr Gale that it's probable that we will need two days, although we may finish a little bit earlier tomorrow.

During the course of today and tomorrow, we will have a number of breaks. We will have a break both this morning and this afternoon, both for the benefit of Dr Croft and Mr Gale, but also obviously for the convenience of the audience.

So, with that explanation, I would invite Mr Gale to begin his examination of Dr Croft.

Mr Gale.

DR ASHLEY CROFT (called)

Questions from COUNSEL TO THE INQUIRY

MR GALE: Thank you, my Lord.

Good morning, Dr Croft.

A. Good morning, Mr Gale.

Q. Just some introductory matters to begin with, please, so that we know what we're dealing with.

You've provided the Inquiry with a report which extends to some around about 70 pages, and attached to that report are a number of appendices which take us up into the hundreds of pages. You've also provided us with a total of 22 scientific papers, which have also been made available on our website and to core participants.

My intention today and tomorrow is to use your report as a guide to take us through your presentation, so everything will largely be under reference to what is in your report. Occasionally, we will divert into some of the documents, but at those points I will make it clear that we are doing that so that you're able to follow that.

So, doctor, can I begin with some formalities.

Your full name is Ashley Marshall John Croft?

A. Ashley Marcel.

Q. Marcel, I do beg your pardon, first mistake.

For present purposes, you've provided your CV, which is contained at appendix 2 of your report, and extends from pages 80 to 100 for those who want to follow it.

For present purposes, you've given an address at consulting rooms at 10 Harley Street in London.

A. Yes.

Q. You've also provided, I think, your GMC number.

A. Yes.

Q. How old are you?

A. I'm 70 years old.

Q. Now, at the beginning of your CV, you tell us that you are a fellow of the Faculty of Public Health Medicine of the Royal College; is that correct?

A. Yes, that's quite correct. Which page is that?

Q. It's at page 82.

A. Oh, that's right, yes.

Yes, on page 82, my Lord, five blocks down, "Professional body: Faculty of Public Health Medicine of the Royal College of Physicians of London", and it is quite correct, I'm a fellow of that by election. I became a member by examination in 1995, and a few years later was elected a fellow.

Q. Now, that organisation -- it may be self-explanatory, but could you tell us what qualifies you for membership and then fellowship of that organisation?

A. Yes, the Royal College of Physicians of London is a long-established Royal College which has a membership consisting of qualified physicians, and they have to pass examinations and prove their competence.

There are various subsections of that Royal College. One of them is a Faculty of Occupational Medicine, and quite a recent subsection is a Faculty of Public Health Medicine, which came into being about 40 years ago. It originally was called the Faculty of Community Medicine, but the name was changed because -- I don't know. I think Community Medicine was a better name. So the two terms are sometimes used interchangeably.

To become a member of the Faculty of Public Health Medicine -- nowadays they tend to call themselves the Faculty of Public Health -- you have to pass examinations, part 1 examinations, in the various specialist disciplines of public health, and in my day the core disciplines particular to public health were medical statistics, epidemiology, communicable disease control, health promotion, health economics and sociology. So it was common to go on a Master's course to prepare yourself for those part 1 exams, which were very hard. Later on, I was a part 1 examiner.

But I passed those exams in 1992, I think -- I've got it down here -- and then became a member -- I'm so

sorry, I didn't become a member. I passed the part 1. There's then a part 2 for the membership of the faculty, and in my day that required you to do two big projects and two big reports, similar to this report, on some aspect of the work you were doing. You were meant to be training in-house and doing public health tasks under supervision, and you could choose any two things that were of interest. The idea was they had to be different. One of them was expected to be communicable disease control, because that's important -- very important -- in our area.

So I did -- I prepared two projects. Would you like to know what they were?

Q. Please tell us.

A. The first one was I looked at -- I was working for the army at the time, and there was a concern about pregnant service women, that's to say women who were in the army, navy or air force, because up until about 1990, if they became pregnant, they had to leave. There was no facility for pregnant service women in the forces. Then this was challenged in the European Court, I believe, around about then, and it was considered illegal to ask women to leave -- quite rightly -- if they were pregnant. So the problem arose as to: how could they be employed safely where they were pregnant and

breastfeeding?

This was a big problem, and because I was the newest arrival, they said to me: right, you can sort it out. So for about a year, I did literature searches and consulted various authorities and produced a report for my department, my army department -- yes, it was the army then -- and this became army policy. I then wrote it up as a scientific paper, which we were encouraged to do, and as one of my first -- yes, I think it was my second research paper that's in my CV:

"Croft AM. The employability of pregnant and breastfeeding servicewomen. [Journal of the Royal] Army Med[ical] Corps 1995 ..."

I think a lot of that is still in military policy.

So that was basic epidemiology, really, just looking at all kinds of environmental infectious disease, ergonomic, occupational factors that might damage the health of servicewomen, and trying to find some way in which they could be accommodated with pregnancy, or not as the case may be.

Then for my second report, I was rather keen on Legionnaires' disease. We had that outbreak in the army computing centre in Worthy Down in Hampshire, and it had closed down the army computing centre for two days, which meant for two days the army couldn't actually

function. So I was keen to do that. But I was told, "No, don't do that; we want you to go and look at a new anti-malaria drug that's just come in called Lariam, and just go and evaluate it, it's a really good drug". So I thought: okay. I wasn't interested in malaria then, but I thought: well, you do what you're told in the army.

So I set up -- because I had been trained in epidemiology, I knew the right way to do an evaluation of a drug or a service or a vaccine is to do a randomised controlled trial. So in 1993, I did a little pilot trial in soldiers going to Kenya who were taking this new drug, and that went well.

Then in 1994 I set up a full-scale randomised controlled trial of this new drug, and the study population were the First Battalion of the Grenadier Guards, who were going to Kenya for six weeks, and there's malaria in Kenya. So there were about 640 in the population, and so I -- I should have said, I got research ethics approval, obviously. So they were randomised into two groups. The first group were randomly allocated to receive the new drug, which they would have got anyway, actually, and then the other group from randomly allocated to receive the old combination of drugs that they would have got the year

before.

So I did this trial —— and this is relevant, I think, to what we're going to talk about later on —— but it was a bit unsatisfactory, because the soldiers going out to Kenya were given a questionnaire on week 2, at the point where they were flying to Kenya, and then again at week 8, when they were flying back, and I entrusted the questionnaire to the Royal Air Force, who were flying them from Brize Norton, and I didn't get a very good response; I got about a 56% response for the first questionnaire and a 48% response rate for the second questionnaire. That's not really very good in a randomised controlled trial; you want to aim for 100%. Another thing that was odd about it was that a lot of the soldiers —— one of the questions was: have you been taking the drugs correctly? And about 17% of them, even though they responded, admitted they hadn't. So this raised concerns.

But anyway, I wrote the study up, and it was published in the Transactions of the Royal Society of Tropical Medicine and Hygiene. I had offered it to the British Medical Journal, and they said, "Well, Dr Croft, Major Croft, this is interesting, but normally we expect a response rate of about 60%. When it falls below that, when the dropout is so high, you can't really

necessarily ascribe validity to your results to the degree we want it."

So anyway, I then did, the following year —— in the meantime, I passed my part 2 exam, putting in my pregnant servicewomen paper and my malaria paper, but I thought: I will do another randomised controlled trial just to sort of get to the bottom of this problem: why are soldiers throwing away their drugs?

The second trial took place between October 1995 and January 1996, and the trial participants were the Princess of Wales' Royal Regiment, based in Dover. On this occasion, I went down to Dover and I spoke to the second in command. I said, "This is a very important trial, we need to know how good these drugs are, how well tolerated they are". So he put it on part 1 orders, which are what soldiers read every day, "You really must take your pills when we are in Kenya, and if you don't like them for any reason, just tell the medics and we will sort it out."

Then I personally went to Brize Norton at 4.00 in the morning on a number of occasions, because they went out to Kenya in waves. I personally gave the questionnaires to the troops, and the idea was they had to fill out a questionnaire or they didn't get on the plane. So I got a 100% take—up rate, and it was the

same coming back; they wanted to come back. So that was very good. But unfortunately the —— sorry, there was a point in the middle where somebody went out and they did a questionnaire in the middle.

Towards the end of the trial, the whole thing collapsed because I was taken off the trial and sent to Bosnia, and also there had been an unexpected event where a soldier had become psychotic taking Lariam, and later on another soldier committed suicide from taking Lariam. So it was very unsatisfactory.

Anyway, I was no longer in charge of the trial and went to Bosnia, came back, and then the following year I wrote a Cochrane systematic review of this particular drug to try and establish what were its proper properties based on randomised controlled trials, including mine, and that's how I got involved in Cochrane reviews.

Q. Right.

You've mentioned there, Dr Croft, a number of expressions that we're going to become familiar with in the course of your evidence.

A. Yes.

Q. Can I just pick up just a few of those ——

A. Of course.

Q. —— at this stage.

Epidemiology ——

A. Yes.

Q. —— as I understand what you've said, was an aspect of public health medicine, a specific aspect of that; is that right?

A. Yes. It's really an aspect of all medicine, and all doctors have an intuitive understanding, or sometimes an academic training, in epidemiology. I'll just refer ——

Q. Well, you've given a definition of epidemiology ——

A. Yes.

Q. —— in appendix 3.

A. Page 101, I think it is.

Q. It is indeed page 101. Perhaps you could just read that out, so we have that in the note.

A. So page 101, this is appendix 3 of my report, my Lord, and in appendix 3 I define key epidemiological concepts, and one of the concepts is the word or the term "epidemiology". The definition I have used here is a fairly standard one, and it's:

"The monitoring and study of factors related to health conditions, and the implementation of control measures to prevent disease occurrence."

So epidemiology might encompass —— often will encompass —— infectious diseases, but it also extends to

noninfectious diseases. So you might study the epidemiology of road traffic accidents, for example, and work out why they're occurring, where they are occurring and how you might try and mitigate them or prevent them.

The word "epidemiology", the Greek actually means, "that which falls down upon us from above". So it's quite a good idea. It's really anything that's unexpected or really unfavourable, we try and work out what it is about it that we can know and then how we can mitigate or even prevent it.

Q. I think, from what you've said, there are probably many aspects of epidemiology that one has to take into account, but I think possibly two that are of significance would be an understanding and an ability to apply statistics and statistical analysis.

A. Yes, indeed.

Q. Also, as you say, looking at control measures ——

A. Yes.

Q. —— to prevent disease occurrence.

A. Yes.

Q. Now, would control measures also include prevention of further infection through disease?

A. Yes. So if we were looking at a noninfectious disease, motor vehicle crashes, we'd look at helmets and seat belts. For infectious diseases, the control measures

might be, if it was food—borne transmission, a disease caused by food—borne pathogens, you would try and implement food hygiene measures; if it was a respiratory pathogen, you would look at maybe air filtration or ventilation, as well as maybe more extreme measures; if it was a blood—borne pathogen, you would make sure that proper sterile techniques were being used and any blood transfusions were free of pathogens, and so on.

So it would be specific to the type of disease and especially the route by which that disease was transmitted. That's really key to mitigating measures for infectious diseases.

Q. Okay.

Two other phrases that you've used so far, and I think we can helpfully find these referred to in appendix 3.

One was randomised controlled trials.

A. Yes.

Q. Now, I think probably most people who are familiar with medical papers and data will know what a randomised controlled trial is, and probably most people in the general public know what a randomised controlled trial is, but you've given it a specific definition. It's at page 102 in appendix 3, and I think if you could just read that out.

A. Yes, "randomised controlled trial (RCT)". A randomised controlled trial is defined as:

"The 'gold standard' research study in evidence—based medicine (EBM); [in a randomised controlled trial] study participants are assigned to the intervention group or to the control group in a random fashion."

Q. So if one is taking, for example, a vaccine ——

A. Yes.

Q. —— you would have a group who had been vaccinated, and there would be a control group who either were not vaccinated or had been given a placebo, as it's frequently termed.

A. Yes. The experimental group, as it's called, the intervention group, receives the vaccine, and the control group might receive a different vaccine, sometimes, but it's not ideal to have a different vaccine, or they might receive saline, some inert solution that looks as though they're getting an injection but isn't a vaccine.

Q. I think if you go back to page 100 in appendix 3 ——

A. Yes.

Q. —— you will also find a specific type of randomised controlled trial, which is a cluster randomised controlled trial.

A. Yes.

Q. Perhaps you could just read that out and, if appropriate, just expand on that a little.

A. Yes. So, my Lord, in a randomised controlled trial, usually they involve individuals, like in the two examples I just gave of the soldiers, and the unit of randomisation for a trial with individuals is the individual. So you would say you've got a —— so my Grenadier Guards, for example, 330 of them are randomly assigned to the intervention, the drug, and the other 330 were assigned to the other drug. The numbers are never going to be exactly the same because the randomisation process means that the two arms never have exactly the same numbers, but they usually differ by only a few. So that's randomisation as it normally occurs.

But in complex interventions, you might want to use a different unit of randomisation. For example, you can do randomised controlled trials in schools, where your unit of randomisation would be the school itself. So, for example, if you were worried about some aspect of school dinners, for example, you could take all the schools in Scotland, and half of them randomise them to this aspect of school dinners you were worried about, and the other half you randomise them to standard school

dinners, and then you have a randomised controlled trial which is a cluster randomised controlled trial, and that is as valid as an individually-based randomised controlled trial. They are more difficult to set up, but they can be set up, and indeed some occurred during COVID and the lead-up to COVID, which we may touch upon later on.

Q. One other expression that you've used so far -- and we will come back to these, obviously, in some detail because there are three papers in those that you have prepared for us --

A. Yes.

Q. -- that have this title -- and that is "Cochrane review".

A. Yes.

Q. Again, there is a useful brief expression of what a Cochrane review is at page 101 of appendix 3. Perhaps you could just read that and then, bearing in mind that we are going to look at these in some detail in due course, just give an indication of what is a Cochrane review.

A. Yes. Evidence from randomised controlled trials is very powerful. We may talk a bit more about that in general terms later.

Q. Yes.

A. It's ideal to -- or often it's very helpful to combine evidence from a number of randomised controlled trials using a mathematical method that's called meta-analysis. Cochrane reviews are an approach to doing that, to first of all gathering all the evidence that's available on a particular topic of concern or of interest, and ideally the evidence should be that from randomised controlled trials, and then the individual trials are assessed for their quality and then they're combined using this method called meta-analysis to produce, in effect, a larger randomised controlled trial, where there's a greater degree of confidence in the findings. That's what a Cochrane review is.

They're named after a Scottish public health man called Archie Cochrane, who was born about 1920 and went to Cambridge and then worked in England and in Wales. He ended up in Cardiff as an academic. He was the first really to highlight that there is an enormous wealth of biomedical knowledge, the amount of scientific data is massive, and no clinician, no policymaker, can hope really to keep up with all that's necessary. So he conceived the idea of having a sort of central point by which all of that data was being systematically assessed and analysed and then summarised, so that individuals -- the individual GP, the individual hospital doctor -- didn't have to go through the process of doing it.

Archie Cochrane died in about 1986, and his work was very influential, and a number of doctors, mainly in England and also Canada, Scotland as well, came together to form the Cochrane Collaboration in the early 1990s, and this is what they set out to do: they ambitiously set out to consider every important clinical question -- and there are tens of thousands of these -- and to gradually and progressively examine them all through systematic review of the evidence for those interventions, focusing on the potential benefits of the interventions, and also, importantly, the potential harms of the interventions.

So the Cochrane Collaboration, of which I have been a member since about 1995 -- I haven't done any reviews for a few years -- they've now produced, I think, about 10,000 reviews. They cover a tremendous number, a range of topics. During COVID, towards the end of the pandemic, an important review came out to do with the physical measures to try and prevent the spread of the virus that causes COVID-19 -- we might be looking at that later, my Lord -- and also last year a review came out, it was a preliminary Cochrane review, looking at the efficacy and safety of vaccines to prevent COVID-19.

So very important, extremely important, sources of

evidence for us.

Q. Can I just take two points from what you've said.

First of all, you've mentioned the expression "meta-analysis".

A. Yes.

Q. I think everybody can probably make a guess at what that is, but can you tell us from your point of view what it is?

A. Yes. If you were conducting a study where you end up with some numbers at the end -- I think it might be helpful if we went into the typical kind of numbers that you might obtain from a study -- you report those numbers and they will mean something to people who understand the numbers.

If you then want to combine the results of that study with a kind of comparable study to get a better, more precise estimate as to what it is that the investigators are trying to find, you use this method which is called meta-analysis. It's to do with mathematics. It's complicated. I have to take a lot of it on trust myself. But it's an accepted method of producing more precise numerical estimates of effect, and "effect" means whatever it is that the study was trying to show.

Q. Well, on mathematics, I'm afraid you're not going to get

any help from me.

But the other point that you've perhaps alluded to is —— I take it that Cochrane reviews are regularly updated?

A. They are. It depends, really, on what the review topic is, because some areas don't generate many new randomised controlled trials, but some areas of medical science are generating randomised controlled trials all the time, and so therefore new evidence comes along that may alter the findings of an existing Cochrane review. So a Cochrane review, where there's new evidence coming along, would normally be updated every three to five years, perhaps.

But what's very helpful about Cochrane reviews is there often will come a point where the reviewers say: the evidence for this intervention is so compelling, there's no need to do any more randomised controlled trials, please stop doing more research, because the evidence is there and research funds are limited, and it's better if you research something else. Equally, they might say: the evidence against this intervention is so compelling that you shouldn't really do any more research. They can say that with authority because they have —— the endpoint of these reviews is one of quite significant precision.

Q. I think, again, this is something that we will come to ——

A. Yes.

Q. —— in some more detail, but in the documents you've provided us with, one of them you've already referred to, which is the 2023 Jefferson, principal, main author, Cochrane review. It's number 9 in the bundle of documents, and that is a Cochrane review, the title being the "Physical interventions to interrupt or reduce the spread of respiratory viruses".

A. Yes.

Q. Now, I think we can see from the date that that is post certainly the worst of the pandemic, if I can put it in those simple terms. But before that, document number 8 in the bundle is Jefferson 2011, with a similar title, "Physical interventions to interrupt or reduce the spread of respiratory viruses".

A. Yes.

Q. So just looking at those two, as I understand it, there was not, between 2011 and 2023, an update of a Cochrane review on the prevention of respiratory viruses.

A. No, that's true. There wasn't. This particular review, the 2011 review, had been updated several times.

Q. Yes, I think we can see that ——

A. And ——

Q. —— it had been updated several times, but I think what is important, at least for our purposes in this Inquiry, is that the 2023 Jefferson Cochrane review did take into account preventative measures and the lessons learned from those preventative measures as a consequence of the COVID pandemic.

A. Oh, the updated one, yes. That covered the entire gap from 2011 to 2022, and then they published their essentially further update of their previous update in early 2023.

Q. Right.

It may seem a little while ago, doctor, but can we go back to your CV. I think it'll probably be useful to set a number of concepts and references that you will make in context.

Your academic qualifications, sir, are at page 83.

A. Yes.

Q. I think we can see, after a year at university in Madrid, you went to Oxford between 1971 and 1974, and you graduated from Oxford in 1974; is that right?

A. Yes, that was my BA, which was my first degree, which was in English.

Q. Yes. So you diverted off after that?

A. I did. I was working in children's publishing for a while after that, and I thought it would be nice to be

a doctor, and so in the evenings I was studying A Levels, which I think you call Highers, in science, and then in 1977 I applied to various medical schools and was accepted at Guy's Hospital medical school.

In fact, there was a course where you could apply directly as an arts graduate, or with arts A Levels, and that was quite common in medical schools at the time. It used to be the standard way of entry to medical school. You did classics at school and you did medicine.

Q. Yes. I was always told that in order to do law, it's good to have the Latin.

A. Oh, yes, sure.

Q. You also say, sir, just to get this clear, at page 84 of your CV, you also obtained a Master of Arts degree from Oxford ——

A. Yes.

Q. —— in March 1984?

A. Yes. Yes. At Oxford and Cambridge, you get a Master of Arts automatically 21 terms after matriculation. I didn't get round to picking it up until 1984, when I went in person and got it.

Q. Okay, thank you. Right.

As you said, you attended Guy's medical school between 1974 and 1984 ——

A. Yes.
Q. −− and obtained your degree in 1984?
A. Between 1978 and 1984.
Q. 1978 and 1984, yes.
A. Yes, correct.
Q. You also subsequently obtained a Master's in community medicine from the University of London in 1990; is that right?
A. Yes, that's right. That's when I started my specialist training in public health medicine.
I should have mentioned that the Faculty of Public Health Medicine encourage doctors to work as general doctors, either as GPs or in some clinical specialty, for a few years before doing public health medicine.
Q. I see.
A. Because, essentially, we're not dealing with patients as individuals, we are dealing with groups of patients, so it's good to have pretty good experience of dealing with patients as individuals.
So I didn't start public health training, which I started with that MSc, until 1990.
Q. I think we can also see that, also from the University of London, you obtained two diplomas: one in the medical care of catastrophes −−
A. Yes.

Q. −− and also in tropical medicine and hygiene; is that right?
A. Correct.
Q. Just to complete your academic background, you obtained a doctorate from Portsmouth University in January 2022, quite recently.
A. Yes.
Q. You've had a long association with the University of Portsmouth. Can you explain that a little?
A. Oh, yes. I worked in the army as a public health physician for 27 years and, towards the end of my time, I started a doctorate course at Portsmouth University part−time, and this continued and it went on for quite a long time, nine years. During lockdown, I was able to complete my thesis. That was part of the, for me, helpful aspect of lockdown, which was otherwise very damaging, for me and for everyone.
So I put in my thesis, and the title of my PhD thesis was, "Evaluating the adverse effects of anti−malaria drugs", which I had been working on for nearly 25 years, but the PhD came in only towards the end of that time. So part of that thesis −− with a PhD thesis, you're supposed to include as part of it three or four scientific papers that you've published, and they will be discussed in the exam. I had 12 papers

that I included, and they covered a range of epidemiology, not just malaria.
So I put in my written paper in 2020, and there was a hiatus because the universities were not functioning. But in 2021 I was told I could now have an oral examination on the paper. So this took place in 2021 remotely, and for PhDs you have three examiners who quiz you on your thesis. Normally, there's one from the university and two external examiners, so I had three examiners. It was done remotely.
At the end of it, they can either reject your thesis or accept it or suggest major changes or minor changes. But in the end, they said, "You can be a PhD immediately", which was very nice, "but do make a few minor changes like typos", and they said, "It would be helpful if you enlarged a bit on" −− there was a section where I talked about the need for further research. They said, "Just write a couple of extra pages for that, but for practical purposes, you can call yourself a PhD from" −− that was December 2021. I actually wrote up the bits they asked me to do in January, after Christmas, and sent it in, and then I got the letter back saying, "That's fine", and picked up my PhD in person in July 2022. By then, everything was open, so it was very nice.

Q. You've mentioned now on a couple of occasions an interest in malaria, and we will come to look at some of your papers, but I think we can see in your published papers that you have had, over a very considerable number of years, an interest in malaria and its treatment; is that right?
A. Correct.
Q. Thank you.
Just for completion, I think you're also a linguist?
A. Yes.
Q. And you're a member of the Institute of Linguists, and you're an accredited interpreter in French and Spanish?
A. Yes.
Q. Can we move on, then, from your academic experience, doctor, to your professional experience.
I think in your CV we can see that, after a year as a house surgeon/physician in Guy's, you then make reference to an engagement −− this is at page 85 of your CV −− in the Falklands.
A. Yes.
Q. I'm inferring from that that that is in connection with your army career?
A. Yes. I trained in the NHS and paid my own way for most of it. I did get a grant towards the very end, happily, but because I had a first degree already, I had to do

the three years self-funding.

So after qualifying as a doctor, you become what was called a house physician, a house surgeon, and during that time you're -- it's called preregistration appointment, so you're working under supervision, but when you've completed that year, you then become fully registered with the General Medical Council, and you can then do whatever you like, emigrate to America or whatever.

I joined the army then, because I had been in London for seven years. I wanted a change. So I joined the army on what was called a short service commission, which was three years, and I rather liked the army, actually. I got married during that time, and my wife liked the army, so I stayed on.

But anyway, so I joined the army in February 1986, after finishing my house surgeon job at Guy's Hospital and Lewisham, and then we had a period of four -- I was with about 20 other doctors, one of them from the University of Dundee, and we had four or five months of specific military medicine training to prepare us for a new role as army doctors. At the end of that, I got what was called a posting order to go to Germany. This was in the Cold War, so I was sent to the front line up against the Russians. But they diverted me to the

Falklands, because they had been told to provide someone. So I didn't go to Germany until the following year. I went to the Falklands for four months, June until October 1986, and worked there. Then I joined the regiment to which I had been assigned, which was the First Regiment Royal Horse Artillery, in Hohne in West Germany.

Q. Right.

Really just taking it short, doctor, you had various appointments, I think in various capacities, in Germany, London, Bosnia, Afghanistan, and the majority of these were as a public health specialist or consultant --

A. Correct, yes.

Q. -- or grew into that role as --

A. Yes, correct, and once I became a public health specialist, from time to time I'd be sent out to the NHS for short secondments, or in one case for a two-month secondment to Heart of Birmingham Primary Healthcare Trust, and that was just really to keep the public health skills up and to help out the NHS, perhaps, and just get the benefit of what they were doing.

But my employer during all of that time was the army.

Q. Yes.

I think you ended your career in the army with two

stints as a consultant public health physician in the Surgeon General's department in both London and Litchfield?

A. Yes, I became a consultant in July 1995 --

Q. Yes.

A. -- after completing, as I was saying, my part 1 faculty exams and my part 2 exams and doing a further exam, and so then I was a consultant for 18 years. So, yes, that takes us through to 2013, when I reached the normal retiring age for army doctors of 60. It's less for non-doctors. So I left the army at that point.

Q. What rank were you when you left the army?

A. Lieutenant colonel.

Q. Thank you.

Now, I think -- and we will look at some of your scientific papers as we go on -- a lot of your scientific papers are either directly or indirectly related to interests that you might have had as a public health consultant in the army.

A. They are quite army-specific, but of course that was my employer and they were the kind of tasks I was being set to do.

Q. Could I look at some of the other appointments that you've had.

At page 86, I think we can see that you were

a visiting fellow at the Effective Healthcare Research Programme Consortium at the University of Liverpool. Just tell me what that was about.

A. Yes. The University of Liverpool tropical medicine department had a very close link with the Cochrane Collaboration's infectious diseases branch, so they hosted that and they provided secretarial support and other support, for example in locating trials and doing library searches and so on.

So for a period of just over a year, I was at that point updating my systematic review that I'd written in 1996, which is one of the first Cochrane reviews to come out and was published in the British Medical Journal at the same time, and the updating process was quite complex because we'd broadened the scope of the review, and so I was appointed just to this title because it then gave me use of the library and use of the facilities at Liverpool while I was doing this task, which took about a year.

So I was still in the army, but I had this kind of extra -- it was an honorary appointment as visiting fellow.

Q. I think also, for a number of years, you were an honorary lecturer in travel medicine --

A. Yes.

Q. —— at De Montfort University in Leicester.
A. Correct.
Q. Finally, for about, I think, ten years, you were also the editor—in—chief of Human Parasitic Diseases. Can you tell us what that is, please?
A. Yes. The editor—in—chief sounds very grand, but really I was there to really oversee the correct conduct of the publication process and the peer—reviewing process that was going on for this journal, Human Parasitic Diseases. It wasn't a paid appointment; it was, again, an honorific appointment.

My role usually was to act as a kind of final arbiter, where a paper had been submitted to the journal for publication and two of the peer reviewers had said, "This is wonderful" and two had said, "This is terrible and should never be published". So, if you like, the managing director of the company would come to me and say, "Here is the paper, here is what the reviewers say, what do you think?" So I would arbitrate like that.

They would also from time to time say to me, "We want to put out a special issue with a call for papers; what are the kind of topics of interest in the field of parasitical diseases?" So I would list topics of interest, and I would also perhaps from time to time suggest possible peer reviewers for papers.

So it wasn't a very onerous task, but it was interesting, and it meant I'd often have to read papers that were —— I'd know about them, but they were to a depth that I hadn't been familiar with, and I would have to kind of really try and nut out what it was that was being said and come to a decision as to whether this was something we would want to publish in that form or not.

In the end, the publishing house that owned Human Parasitic Diseases, which was based in New Zealand, they sold out their titles to Elsevier, which is like a big publishing giant, and so this journal was merged with an existing Elsevier parasitical diseases publication, so it doesn't exist anymore, and I wasn't required because they already had an editor—in—chief for their new journal.

Q. Again, it's probably a useful interjection because you've mentioned, in relation to your position as editor—in—chief of Human Parasitic Diseases, peer reviewing papers.
A. Yes.
Q. Now, again, for many of us, this is a probably a concept we're all relatively well familiar with, but it perhaps does need a little explanation.

So can you just tell us, what is peer reviewing for

the purposes of publication? How does it proceed? Who is it done by? Really as much information as you can give us about it.
A. Yes. Yes, "peer reviewing" is a term which means that when a scientific paper is put forward to an editor of a journal, generally before the editor makes a decision, he or she will send it out to a number of acknowledged experts in that particular field, and they may be people that the editor knows about or they may be experts that they find by seeing who else has published in this field, and the peer reviewers —— they do it for nothing. I've done a lot of peer reviewing in my time. They do it for nothing. It's just meant to be part and parcel of what you do if you're a responsible scientist. They will read the paper, they will often be told to try and do it within a week or so, and they will often have a checklist that's provided by the editor to say: well, are the methods set up correctly? Are the results reported properly? And so on. Are the statistics sound, as far as you can tell? There will often be a separate statistics peer reviewer, because statistics is quite a specialised area. And then at the very end you will be given, usually —— this is what we had in my journal —— a list of options: publish as it is, or publish with major revisions, or publish with minor

revisions, and you could specify what those are, or don't even think about publishing it. But you would normally have to give your reasons. So you send that in, and other peer reviewers will be doing the same, and then the editor makes a final decision as to whether or not to publish.

They have to do that, firstly to guard against research fraud and possible —— or unintentional errors that might have been made by the investigators that perhaps they weren't aware of, and so to some extent it's protecting the editor's own back. But it acts as a sifting —out process. Really, the idea is that the best ideas get published quicker in the best journals. That's the idea of it.

But the top journals will reject 90% of the papers submitted to them, usually after peer review, because there's just too much science that's being produced all at once to get into the most prestigious journals.
Q. So can I just ask you, do I take it from what you're saying that you've been on both sides of the peer reviewing exercise, both as a peer reviewer and submitting papers that are subject to peer review?
A. Of course, yes. I have been —— exactly, I have had papers peer reviewed. Unfortunately —— I think it's unfortunate —— peer reviewers tend to be anonymous, so

you don't know who has actually reviewed your paper, and it could be your worst enemy who has reviewed it, and this does happen. So your worst enemy, a rival in your field, could peer review your paper because he's the only other person who knows about this unique topic, and they could just review -- they could say to the editor, "Don't publish this", and so there's no real redress against rejection.

So I have been in the position of having papers peer reviewed and accepted by the editor, or sometimes not accepted, and I have been a peer reviewer for about a dozen journals, and then I have been at the stage beyond that, where I have been the arbitrator, where peer reviewers have reached an impasse where they couldn't decide amongst themselves whether to publish or not. So I think I'm familiar with the process.

Q. Thank you.

Just moving on to one other appointment, you mentioned that you have been an appraiser of General Medical Council registered consultants and general practitioners from April 2021 to date. This is again at page 86 of your CV.

Now, I don't wish you to breach any confidences, either personal or professional, but can you just tell us what that role involves?

A. Yes. About ten years ago, the General Medical Council and also, I believe, the General Nursing Council, introduced the idea of annual appraisals -- I'm sorry, nurses don't do annual appraisals; they do three-yearly revalidation. But doctors were required to do annual appraisals to a certain format, and the format is dictated by a document called "Good medical practice", which is produced by the General Medical Council. So you have to show during your annual appraisal that you've conformed to the principles of good medical practice, and it's set out in various domains, and they cover areas such as courtesy to patients, good record-keeping, clear handwriting, keeping up with your topic, keeping up with your area, and patient confidentiality and so on.

So that's the background to doctors' annual appraisal. Everyone has to do it, and you have to do it with an appraiser who is also a GMC doctor.

Then after five years, your responsible body -- which is the body that you belong to that, in a way, guarantees your professionalism, your competence -- will make a recommendation to the GMC: this doctor, Dr Smith, has undergone the five year appraisals.

Also, yes, during that period you have to do what's called a 360-degree reflection, which means your peers

are meant to comment on your performance, patients are meant to comment on your performance, or nurses, and that's part of the revalidation process. You're also meant to conduct a quality assessment exercise of your own practice to try and improve your practice.

So, provided all those criteria are met, the responsible body will make a recommendation as to whether or not you should carry on for another five years as a GMC registered doctor.

So it's quite bureaucratic, but I think it's good. I think it actually does improve medical practice.

Q. Just, again, diverting away briefly from the GMC, if we go back to page 82 of your CV, I think your responsible body for appraisal and revalidation is the Independent Doctors' Federation in London.

A. Yes, it is.

Q. So you undergo this process?

A. Oh, yes, certainly, I undergo it every year, and my appraisal is coming up in October. So there's quite a lot of bureaucracy I've got to go through then, and you have to show your appraiser that you've kept up to date with your -- well, your faculty normally will have a requirement to do a certain amount of CPD every year. In my case, we're expected to do about 50 hours of continuous professional development of various kinds,

but the aim is to do 100 hours. So you show that you have done that and that your faculty has confirmed that, and then they will ask you, killer question: are there any investigations against you? Are there any complaints against you? And if there are complaints against you with the GMC, you have to declare them. You can't conceal them because they already know, because if there's a GMC investigation against a doctor, the GMC will notify the doctor's responsible body, and so the appraiser will already know. So if there is an investigation, it's not necessarily the end of the world, because often the investigations don't come to anything, but you have to discuss it with your appraiser and you reflect on what you might have learned or the background, and then that's recorded. You also tell them about your general health.

I'm happily in the position there has never been any complaint against me to the General Medical Council, and I think I'm right in saying that all General Medical Council investigations are logged and registered in perpetuity, so it's not something that one can really get away from if it should ever occur.

Q. Okay.

Can we go back to the GMC, please.

A. Yes.

Q. Can I ask: what qualifies you for a role with the GMC as an appraiser?
A. Actually, I believe any doctor can appraise another doctor, as long as it's done in the correct way, with the recognition of a responsible body, but I myself went on a three—day training course with the Independent Doctors' Federation because they needed some appraisers, and then I did some appraisals after that, based on that training, which very closely followed what I was just mentioning, the good medical practice guidelines.

So the appraiser doesn't actually —— it's not the appraiser who says at the end, "You're fit to go, carry on for another year", they just go through the process. It's the responsible body that, on the basis of the five successful appraisals, will say to the GMC, "Right, we recommend the doctor for revalidation for a further five years".
Q. Can I ask —— again, without involving you in any compromise of confidentiality —— can you indicate the areas in which you may have been an appraiser?
A. As an appraiser, you can appraise any doctor in any discipline, either a GP or a consultant, because the principles of good medical practice apply to all doctors. So let's say you are a psychiatrist. You don't have to be appraised by a psychiatrist. You can

be appraised by a GP. I myself have been appraised in the past by a psychiatrist —— really good, excellent, best appraisal I have had —— and by GPs and by rheumatologists, and my current appraiser is an occupational physician. So the specialty doesn't matter, as long as they follow the format that's approved.
Q. So would I take it from that that, in order to be an appraiser, you would have to have a certain standing within the profession?
A. You would have to be registered with the General Medical Council. Yes, that's what you have to do to be an appraiser. Because you're doing this on behalf of the General Medical Council, you have to have a GMC number.
Q. Also, would I be right in thinking that you would have to have the quality of independence?
A. Of course. And —— thank you very much —— so really the appraiser shouldn't be known to you. It should be somebody you don't know. And every three years, you ought to change your appraiser. I think that is a requirement. So you can't have the same appraiser for 20 years. That wouldn't be appropriate.

The system isn't perfect, and clearly sometimes it breaks down, and doctors are charged with the most heinous crimes, correctly, and that's terribly

unfortunate. But it's rare, I believe.
Q. Briefly, can I look with you at your postgraduate awards and decorations, which are at pages 87 to 89.
A. Yes.
Q. Really, again, just taking these relatively briefly, you've had two decorations specifically in relation to your military career. I think you received the NATO Medal for service in Bosnia in 1996, and also the Campaign Medal for active service in Afghanistan in 2008.
A. Yes.
Q. I'm particularly interested in the last reference on page 89 to the Cochrane Club award. Obviously there's a similarity in the name. Could you explain what that was for?
A. Yes. The year before —— so I was given this award in Auckland in New Zealand at the Cochrane annual colloquium. That's the big meeting they have every year, which moves around to different Cochrane centres around the world. So that year it was in Auckland, and I'm just going to look to see what Cochrane review I was given it for. It was for doing a podcast in relation to ... Yes, I produced a Cochrane review about the use of helminth —— so here we are. So page 93, that's right, the fourth one down. I produced, with two

co—authors, a Cochrane review which was titled, "Helminth therapy (worms) for allergic rhinitis". We looked at various trials where people suffering from allergic rhinitis were assigned to be given helminth therapy or placebo to try and improve their allergic rhinitis. We found there was a modest effect in improvement of the hay fever, and I produced a podcast.

I think I was given an award because it was such a novel area, said to be interesting and out of the usual run of Cochrane reviews, so it was very nice.
Q. You've also appended to your CV an extensive list of publications ——
A. Yes.
Q. —— which are divided into what you describe as main scientific publications; then there's a section of research letters, which I understand they are what they say they are: they're letters which are submitted to medical publications relating to areas of research ——
A. Yes.
Q. —— and there is then a list of books that you've made contributions to, and then a list of national and international presentations.

I'll come in a little to look at the list of occasions on which you've been invited to be an expert adviser to official inquiries, but obviously everybody

can read the list of your publications and those with which you are associated.

As I have said earlier, you appear to have an extensive interest and have written extensively on malaria. Again, can you confirm that?

A. Yes.

Q. Again, also a lot of your papers are associated with your time in the military ——

A. Yes.

Q. —— and relate to circumstances experienced in the military.

A. Yes.

Q. I think you've also made reference to one paper in relation to pregnancy and breastfeeding women, who at that time, their careers came to an end in the military. That's paper number 2 at page 90.

There's another paper, I think, that relates to —— I'll just find the reference.

Yes, there's a reference at page 91. It's the third paper from the bottom, in which you were a co—author. It's entitled:

"Does military service damage females? An analysis of medical discharge rates in the British armed forces."

A. Yes.

Q. Can you just tell me what journal that was published in?

I assume it's Occupational Medicine.

A. That's right, yes.

Q. Can you just indicate what was the subject matter beyond the title of that paper?

A. That's one of the few papers I didn't write entirely myself. I contributed to it, but the lead author there was Squadron Leader Katie Geary, who was my public health trainee. She had an interest in this. She was doing this as one of her big project, Katie. And then David Irvine, the second named author, he was a civilian epidemiologist who was working with us in the Surgeon General's department of the Ministry of Defence.

So Katie Geary just set out the information she had about medical discharges from the armed forces. This is when somebody joins the armed forces and carries on for a little while but then has to be sent back to civilian life because they're not medically fit. It was a concern at the time because the rates of medical discharges were going up, and so she, I think, had been told to look into this particularly and try and draw some conclusions. I can't actually remember in detail what her conclusions were, but it led on to some other research which you might be coming on to, Mr Gale, which was to do with training injuries.

Q. Okay.

Just finally, in relation to your papers, you also presented a paper —— this is at page 95, the third from the bottom —— entitled, "Trends in post—deployment mental disorders".

A. Yes.

Q. Can you explain what your contribution to that as a public health consultant would be?

A. Yes.

Again, I was reporting on data that was being routinely collected at the time by the medical statistics department in relation to the incidence of mental disorders in troops. They were rising then and they continued to rise over the next decade, and there are a number of reasons for that; amongst them the fact that there were still many troops who had served in the Falklands, where they'd been exposed to traumatic events, and many who had been in Northern Ireland, where they'd been exposed to traumatic events, or, again, Iraq. So they were the main contributors to the rising trends, and I was simply describing what was being observed without actually —— it wasn't based on my own primary research into that area, other than just really summarising what other people were finding and trying to fit that into some kind of pattern and sharing that information with other NATO colleagues.

Q. I think we can divert from your CV now briefly, Dr Croft, and could we go back to the very beginning of your statement ——

A. Yes.

Q. —— and the circumstances of your instruction for this Inquiry.

I think at preface page i, under the heading "Scope of this report", you say that:

"This report was commissioned in May 2023 by the Scottish COVID—19 Inquiry. The Inquiry's Letter of Instruction is reproduced at Appendix 1."

If you could bring up, please, appendix 1 so that you can look at it, we just see the terms of that instruction.

This was a letter to you from Ms Clements, who is the interim Deputy Solicitor to the Inquiry, and it reads:

"Dear Dr Croft

"As the interim Deputy Solicitor to the Scottish COVID—19 Inquiry ... I would be grateful if you would accept this letter as your instruction to utilise your expertise as an independent Consultant in Public Health Medicine and provide the Inquiry with a written report which will subsequently form the basis of ... evidence to be given at the Inquiry which is likely to take place

in late July 2023."

And that's where we are.

Then there's a passage on the scope of your report, and there's a reference to discussions that you had with Ms Soper, the co-secretary of the Inquiry, and indeed with myself as the co-lead Counsel to the Inquiry.

After the sentence that ends with my name and co-lead counsel, it continues on:

"The report that the Inquiry wishes you ..."

Could you just read the remainder of that paragraph out to us, please?

A. Yes:

"The report that the Inquiry wishes you to provide is one which will provide the Inquiry with a factual narrative detailing the state of accepted scientific knowledge concerning Coronavirus and COVID-19 as that knowledge was understood by public health practitioners in the period between late 2019 and the end of 2022."

Q. Would you just go on, please?

A. "In particular, your report will include the evolving state of scientific knowledge around (a) the nature of Coronavirus and COVID-19 and its pathogenicity; (b) the ability or otherwise of masks and other forms of PPE or other measures as recommended to medical, nursing and care practitioners and the public at various stages

during the period from late 2019 to the end of 2022 to prevent or restrict transmission of the virus; and (c) the utility or otherwise of handwashing, social distancing rules or guidance, social isolation measures or guidance for those at risk and/or those infected, COVID-19 specific treatments and vaccines at various stages during the period from late 2019 and the end of 2022 to prevent or restrict transmission of the virus."

Q. Right. I think we can leave it there.

As is inevitable, there is a word used in that section which perhaps it is useful to get your definition of at this stage, or your understanding of, and that is "pathogenicity".

A. Oh, yes.

Q. Now, just before we do that, there is a definition within your appendix 3 at page 102 of "pathogen".

A. Yes.

Q. Now, it may be my simplistic approach to matters, but the extent to which "pathogen" and "pathogenicity" are related may exist in my mind, but perhaps not in yours. So perhaps you could just explain, first of all, what a pathogen is --

A. Yes.

Q. -- and then what you understand by pathogenicity.

A. Yes.

A pathogen, as I have explained, my Lord, is a microorganism, so it's a small organism that -- I was trying to avoid the word "living", because of course viruses aren't living -- a very small organism that causes infection. Pathogens are generally divided into fungi, like candida, for example, aspergillus; bacteria, we know about those; and viruses; and also protozoa, such as the malaria parasite, which is to say more parasites.

So "pathogenicity" is the term that describes how grave a threat are they to the potential host, the humans or the animal host, and that is an umbrella term that will include their transmissibility and also their lethality or otherwise. So it's a rather broad term that, in a real-life context, you would break down into what exactly it is that you're -- what aspect of their disease-causing ability is the one that you're interested in.

Q. Thank you.

Now, going back to your instruction, obviously by accepting that instruction you accepted that you required to have a sufficient degree of expertise from the standpoint of a consultant in public health medicine, as you say, in the pathogenicity of COVID-19 and coronaviruses in general.

I would like to just investigate with you briefly, doctor, where that knowledge and expertise has come from.

You've said in your disclaimer at preface page i of your report, at the bottom of the first full paragraph, that you have acted as an adviser in a medicolegal capacity for both sides in a number of legal actions relating to COVID-19.

A. Yes.

Q. Now, again, conscious of confidentiality here, but could you give us some indication of what that has involved?

A. Yes. If you're instructed in a medicolegal action by either party, or jointly instructed, you, as an expert, will write a report addressed to the court, and it's important that you are independent as an expert. So perhaps the wording there might have been phrased slightly differently. So the focus of whatever advice you are giving is in fact the judge or the court as a body, and I was approached a number of times during 2021 onwards to give advice of this kind for civil actions and took on those instructions. And there were other advisory roles that I had taken on as well, which we may come to, where I acted as an independent adviser to, shall we say, established bodies.

Q. And do I take it, by accepting instructions in those

situations ——
A. Yes.
Q. —— you require to inform yourself of in general, as we're talking about COVID—19 and coronaviruses in general, of the pathogenicity of those?
A. Of course, yes. In fact, the first approaches I had were in 2020, I had some very early approaches, and those I declined because I said: well, the knowledge is still evolving, and I wouldn't be in a position really to assist you helpfully, and I might have to revise my position as time went on. So I didn't accept instructions, though I did have some approaches, really until the middle of 2021. By then, I'd also —— we might come on to this —— been advising the General Medical Council on some general matters to do with COVID.
I'd also advised a big insurance company. Insurance companies were caught out by COVID—19 and they had a lot of business interruption claims, which I believe is possibly going to be part of this Inquiry, and one of the big insurance companies came to me —— I don't know how they got my name —— and they said, "Could you do a horizon—scanning exercise for us of all the infectious diseases that there are, and which of them might become a pandemic in the future?" So that was quite a challenge, and they wanted it in two weeks, of course,

but it took me about a month.
So that was helpful in terms of crystallising my thoughts and my knowledge as to every infectious disease, and I came up with a list of about 12 —— top of the list was influenza. I thought influenza is always mutating and potentially could cause a serious epidemic any time. That was amber to red. I had about 10 for 12 amber infections that potentially could cause serious epidemics. One of them was monkey pox, which was interesting, before it came a problem. And then the rest of the infections, I said these are not ever going to cause a pandemic because they are not pathogenic enough. Their pathogenicity is not sufficient that they will ever be a major problem. They will cause minor problems, but there won't be business interruptions on a large scale.
LORD BRAILSFORD: It's approaching 11.30.
MR GALE: Can I just take one more matter, my Lord?
LORD BRAILSFORD: By all means, yes.
MR GALE: It will be fairly brief.
Dr Croft, just to conclude this section and conclude this session, you have provided us with obviously an extensive list of your medical publications.
Could we go to page 93, please.
A. Yes.

Q. Can we look at the last two articles of which you are a co—author with Dr Mawson and Dr Gonzalez—Fernandez.
A. Yes.
Q. There are two there. The first is, "Clues to understanding the pathogenesis of coronavirus infection", and then you give it the COVID—19 and SARS—CoV abbreviation, and then the second is —— again, with the same two co—authors —— "Liver damage and exposure to toxic concentrations of endogenous retinoids in the pathogenesis of COVID—19".
Can you briefly tell us what those were about, beyond the terms that we can read there?
A. Yes. These two papers, which are publicly available, they were —— the first one was published in the BMJ online quite early on in the COVID pandemic, I think it was March 2020, and the second paper was published in a peer—reviewed journal, Viral Immunology, in 2021. But they dealt with a common theme, and that was the proposal that I and my co—authors were putting forward that one aspect of COVID—19 that was puzzling then, and still is puzzling to some extent, could be explained if we consider the disease as being in part an assault on the liver, a virological assault on the liver, such that the liver, which stores retinoids, which are vitamin A precursors, normally in a safe form, the liver becomes

inflamed, and the retinoids, which potentially are toxic, spill into the general circulation and then cause distant systematic effects throughout the body. We simply reviewed the biochemical and clinical literature to explain how we arose at this hypothesis, and we set out various strategies by which the hypothesis could be potentially tested.
Q. The first of your papers, I think, was published in the BMJ; is that right?
A. It was the BMJ online, yes. Because of the peer—review process that we were talking about earlier, which is quite long—winded and laborious, many journals now have an online section where they will publish papers more quickly. They're still subjected to peer review, but that was where that was published.
Q. The second paper is in, I presume, a publication called Viral Immunology.
A. Yes.
Q. Where is that published?
A. I think it's published in America. It's a hard copy paper, but there was also, as is often the case now, a pre—print electronically a few weeks before it became hard copy. But, again, a peer—reviewed journal.
Q. So, against that background, Dr Croft, and going back to the terms of your instruction, are you satisfied that

you have the requisite degree of expertise to inform this Inquiry in the context of what you've been asked to advise on?
A. Yes, I have. I set out my qualifications frankly at the time I was approached and there was a period of consideration, and then the Inquiry team came back to me and appointed me, and I do feel I have those qualities.
The main quality I feel I have which is important is independence from any lobbies or factions, and I wasn't giving advice formally during the pandemic to any government bodies or commercial organisations. So really, like other people, I was really an observer of what was going on, but I hope an educated observer, and a self-educated observer. So I now come to the Inquiry from that standpoint, as a, if you like, qualified public health physician who experienced and studied what was happening, and coming to explain what the general scientific background was to the COVID-19 pandemic.
MR GALE: Thank you very much, Dr Croft.
My Lord, perhaps that's a useful point to stop.
LORD BRAILSFORD: It is indeed. Thank you very much indeed.
Very good, ladies and gentlemen. We will have a break now for 20 minutes, please. We are actually a minute slow. I apologise. If you could be back at 11.51. Thank you.

(11.32 am)
(A short break)
(11.52 am)
LORD BRAILSFORD: Before we start, I'm terribly sorry, but I have an apology to make. I have been informed that I made a mistake in my brief opening remarks. I said that the preliminary hearing on 28th and 29th was in Meadowbank Stadium. I cannot imagine how I made that mistake. I genuinely can't imagine. I have never been in Meadowbank Stadium in my life. It really is in Murrayfield, where I have been on several occasions -- not in a team, I should say, simply to observe.
So the preliminary hearing is in Murrayfield Stadium, my apologies.
Yes, Mr Gale.
MR GALE: Thank you, my Lord.
Dr Croft, having looked at these matters in your background and your qualifications before the break, there is one matter that I would like to raise with you before we go into the substance of your report.
You have been made aware that your engagement as a scene-setter in this Inquiry has been the subject of some recent comment in the press.
Can I first of all refer you to an article which appeared some two weeks ago, and I think you've seen

a copy of this. You don't need to have it in front of you, but if I can just read some passages from it for your comment.
The article is in these terms or contains these terms:
"A doctor commissioned as an expert witness for Scotland's Covid-19 Inquiry claimed just four years ago that routine childhood vaccinations 'could be contributing to increasing rates of autism'."
Then it is said that -- and again, I'm quoting from the press report:
"Medics have expressed concern that Dr Croft was still referencing the vaccine-link claim, which has been widely debunked and led to its originator being struck off."
I think that's a reference to Dr Andrew Wakefield, who has been struck off.
A. I presume so, yes.
Q. The article goes on to say.
"A recent paper, by Dr Croft, published in 2019 - 'Rubella Virus Infection, the Congenital Rubella Syndrome and the Link to Autism' - includes claims that rapid increases in autism coincided with the expansion of the vaccination schedule."
And it goes on:

"Two more papers published by Dr Croft and a co-author, Anthony Mawson from Jackson State University in the USA, also include claims about an increased risk of autism in vaccinated children.
"Claims of a link between the MMR vaccine and autism were initially promoted by Andrew Wakefield, a doctor who was subsequently found guilty of fraud and serious professional misconduct.
"Wakefield was struck off the medical register by the General Medical Council in 2010."
So that's really the context that I would like to ask you some questions.
Could we go to your list of papers, and I think we can see on page 93 of your CV that the paper that is in fact referred to in the press article is the fifth article from the bottom of that particular section and is, as is said:
"Rubella virus, the congenital rubella syndrome, and the link to autism."
A. Yes.
Q. That appears to have been published in something called the IJERPH. What is that publication?
A. Yes, I have a copy of the paper here.
Q. Yes.
A. And that stands for the International Journal of

Environmental Research and Public Health, 2019.
Q. Is that an American Journal?
A. I don't know whether it's American or not. It's not clear from the ——
Q. Do you know ——
A. Beg your pardon: "Licensee: MDPI Basel, Switzerland", so it seems to be a Swiss journal.
Q. Does that have, so far as you're aware, any particular status in the field of public medicine?
A. I believe it has, yes. It's a peer—reviewed journal. The publications of the journal are available online, which is always a good thing, because it means that they're being transparent in what they publish. My own journal, Human Parasitology, was one of the first online journals in this field. So it's one with credibility and authority.
Q. Right.
Now, can you just tell us, in as brief terms as is possible, what that article was about?
A. It was on the same lines —— it was developing the same theme, exploring the same theme, that I've brought up earlier in regard to my two coronavirus articles.
It might be best if I read the abstract, or part of the abstract. Would that be all right?
Q. That would be very helpful, yes, if you would.

A. That way I couldn't be said to be misremembering it or getting key ——
Q. That would be very helpful.
A. Yes. So I happen to have it here. I don't carry it around with me all the time, but I've got it here because I thought I might be asked about it.
So the article is called "Rubella Virus Infection, the Congenital Rubella Syndrome, and the Link to Autism", and the authors are Anthony R Mawson and Ashley M Croft.
The abstract is quite short, about half a page, but I'll read it all. If there's anything that you want clarifying, I would be happy to do so.
The paper, by the way, is very long. It's 28 pages and there are 198 citations. So it's not an easy read, even for me. But the abstract is short.
Q. Before you do, doctor, was that paper peer reviewed?
A. Of course, yes. Yes, certainly, yes. Yes. Yes. Yes.
Q. Please continue.
A. Okay. So abstract:
"Rubella is a systemic infection that is usually mild. It can, however, cause severe birth defects known as the congenital rubella syndrome ... when infection occurs early in pregnancy."
I should say at this point, I have perhaps

a conflict here, in that my own brother, my youngest brother, had congenital rubella syndrome. He was born in 1963, and he must have acquired rubella in utero from my mother in 1962, when she was carrying him. So he was born with this syndrome which I'll go on to discuss, and he had some of the disabilities that we talk about in this paper.
Q. I mean, I don't wish to pry into your personal background and familiar background. Could you just tell us what the symptoms that your brother had?
A. Indeed, yes. Okay. Right. Oh, he had deafness, and he had locomotive problems, so he was in and out of orthopaedic hospitals as a child.
With hindsight, because he's now dead, he had many endearing qualities, but he probably had a degree of autism, I think, because he didn't go to university —— he went to school and got some O Levels —— he didn't ever marry, and he didn't hold down a job for any length of time. Towards the end of his life, he was effectively the carer to my parents, who both predeceased him. So that was his case.
Q. Sorry, I have interrupted you. Carry on.
A. Not at all.
So this is the next bit:
"As many as –8%13% of children with [congenital

rubella syndrome] developed autism during the rubella epidemic of the 1960s compared to the background rate of about 1 new case of autism per 5000 children. Rubella infection and [congenital rubella syndrome] are now rare [and that's because of vaccination, which is good] in the U.S. and in Europe due to widespread vaccination. However, autism rates have risen dramatically in recent decades to about 3% of children today, with many cases appearing after a period of normal development ('regressive autism'). Evidence is reviewed here [in this paper] suggesting that the signs and symptoms of rubella may be due to alterations in the hepatic metabolism of vitamin A (retinoids) ..."
That's what I and my co—authors were talking about also with regard to coronavirus:
"... precipitated by the acute phase of the infection. The infection [rubella] causes mild liver dysfunction and the spillage of stored vitamin A compounds into the circulation, resulting in an endogenous form of hypervitaminosis A. Given that vitamin A is a known teratogen [that means it can cause foetal malformations under certain conditions], it is suggested that rubella infection occurring in the early weeks of pregnancy causes CRS through maternal liver dysfunction and exposure of the developing fetus to

excessive vitamin A."

That's the basis of our hypothesis:

"On this view, the multiple manifestations of [congenital rubella syndrome] and associated autism represent endogenous forms of hypervitaminosis A. It is further proposed that regressive autism results primarily from post-natal influences of a liver-damaging nature and exposure to excess vitamin A, inducing CRS-like features as a function of vitamin A toxicity, but without the associated dysmorphogenesis [the physical abnormalities that occur]. A number of environmental factors are discussed that may plausibly be candidates for this role, and suggestions are offered for testing the model. The model also suggests a number of measures that may be effective both in reducing the risk of fetal [congenital rubella syndrome] in women who acquire rubella in their first trimester and in reversing or minimizing regressive autism among children in whom the diagnosis is suspected or confirmed."

That's the end of the extract.

Q. Thank you.

Now, you mentioned, in connection with that article, the word "hypothesis".

A. Yes.

Q. I think you have discussed in discussions that we've had

the concept of a hypothesis paper.

A. Yes.

Q. Will you just explain what that is, again for those of us who aren't as familiar with these papers as you are?

A. Yes. "Hypothesis", again, is a Greek word. It means an idea, an abstract idea, that potentially can be tested experimentally or through other laboratory methods and may or may not turn out to be correct, or part of it may turn out to be correct, and it's a very common sort of paper in medical science. There are entire journals that are called a journal of medical hypothesis, and in those journals scientists will put forward ideas, often of a revolutionary nature, and often wrong in fact. But, nevertheless, they explore various ways by which observable medical or physiological events plausibly could be explained biochemically or through what's known about the normal bodily functions.

So it's a kind of blue-sky thinking sort of paper, which is rather long, but we had to -- or, as will be usual with a hypothesis paper, explain every link in the reasoning through reference to existing research that would support the hypothesis, and it's customary -- it's normal with a hypothesis paper to end by saying: this is the hypothesis, and this is how it could be tested, and

if it was tested and found to be true, this would be the implications for clinical practice.

Q. Now, looking back to what I quoted to you from the newspaper article, on one reading --

A. Yes.

Q. -- there may appear to be within that article a suggestion that you are a fellow traveller of Dr Wakefield in relation to, as it said, his widely debunked theory which led to his being struck off; are you?

A. Not at all. No, I have never met Andrew Wakefield, who was a gastroenterologist, and his theory, I accept, has been debunked and has no credence.

Q. Can I just pause again. Can I go back to page 90 of your CV.

A. Yes.

Q. Because I think you've written on rubella before.

A. Yes.

Q. And I think if we look just about halfway down --

A. Yes.

Q. -- you are the co-author, with Adams, Winfield and Richards, again, obviously a paper written with your military experience --

A. Yes.

Q. -- called, "An outbreak of rubella in British troops in

Bosnia", and I assume that's Epidemiological Infection. Again, is that another academic journal?

A. Epidemiology and Infection.

Q. Can you just give us a little background to that?

A. Yes. Again, I've got the paper here. But in 1996, the year before, I was in Bosnia, having been sent there at very short notice, and I was there for about seven months. In April of that year, a soldier who was in the army air corps developed rubella. This was before -- no, I'm sorry, there was MMR vaccination at that time. So he developed rubella. He obviously hadn't been immunised against rubella at any time because he was 24, I think. And this was of grave concern, because the period of deployment for the army was usually six months, and in the middle of it you would go back to wherever you came from, Germany or Britain, to be with your spouse or girlfriend, and potentially, if soldiers were acquiring rubella in Bosnia through living in close confined quarters, as they were, then there was a potential for them to go back and infect their spouse or partner, who might have been in the early stages of pregnancy, and then she would then potentially be at risk of congenital rubella syndrome.

Q. Yes.

A. Had she not been vaccinated against rubella, that was the key thing. And there had in fact been a case like this in the German army, where a German soldier had gone back and exactly that had happened. I think the spouse there had been vaccinated, but she hadn't mounted an immune response, so they had a second child who had congenital rubella syndrome. So this was a matter of concern.

So the paper just describes what mitigation measures we took as epidemiologists, and I had to go round the various sort of camps where the army air corps were. We anticipated there would be more cases coming up, and we tried to do a proactive case finding of the cases and then isolate them in Bosnia until their rubella had cleared up before allowing them to go back home.

We made recommendations for the future as to how to prevent this possible scenario of soldiers acquiring rubella on deployment or on exercise and then going back and infecting their spouses, one of the recommendations including MMR for all troops, MMR for all recruits, regardless of previous vaccination status. That, in fact, the very last phrase of that sentence, we say -- and in fact, the Canadian forces were doing that at this time. All their recruits, men and women, were all given MMR, even though -- really to protect against congenital

rubella system. MMR stands for measles, mumps and rubella. And even though for adults it's a mild condition, the danger is if the mother develops the condition in the first trimester of pregnancy.

So our last sentence in this paper, Adams and Croft et al:

"Alternatively, military planners could choose to act now by adopting the Canadian strategy of administering MMR vaccine to all recruits regardless of any history of previous vaccination."

Q. That approach that you've referred to in your 1997 paper, is that an approach that you repeated in your most recent paper that has been referenced in the press article?

A. The general idea is the liver being damaged by external factors and then spilling over the retinoids into the circulation was at the heart of the papers. But the recent papers didn't mention vaccination, as far as I can recall.

Q. Did you in fact say, looking at what you actually said in that article, in that paper, that the proven primary prevention strategy for congenital rubella syndrome is and will continue to be the vaccination of young women?

A. We did say that, and that's obviously correct.

Q. Right.

Can we move on, doctor, and can we go to finally, you will be pleased to know, the substance of your report.

A. Oh, good.

Q. If we go to page 2 at part 1 of your report, this is headed "Evidence-based medicine". We will look at this in a little more detail but, as a principle, is this a principle which you, as a public health physician and an epidemiologist, regard as particularly significant?

A. Yes, evidence-based medicine is the underlying philosophy, operating principle, of medical practice throughout the world.

Q. I think within your report you begin with a discussion of evidence-based medicine, and then you go on to certain aspects of evidence-based medicine.

A. Yes.

Q. So can I just ask you to read through, just to begin with, section 1.1, please.

A. Yes. Would you like me to read the whole section?

Q. Yes, if you would.

A. So section 1.1 -- and, of course, here I'm citing from standard textbooks, so none of this is my own opinion; I'm simply setting the scene for the Inquiry, and I'm conveying the accepted, undisputed principles of evidence-based medicine as understood everywhere.

So:

"Evidence-based medicine (EBM) derives from the understanding that there exists a hierarchy of scientific evidence. All clinical and medical policy decisions should be based on the best available research evidence."

And there's a reference to a very short paper by Torpy of one page:

"Contrary to popular belief, not all scientific evidence is of equal merit. Many scientific studies are prone to bias (e.g. commercial bias ...)"

Bias means sort of incorrect influences coming to bear on the results which might transform those results in a negative way. That's what bias is in a nutshell:

"Some scientific evidence is more reliable than other evidence. Many studies, and perhaps the majority, incorporate 'findings' that are false."

And there's another reference there:

"EBM [evidence-based medicine] denotes the principle, now accepted by all modern medical practitioners, that clinical practice and health policy decisions should be informed by high-quality research into the benefits and harms of healthcare interventions, rather than be informed by low-quality studies, theoretical speculation, expert committee reports or

anecdote.

"While the concept of EBM is simple, an obstacle to its implementation in clinical practice is the uncontrolled explosion that has occurred in scientific data. Over 30,000 biomedical journals are currently in circulation, and over 17,000 biomedical books are published annually. As long ago as 1992 it was calculated that a physician would have to read approximately 11 scientific articles per day to maintain their scientific currency; the challenge now is exponentially greater."

Just as an aside, I understand during the COVID pandemic 2 million scientific articles were written about COVID. No one could read 2 million scientific articles, so we have to focus on the ones that are the most credible, give the best results, the most reliable ——

Q. Can you just pause there and look at two of the papers that you refer to.

Could we look at Torpy ——

A. Yes.

Q. —— which is paper number 20 in the bundle, and it's at page 950.

A. Yes.

Q. I think this is a single page ——

A. Yes.

Q. —— from a publication called —— assuming one takes the letters together —— JAMA, a patient page; is that correct?

A. Yes, JAMA is the Journal of the American Medical Association, and it's the number 2 most prestigious journal in the United States.

MR GALE: Thank you.

LORD BRAILSFORD: New England Journal of Medicine being the most ——

A. Yes, quite right. The New England Journal of Medicine resisted evidence—based medicine for a few years, funnily enough, but they are now on board.

MR GALE: Right.

Again, if we can just look at what's said there, I think we can see the author is Dr Janet Torpy.

A. Yes.

Q. And interestingly, perhaps, in the block on the right—hand side of that page, there is a statement, "For more information", and the second of those is the Cochrane Collaboration.

A. Yes.

Q. Also, I think we can tell, perhaps, from the wording of what is on that page, this is directed towards practitioners ——

A. Yes.

Q. —— largely.

A. Well, JAMA, at that time —— recently they've stopped, unfortunately —— towards the end of every —— the journal comes out every week, and the last few pages there would be a page that would be for your patients, and it would talk about prostate cancer or pneumonia or whatever it was, and the idea was that you would keep these in a file on your desk, and if a patient came in who had prostate cancer, you would give them this information page and there are websites there they could follow.

So it was primarily directed to patients, but the initial reader would be doctors.

Q. And hence the red stamp at the bottom of the page ——

A. Yes.

Q. —— "JAMA copy for your patients".

A. Yes.

Q. Would you just read through the first paragraph and then the second paragraph of "Looking for evidence", so we just have that in the notes.

A. "Looking for evidence"?

Q. No, sorry, start at the beginning.

A. Oh.

Q. Under the block heading "Evidence—Based Medicine", "In the 1990s". If you just read that paragraph and then

the next paragraph of "Looking for evidence".

A. Of course:

"In the 1990s, evidence—based medicine [which is in bold print] emerged as way to improve and evaluate patient care. It involves combining the best research evidence with the patient's values [very important] to make decisions about medical care. Looking at all available medical studies and literature that pertain to an individual patient or a group of patients helps doctors to properly diagnose illnesses, to choose the best testing plan, and to select the best treatments and methods of disease prevention. Using evidence—based medicine techniques for large groups of patients with the same illness, doctors can develop practice guidelines for evaluation and treatment of particular conditions. In addition to improving treatment, such guidelines can help individual physicians and institutions measure their performance and identify areas for further study and improvement."

Then it says this article is:

"... about the importance of using evidence—based medicine to develop practice guidelines."

And there seems to be a condensation of a larger article published a few years earlier in JAMA, in 2006. This is distilled into one page.

Q. Yes. Then the next paragraph.
A. Yes. So it's "Looking for evidence in medical literature". It talks about -- so it says:
"Systematic reviews of the medical literature, large randomized controlled trials (the best way to assess the efficacy of a treatment), and large prospective studies (followed up over time) are types of research published in the medical literature that can be helpful in providing evidence about tests and treatments. Reports of the experiences of individual patients or small groups usually provide less reliable evidence, although they may provide important clues about possible adverse effects of treatments.
"Using evidence-based medicine.
"Practice guidelines developed using evidence-based medicine have helped to reduce mortality (chance of dying) from heart attacks. Evidence-based medicine guidelines have also improved care for persons with diabetes and other common medical problems.
Evidence-based medicine does not replace physicians' judgment based on clinical experience. Any recommendations taken from evidence-based medicine must be applied by a physician to the unique situation of an individual patient. Sometimes there is no reliable research evidence to guide decision making, and some

conditions are rare enough that there is no way to do large studies."
Q. I think I can stop you there, doctor.
Just one phrase that I think we can see there and which we haven't, I don't think, looked at a definition of is "systematic review". I think you will find a definition of that in your appendix 3 at page 103.
A. Yes.
Q. And I think, to save you looking at it, it's:
"A type of scientific study which summarises the existing research in a particular area in a comprehensive and impartial way; known as 'evidence synthesis' or 'meta-analysis'."
A. Yes.
Q. Right.
Passing on from the reference to Torpy, could we go to the reference to the paper by Ioannidis, which is number 10 in the bundle. It's at pages 806 and 807. It begins, I'm sorry, at page 802.
It's under the headline, if I can put it that way, "Why Most Published Research Findings Are False" --
A. Yes.
Q. -- which might send most people into a spiral of concern.
Can you just explain what -- I think it's now

Professor Ioannidis, who I think is now attached to Stanford University in the States.
A. Yes.
Q. I think at the time of writing he was attached to Tufts New England Medical Center. You find that in the footnote on the first page.
Could you just read out the summary, please?
A. Yes. This is a summary of Professor John Ioannidis' paper and he says:
"There is increasing concern that most current published research findings are false. The probability that a research claim is true may depend on study power [that essentially means the size of the study] and bias [we mentioned bias], the number of other studies on the same question, and, importantly, the ratio of true to no relationships among the relationships probed in each scientific field. In this framework, a research finding is less likely to be true when the studies conducted in a field are smaller; when effect sizes are smaller; when there is a greater number and lesser preselection of tested relationships; where there is greater flexibility in designs, definitions, outcomes, and analytical modes; when there is greater financial and other interest and prejudice; and when more teams are involved in a scientific field in chase of statistical significance.

Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true. Moreover, for many current scientific fields, claimed research findings may often be simply accurate measures of the prevailing bias. In this essay, I discuss the implications of these problems for the conduct and interpretation of research."
MR GALE: So what do you take from that?
LORD BRAILSFORD: Do you happen to know what Professor Ioannidis' academic background is? Is he a statistician, a mathematician?
A. Oh, he's an epidemiologist.
LORD BRAILSFORD: He's an epidemiologist, is he?
A. Well, I presume he is because he writes from the Department of Hygiene and Epidemiology at the University of Ioannina, Greece, and then later on he's moved to the United States.
LORD BRAILSFORD: Sorry to interrupt you.
MR GALE: Dr Croft, what do you take from that?
A. Well, of course, this needs to be interpreted carefully because he's not saying research mustn't be done. He's focusing really on pure biomedical research, which is exploring entirely new areas, new concepts, and he makes that clear further on. Further on in the paper he does talk about randomised controlled trials as being the

type of research that is most likely to yield accurate results.

But it's really pure and investigative research that is the real focus of what he's exploring there, and this was written when sort of molecular medicine was in its infancy, and the idea of that is you explore thousands or millions of hypotheses connecting a particular gene to a particular disease or a particular aspect of disease, and essentially what he's saying is that if you were exploring on a massive scale, on an industrial scale, you will find apparent associations that are actually not true but have just arisen by chance. That is his key message, as I understand it.

Q. I think if you go to pages 806 and 807 of that document, I think we can see on the right-hand column of 806 a section headed "How Can We Improve the Situation?"

A. Yes.

Q. And perhaps you would just read the -- well, perhaps read until I ask you to stop, is probably the best thing.

A. Okay:

"How Can We Improve the Situation?

"Is it unavoidable that most research findings are false, or can we improve the situation? A major problem is that it is impossible to know with 100% certainty

what the truth is in any research question. In this regard, the pure 'gold' standard is unattainable. However, there are several approaches to improve the post-study probability."

That is the mathematical concept he discusses earlier:

"Better powered evidence, e.g., large studies or low-bias meta-analyses, may help, as it comes closer to the unknown 'gold' standard. However, large studies may still have biases and these should be acknowledged and avoided. Moreover, large-scale evidence is impossible to obtain for all of the millions and trillions of research questions posed in current research. Large-scale evidence should be targeted for research questions where the pre-study probability is already considerably high, so that a significant research finding will lead to a post-test probability that would be considered quite definitive. Large-scale evidence is also particularly indicated when it can test major concepts rather than narrow, specific questions."

Q. Can I just stop you there, doctor, and then can I ask you to read on at the bottom of that column, the paragraph that begins "Second"?

A. So:

"Second, most research questions are addressed by

many teams, and it is misleading to emphasize the statistically significant findings of any single team. What matters is the totality of the evidence. Diminishing bias through enhanced research standards and curtailing of prejudices may also help."

Q. Can I stop you there. I think that's probably all I need to ask you about there, unless there's anything further that you would wish to draw to our attention?

A. Just at the very bottom of that section, he says:

"... in other fields, the principles of developing and adhering to a protocol could be more widely borrowed from randomized controlled trials."

Randomised controlled trials, you normally define what you're going to do before you do it and you don't start changing what it is you're measuring because of what's emerging. That's part of the rigour of randomised controlled trials.

Q. So the idea is to have a defined protocol before you start?

A. Yes, and not move the goalposts as you proceed.

Q. Exactly. Right, thank you for that.

Can we go back now to your report. Can we go to the top of page 3 and paragraph 1.2, and would you read on there.

There is in that page a table taken from a standard

textbook for medical students which is referenced at the bottom, I think it's the -- yes, it's the bottom, "Good medical practice" textbook, and we will look at that table perhaps in some detail in a moment, but if you just read through what you say in 1.2.

A. I'll just wait for the screen to change.

(Pause)

Shall I start reading, my Lord? 1.2:

"What are systematic reviews?"

Thank you:

"A pragmatic solution is the systematic review (also known as an evidence synthesis or meta-analysis). Systematic reviews are a relative new form of research. Their aim is to present a balanced and impartial summary of the existing research, enabling decisions on effectiveness to be based on all relevant studies of adequate quality.

"The systematic review has established itself at the highest level of evidence in the [evidence-based medicine] hierarchy because it summarises the available evidence on a particular topic, in a comprehensive and up-to-date manner. Properly-conducted systematic reviews constitute Level Ia evidence. The bottom rung in the EBM hierarchy is Level IV evidence, obtained from expert committees, authoritative opinions and the like.

This is demonstrated in the table below, [which is] taken from a standard textbook for medical students."

Q. Could we just look at that table. As you say in your text, the gold standard is Ia, and we see that as:

"Evidence obtained from meta-analysis of randomised clinical trials."

A. Yes.

Q. And there are then various intermediate standards, if I can put it that way --

A. Yes.

Q. -- down to Level IV, which is, as you've said:

"Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities."

Now, that might seem slightly counter-intuitive. Those qualifications, expert committee reports, clinical experiences of respected authorities, might suggest that they are worthy of a higher ranking than the lowest ranking that is given in that category. Can you explain why that is?

A. Well, it's a paradox because often the randomised controlled trial might be being done by some junior registrar and it's producing a surprising result that the respected authorities, the senior consultants, may choose to disagree with.

But the point of the hierarchy is that the traditional way of developing medical decisions was often for, in a hospital setting, for example, the senior consultants to sit around and agree between themselves as to what was the best surgical approach to appendicitis or the best antibiotic to give osteomyelitis, shall we say. And that kind of approach -- by the way, it's sometimes called in the medical literature the GOBSAT approach. GOBSAT, G-O-B-S-A-T, means "good old boys sitting around a table". It's a bit --

Q. Probably a relief it wasn't something else.

A. But it's a recognised term, and obviously it sounds -- you know, they must know what they're talking about because they're professors and they're senior consultants. But in reality biases can creep in, not only of a financial nature, but just of a chance nature. You know, the senior professor might just happen to have used a particular antibiotic on five not very sick patients because he didn't get the very sick patients, he gave them to the juniors, and so this antibiotic just worked well for him but that was chance.

So this is what the concept of evidence-based medicine is trying to disentangle: the authoritative opinions that come from experience, but are liable -- often very strongly liable -- to be influenced by factors of bias coming from various directions.

Q. By according that the lowest level in that table, is that suggestive that one ignores it?

A. No, and when there is no good quality Level Ia or Level Ib evidence, or Level II or III, that would be a reasonable starting point. But at the same time it would be necessary to qualify very carefully any interpretations that one could put on the weight of evidence that's coming from that kind of source. It would need to be managed in a very prudent way with a lot of caveats.

Q. And those levels are then translated into grades of recommendation at the bottom of the table --

A. Yes.

Q. -- which simply follow the levels of evidence themselves.

A. That's right. And nowadays, with clinical guidelines, of which there's a vast number, the best guidelines will say: if a patient presents with these series of symptoms, consider doing this test, and then they will put in brackets "Grade A" or "Grade B", and that will indicate the kind of strength of the recommendation based on this hierarchy, and so therefore being explicit about the nature of the advice that's being given to

those who will be reading the guidelines. That's often called the grade approach to evidence. The two terms are interchangeable.

Q. Right.

Can we pass on to page 4 and paragraph 1.3, which is in relation to randomised controlled trials.

Now, to a certain extent we've looked at this a little in what you've already been telling us, but just so that we again have it in the note, can you read through 1.3, please.

A. "1.3 What are randomised controlled trials?

"Systematic reviews seek evidence of benefit from randomised controlled trials (RCTs).

"In an RCT, participants are allocated randomly either to the treatment (or intervention) of interest, or to the existing standard treatment, or to a placebo. The purpose of randomisation in [randomised controlled trials] is to minimise bias and confounding. In order to minimise patient bias, the participants are unaware of their treatment allocation; this is termed a single-blind RCT."

Some of the vaccine trials look at single-blind RCTs because if the doctors knew -- so:

"In order to minimise doctor bias, treatment allocations are also withheld from investigators; this

then is termed a double−blind RCT. To recruit sufficient numbers of patients, and to examine the effects of treatments in different settings, it may be necessary to conduct the trial at several locations; this is termed a multicentre RCT."

Or sometimes it's called an international RCT:

"To determine the reliability of a particular [randomised controlled trial], a number of features in the study design need to be assessed. To ensure that there is no selection bias, the process of randomisation must be seen to be robust."

So it's easy for authors to say, "We randomised patients to receive the drug or the placebo", but they have got to be more specific. They have got to say how did they do it, because often investigators, they don't really know how to do randomisation. But there are correct approved and non−approved ways of doing it. It must be done in a proper way, because randomisation is really the key to why randomised controlled trials (inaudible).

And then blindness of allocations means that the person doesn't know whether they are on drug A or drug B, and that should be imposed rigorously at the start of the randomised controlled trial, and it ideally should be maintained throughout this study, especially

if a subjective outcome is being measured, such as relief of pain or alleviation of depression:

"All the patients enrolled into a trial should be properly accounted for, at its conclusion. Finally, the trial must be reported adequately − and as a minimum, it should include a flow chart ..."

Also called a trial profile, there should be a flow chart which has various arrows coming out of it:

"... depicting the progress of participants through the trial.

And I finish here by saying:

"The need to report [randomised controlled trials] accurately was recognised in the mid−nineties and has been reiterated many times since then."

Q. I think the paper that you refer to as Altman, that is the first paper in the bundle, and it's at pages 1 to 2. Sorry, it's not −− it's at pages 3 to 4.

A. Yes.

Q. And I think it's an entitled "Better reporting of randomised controlled trials: the CONSORT statement".

What does one attach to the CONSORT statement?

A. The CONSORT statement was a statement put out by clinicians and epidemiologists and statisticians around about this time, and it was published in various journals, including the British Medical Journal, the

Lancet, JAMA. It wasn't published at that time in the New England Journal, because they were resisting evidence−based medicine, but eventually they came around.

Douglas Altman, who is a statistician, who used to write beautiful little articles in the British Medical Journal of half a page on medical statistics every few issues, he was a great proponent of evidence−based medicine. One of the founders of the Cochrane Collaboration. I don't know him personally, but I went to some of his workshops.

So what he's saying is that not only must the randomised controlled trials −− this is what we want, we want RCTs because they are the best form of evidence, but not only must they be designed correctly, they must also be reported fully and accurately. That's essentially what he's saying there.

And really −−

Q. I think if one is interested, one really −− I don't need you to read through it, but one finds that in the first paragraph and the beginning of the second paragraph in his paper.

A. Yes. Could I just read out one sentence?

Q. Yes, please.

A. Key sentence. This is his starting point, and it's

indisputable. This is 1996. It's even more indisputable now than it was then:

"Only randomised trials allow valid inferences of cause and effect. Only randomised trials have the potential directly to affect patient care ..."

So only from randomised trials can we have valid inferences of cause and effect.

Q. So that's the second sentence in the first paragraph of that paper.

A. Of course. But he goes on to say there still could be bias in them.

Q. Yes.

Right, can we then move on to section 1.4, "Pooling scientific evidence". There's again a reference to Altman there, but could you read through what you say there, please.

A. So section 1.4, "Pooling scientific evidence". So pooling means merging scientific evidence, really means merging numbers to get a slightly better number. So:

"In recent years, systematic reviews have sought to pool evidence from RCTs. This is done through meta−analysis, which is a statistical method that quantitatively summarises the systematic review findings ... Unpublished trials should ideally be identified and included in the meta−analysis to avoid publication bias

(i.e. non-inclusion of 'negative' trials that are less likely to have been published ...)"

So when you do a systematic review, you not only try and find all the papers that have been in print, but also the ones that never saw the light of day because the journals rejected them or the authors got discouraged because they weren't showing what they expected, and that's all relevant evidence if it is a randomised controlled trial.

"Meta-analysis results in a pooled estimate of effectiveness which is more precise than the effect estimates from the individual [randomised controlled trials]. This is because the pooled estimate is based on a larger number of participants, and hence is less liable to random error.

"... [some] systematic reviews also assess non-[randomised controlled trial] evidence; these additional sources of evidence include qualitative research, animal studies and modelling."

But the core of the symptomatic review will be randomised controlled trials, and the review:

"... should systematically identify and evaluate (i.e. through an explicit and prespecified and well-validated methodology) all appropriately-designed studies that address the clinical question being

considered. Where appropriate, the results of these included studies should be combined.

"To be fully valid, a systematic review must satisfy a minimum of three criteria:

"i. It must try to identify all relevant studies [the published ones and the unpublished ones].

"ii. It must assess the quality of the included studies [because some randomised controlled trials are better than others].

"iii. It must try to combine the study results [through meta-analysis], as long as it is reasonable to do so."

Q. Right. Against that background, you go on to the Cochrane reviews.

A. Yes.

Q. Can we just start a little about the Cochrane reviews. I think we will need to pause because there are various matters that I need to look at in some detail with you --

A. Yes.

Q. -- in relation to Cochrane reviews, but perhaps you can just read on to page 6 of your report, please.

A. So:

"A Cochrane review is a systematic review that uses methodology that has been tested and refined over three

decades by the Cochrane Collaboration. [These] reviews are prepared and maintained, usually on a pro bono basis [pro bono meaning the reviewers just volunteer, they're not paid], by members of the collaboration working in small teams; in 1993 the active members of the Cochrane Collaboration numbered less than 100, but by early 2016 this number had grown to over 30,000 reviewers in more than 100 countries."

Q. Just pausing there, am I right in thinking that you are a Cochrane reviewer?

A. Yes, I am, yes. I have written five or six Cochrane reviews. Yes, I'm a reviewer in various fields, infectious diseases but also airways and guts, the gut field. So I have been involved in different branches of the organisation, yes.

Q. Did I pick you up right by you saying that you've been a reviewer in relation to airways?

A. Yes, I wrote a Cochrane review that was to do with -- exploring the same idea we had earlier about helminths treatment for allergic rhinitis.

Q. Oh.

A. Actually, that was done under the auspices of airways. We prepared another review that was looking at helminths treatment for asthma.

Q. All right.

If you just carry on, doctor.

A. Yes. So:

"Historically, the focus ... has been on quantitative data, with study results combined using [a software program called] Revman ... Since 2003, the quality of included studies [randomised controlled trials] ... has been assessed through the Cochrane risk of bias tool; this automatically grades each included study into a High risk of bias, Low risk of bias or Unclear risk of bias category, and [that then] allows [the reviewers to do] a reliable appraisal of the overall robustness or otherwise of the accumulated evidence."

So if the accumulated summary evidence is based on not very reliable randomised controlled trials, they will place less confidence in that particular outcome, whereas if it's based on very low bias studies, they will have more confidence in the outcome.

Then:

"An important feature of Cochrane reviews is that they are published electronically in the Cochrane Library, and ... clinicians, policymakers and researchers [can access them]. In most countries [including Britain] ... [they] can be downloaded free of charge."

That's because the costs of the Cochrane Collaboration's overheads are met in part by the Department of Health, or the Department of Education. But there's a lot of government funding to support Cochrane reviewing in this country, and most countries. Not all countries, but most countries:

"For better accessibility, every Cochrane review since 2001 has included [what they call] a Plain Language Summary ..."

So it's like an executive summary, a simple one– or two–page ––

Q. A summary to which I automatically go when I'm trying to understand it.

A. Of course, yes. Of course. Because that's actually –– trying to get away from the jargon, that is inevitable in scientific work, and it's trying to say: what does this actually mean in practice to the ordinary consumer of health, which is clearly the end user of these medical interventions? So they're always well worth reading.

In addition, they have the standard abstract, which is introduction, methods, results and conclusions.

"The collaboration has its own press office, which promotes new reviews ..."

And then Cochrane reviewers are –– they are expected

to:

"... update their review as and when there is a substantive new body of evidence ..."

Which means, for many reviews, about every three to five years.

Q. Yes.

A. And that means actually, my Lord, that the reviews that we might be looking at later on, by the time this Inquiry finishes, will probably have been updated. But it's unlikely there will be significant differences, I think, because the time to do randomised controlled trials in a COVID arena was in 2021 and 2022. We are moving to a different phase. So there will be some modifications to opinions, but I wouldn't have thought they would be that significant.

Q. I think, just to conclude, doctor, you refer to three Cochrane reviews: the two Jefferson reviews that we've looked at briefly ––

A. Yes.

Q. –– in 2011 and 2023 ––

A. Yes.

Q. –– and Graña, which is 2022, which relates to vaccines.

A. Vaccines for COVID–19.

MR GALE: I'm sorry, yes, COVID–19.

We will look at those, my Lord, I would suggest

after lunch.

LORD BRAILSFORD: Yes, by all means.

We are a little early. So I had indicated that we should try and come back, or would have indicated we should come back, at 1.45, but could we make it 1.40, given we've got five minutes at this end.

So 1.40, please. Thank you very much.

(12.54 pm)

(The short adjournment)

(1.40 pm)

LORD BRAILSFORD: When you're ready, Mr Gale.

MR GALE: Thank you, my Lord.

Dr Croft, we finished before lunch by looking at Cochrane reviews, the three that you have produced for our consideration: the two by Jefferson and the Graña review.

I would like to ask you a little bit about the approach that one takes to those reviews, and can we do this under reference to appendix 4 to your report, which is at page 105 and 106.

A. Yes.

Q. I think here you get into what are for most of us probably the dreaded statistics and analysis of that nature.

A. Yes.

Q. Can we just look at what you set out there. You look at, I think, three concepts: odds ratios, risk ratios and confidence intervals.

To begin with, can you explain and read what is meant by odds and odds ratios?

A. Yes. So all of these terms are used regularly in statistical analysis which is, as I was explaining, the process by which you analyse the numbers that have derived from your studies, and they're common terms used by all investigators everywhere.

So, first of all:

"What is meant by odds and odds ratio?

"Odds and odds ratio are effect measures which are commonly used in the statistical analysis of research ...

"[For a particular group] The odds for a particular group is defined as the number of patients in the group who achieve the stated end point, divided by the number of patients who do not."

So there's an example here:

"... the odds of acne resolution during treatment with an antibiotic in a group of 10 patients may be 6 to 4 (6 with resolution of acne divided by 4 without = 1.5); in a control group the odds may be 3 to 7 (0.43).

"The odds ratio ... is the ratio of two odds."

And those are the figures, if you're going to try and summarise statistics from different studies, you will use, and the odds ratio is just a ratio of the odds of the treatment group to the odds of the control group. So in this case the odds ratio would be 3.5, so that's 1.5 divided by 0.43. It's actually 3.488, but 3.5 for practical purposes.

So if you have a study where you end up with an odds ratio of 1, that means there's no effect. What's happened in the treatment group, the intervention group, is really the same as the comparator group.

People who are gamblers understand these terms instinctively, I'm told. But most of us struggle. But there is a logic to it.

Q. I am glad you say that.

A. Yes. Okay.

So relative risk is -- risk and relative risk and risk ratio. Risk ratio is equivalent to relative risk. It's approaching the same goal by slightly different means. They are also used by researchers. Risk is slightly different to odds. So it's the number of patients who achieve the stated endpoint, divided by the total number of patients.

So in the first example, the risk -- those who achieve the stated endpoint, who got better with the

antibiotic, would be 6 out of 10, so the risk is 0.6. You could think of risk, in a way, as: what is the likelihood of achieving it? What is the absolute likelihood? So the likelihood of achieving it is 0.6, which is you've got a 60% likelihood that you will get better with the antibiotic, whereas those in the control group, 3 out of 10 of them got better anyway, so their risk of getting better was 0.3 or 30%. So even if you don't take the antibiotic, there's a 30% chance your acne will get better anyway, so therefore that gives you a risk ratio of 6 divided by 3, which is 2, a relative risk of 2, or risk ratio of 2.

So, again, if you're using this approach to analyse your statistics, if you end up with a relative risk of 1, it means there's no difference between your two groups, and often at that point people are so discouraged by the negative results of their trial that they just don't bother to get it published, which is a shame, because it nevertheless contains important information about the merits or otherwise of that particular intervention.

Q. Can we move on to confidence intervals, please.

A. Yes.

So confidence interval is the next logical step, and the last step that we need to go into here, and that

really means: how much confidence can you put in your findings? By convention, by statistical convention, what you -- well, I'll read it:

"... all studies with a control group, such as randomised controlled trials ... are based [only] on a sample of the population, [not based on the whole] population ... [so] there will always be some uncertainty around the reliability of the effect measures ... [based on the fact that it is just a] sample. The true effect measure may be larger than the estimated effect measure – or ... it may be smaller."

So as well as measuring the odds ratio or the relative risk, nowadays investigators are expected to calculate the parameters within which the true effect measure must lie with a 95% degree of confidence. These parameters are known as the 95% confidence interval. I notice Pfizer call them the 95% credibility interval, which is fine, but it's a new term to me.

So:

"The true effect measure may be higher than [that you've] estimated ... or it may be lower – but there is a 95% chance that [the true measure] will lie somewhere between the upper boundary and the lower boundary of the 95% [confidence intervals]."

Q. Can I stop you there.

A. Sure.

Q. Who came up with the 95% figure?

A. I don't know whether anybody particular came up with it, but there was a time when 99% confidence intervals were much spoken about. But 95% just seems to be a pragmatic measure that is useful in clinical terms.

But you're quite right, Mr Gale, it's arbitrary. It's arbitrary, but it's universal.

Q. It's universal, but arbitrary, and --

A. Exactly.

Q. -- accepted.

A. Oh, absolutely. Absolutely. Every scientific paper will have a 95 -- well, the good ones will have 95% confidence intervals attached to the data. If they can be calculated. It's not always possible to calculate them, but nearly always it is.

Q. Right.

Please continue, just the last paragraph.

A. Yes. So in general, the larger the study -- the larger the randomised controlled trial, the greater the likelihood that your estimated effect measure will be close to the true measure, because you're doing multiple observations in a rigorous and scientific way, whereas if you've only got a very small study, the effect measure you've calculated may actually be inaccurate

because it's based on small numbers.

So for small studies, you have wide confidence intervals, and for larger studies, you have smaller confidence intervals. So you have more and more and more confidence in your finding, in your calculated finding, if either you have done a large randomised controlled trial, or you've done a systematic review combining trials of a similar kind through meta-analysis that gives you a more precise estimate with smaller confidence intervals.

I'll just go through this again, because it's quite complicated.

So let's say you're covered with acne, Mr Gale, and you went to the GP and the GP said, "I've got a really good antibiotic for you, Mr Gale, here it is, it is going to make you better", you could say to him, "Right, what are the odds I will get better?", and the GP would look at the trial on the screen and say, "Right, the odds are 6 to 10 you will get better". So he would say, "Right, okay, the odds -- and so therefore your odds would be 1.5, and that's quite good". But you could say, "What are the odds of my getting better, even if I don't take the antibiotic?" And the GP would have to admit that it was going to be about 0.45, because some people don't take the antibiotic and they get better

anyway.

So you would ask about the -- you would say, "What's the odds ratio, doctor?" So the doctor would say, "Right, okay, 3.5". So you think that was pretty good. And then you might say, "What about the risk? What's the risk? What's the risk I would get better?" You would get a funny look from the GP, but they would say: "Right, okay, the risk" -- so what you mean is what is the likelihood you're going to get better, the absolute likelihood, and they'd say, "The risk is 60%". So your likelihood you're going to get better is 60%. And then you would say, "Right, okay, in the control group, what was the risk that they got better?", and the GP would say, "The risk was 30% of them got better anyway". So then you would say, "Right, okay, so the relative risk is only 2", things aren't looking that good, but still in the same order of magnitude.

So you could then say, "Right, okay, what's the confidence intervals?" And at that point the GP would think, "Who is this crazy lunatic who is asking me this?", but it's a reasonable question to ask, because the confidence you could have in those small numbers wouldn't be that great, so the GP would have to concede there wasn't much confidence. Therefore, they would have backtracked from their original position, which

was, "Here is a really good antibiotic", to saying, "Well, there's some evidence that it will help you, but I don't have much confidence in the results".

So that's why you really need large trials and systematic reviews, and that's what evidence-based medicine is about. We probably ought to use them more in our encounters with clinicians than we do, but we rely on their -- we rely really on them having sifted the evidence for us and arrived at those kind of conclusions.

Q. And perhaps rely on the fact that a patient may not have the level of understanding to ask those questions.

A. Sure, yes. Yes, indeed. And one could say, well, individual patient encounters aren't that important, because of course they are. But by the same token, population-level decisions are very important, and they should really be based on this kind of very careful weighing up of the pros and the cons and the confidence we can have in the scientific evidence behind the apparent measures of effect.

Q. Right.

Can we perhaps look at this in operation.

A. Mm.

Q. As I say, we have three Cochrane reviews, and can we look at just an example from the third of the Cochrane

reviews, at least chronologically, and that is the Jefferson 2023 review, paper 9 in the bundle.

I wonder if we could look at an example that is summarised at page 659.

A. Yes.

Q. It is in the second volume, if anyone is looking at the references in the volumes.

A. Yes.

Q. It's headed "Analysis 6.2".

A. Mm-hm.

Q. The title is, "Comparison 6: Randomised trials: gargling compared to control, Outcome 2: SARS-CoV-2".

A. Yes.

Q. Now, first of all, we can see that there are two trials that are referred to there. One is Almanza-Reyes 2021 --

A. Yes.

Q. -- and the other one is Gutiérrez-García 2022.

A. Mm-hm.

Q. Just so we understand what these are, we can find the Almanza trial at pages 539 to 540.

A. Mm-hm.

Q. Perhaps we could just look at that, so we know what the context is.

Almanza-Reyes 2021 is at the bottom of page 539.

A. Yes.
Q. And we see there the methods:
"[Randomised controlled trial] randomised using a computer−generated block scheme and stratified according to duty position, work shifts and the area/department of the service."
We have to read that in context of what followed on, although I think the follow−up duration is said to be nine weeks; is that right?
A. Yes.
Q. And at the bottom we have a note of participants.
A. Mm−hm.
Q. And it says:
"Workers (doctors, nurses, administrators) in a hospital for the exclusive recruitment of patients diagnosed with COVID−19 'General Tijuana Hospital'."
Moving over, I think we can see that the interventions are then described, including:
"Experimental group: mouthwash and nose rinse."
And then silver mouth wash, details are then given of that, and then mouth spray, and then:
"Control group: instructed to do mouth wash and nose rinse with a conventional mouthwash the way they normally did before the study."
So, essentially −− perhaps you can probably describe

it much better than I can −− what is being compared there?
A. What they call the experimental group are asked to use the sodium −− sorry, silver nanoparticle solution, to mix it up with 20 ml of water and to gargle it for 15 to 30 seconds three times a day. That's, if you like, the treatment that's being tested here. Or, alternatively, they could wash the inner part of their nose with it with a cotton swab twice a day.
So there are two −− basically, the idea seems to be to sterilise their nasal passages and, as we will learn later, the virus that causes COVID−19 is predominantly in the nasopharynx in the early stages. So it's kind of a reasonable thing to do, one would have thought.
The control −− what did the control group do? The control group just do the mouthwash or the nose rinse or both, using a conventional mouthwash the way they normally do it. So they could use Listerine or water or anything that they might normally use as a mouthwash.
Q. And the other trial is the Gutiérrez−García trial, which I think we will find at page 567.
A. Yes.
Q. At the top of 567.
A. Yes.
Q. And it's a:

"Single−blind (analyst) randomised controlled trial carried out in a single centre in Mexico City during September to November 2020. Randomisation was through tokens in opaque envelopes but the trial was open to all except the data analysts. There were some imbalances in age groups post−randomisation at baseline in age and comorbidities."
Can you translate that for us, please?
A. Single−blind means that those who were analysing the data, the statisticians, didn't know what particular arm of the trial the participants belonged to, but the participants weren't blinded themselves because, as might become apparent, it might have been difficult to try and conceal what arm of the trial they were in. But that shouldn't matter as long as the randomisation has been done correctly, and that's what we come on to next, I believe.
Q. Right. I think probably that's sufficient, just looking at those.
Can we go back, please, to page 659.
A. Yes. Yes. So the −−
Q. And just before we do, I think the reason that this has been selected is that it's a two study or group comparator, and frankly it's relatively straightforward.
A. Yes.

Q. At least −−
A. Exactly. It shows striking results.
Q. Yes. So perhaps you can just take us through what is shown on that page.
A. Yes. So this is one of the analyses that the reviewers of this systematic review undertook, and when you do a systematic review, you do sometimes several dozen or even 100 analyses, and you're encouraged to present the most compelling ones in a chart like this, which is called a forest plot. You don't want to have 100 forest plots; you just want the most important ones. So they've chosen this one because they obviously found it of interest.
What they're comparing is gargling compared to control, which in this case was gargling with ordinary water or ordinary solution, and −−
Q. Can I just pause you there. What was the −− I'm putting it this way −− the end product or the aimed−for end product in this? What were they trying to seek to do?
A. They were trying to seek if SARS −− ah, interesting. Well, let's look again. The outcome is whether the people who were gargling were less likely to develop COVID−19, the people who are gargling with the approved solutions, than the control group.
Q. Right.

A. So the outcome was COVID−19 assessed through different methods.
Q. Yes.
A. Some of the trials, the COVID−19 is assessed subjectively by whether people felt they had a new onset cough and loss of smell and taste, but in other trials it was assessed through laboratory measures. We haven't looked exactly to see how, but I think for these two it was assessed by laboratory measures. So it was assessed quite robustly, I believe.
Q. Yes. And what was the outcome?
A. Well, looking at the −− going back to the forest plot, which is on page 659, both of these trials, randomised controlled trials, were carried out in Mexico, it seems, which is interesting, and the numbers are quite large, and the square boxes give an indication of the size, the numbers of participants in the individual trials. The diamond at the bottom indicates the combined effect of the trials.
So the first line −− if I read across it, my Lord. So Almanza−Reyes, that was the one Tijuana City, which is Mexico, I believe. Right. So they were looking at −− what they wanted to find out was: was gargling with this silver nanoparticles solution likely to have fewer people getting COVID−19 as compared to those who

were gargling in the ordinary kind of way? And they had two events with the mouth rinse. I hope you can see that, two events?
Q. Yes.
A. There are 114 people in total, so 2 out of the 114 acquired COVID who were gargling with the silver nanoparticles.
Would you agree with that, Mr Gale?
Q. I'm taking your word for it, Dr Croft. I can see what it says, yes.
A. Well, what about the control group? Remarkably, the control group had 33 cases of COVID−19 out of a total of 117. So the total number of participants was 231, and they'd been randomised into the gargling group and the control group, and the gargling group had very few cases, just 2, compared to 33, a much higher number of cases in the control group there.
So they did the calculations we were just describing now, and they came out with a risk ratio of 0.06. That means −− I think this is right −− you're 94% more likely to get COVID if you're not gargling with a special solution than if you are.
So Gutiérrez−García, who did something similar, but they used a different solution, they were using −− they weren't using silver nanoparticles; they were using

neutral electrolysed water to prevent COVID, and what did the −− the control people must have used something else. It's not clear what the control group −− anyway, the control people weren't using neutral electrolysed water. They were followed up for only two weeks.
They had similar results. Yes, similar results. Slightly smaller numbers, so −− oh, sorry, I should have said −− beg your pardon −− with the first one, Almanza−Reyes, the horizontal line there, my Lord, represents the 95% confidence interval for their calculated risk ratios. So the calculated risk ratio was 0.06, but the 95% confidence that they had in that ratio indicated that the true effect may lie anywhere between 0.02 to 0.25. But the key thing is that the confidence interval doesn't cross the line of no effect. The line of no effect is that central vertical line, which is 1. If it crossed 1, then you would have to say the results suggest there might be an effect from gargling, but it's not statistically significant. But in this case it is statistically significant.
So Gutiérrez−García, the gargling group comprised 84 people, and these were healthcare workers, I believe. Yes, they were frontline healthcare workers, so very highly exposed to COVID. I understand this was carried out in the first half of 2020. So those who were

gargling had only one event where the individual received −− 1 out of 84 acquired COVID, and those who weren't gargling or who weren't using the neutral electrolysed water had 10 events. So they had 10 out of 79.
So the risk ratio there was 0.09, so not quite as good as the other people, the silver seems to be better, and that's plausible because silver seems to have virucidal and antibacterial properties. Nurses use it for silver dressings for burns. They're expensive dressings, but where you don't want any bacteria or viruses, you might use dressings. So their risk ratio wasn't quite as compelling, but nevertheless, there it is: it's 0.09. So the study authors could say that this shows statistically that gargling using this neutral electrolysed water will protect you from COVID within 95% bounds of credibility or probability.
Then the Jefferson −− the review authors have summarised this, have pooled these results, and that's shown by the diamond there, which really gives a more precise measure of effect because the confidence intervals have been narrowed. The two horizontal corners of the diamond indicate the extent of confidence, and so therefore there's even more confidence now in this pooled result than there was in

the individual results, and here we are. The risk ratio is 0.07, so they consider there's a 93% chance you won't get COVID under these circumstances, and it might be as much as 98% chance you won't get COVID, but it might be as little as 77% chance. But the best estimate of effect is that 0.07 risk ratio that's been calculated in that way.

Q. Given that there were two trials that were in comparison ——

A. Yes.

Q. —— there, and relatively small numbers ——

A. Yes.

Q. —— in the intervention group of 114 and 84 and the control group of 117 and 79 ——

A. Yes.

Q. —— what degree of confidence would you take from a result such as that and a comparison such as that?

A. Yes. Well, I take a lot. And there are some numbers underneath that, my Lord —— tau, I—squared —— and those numbers are indicating —— they are different mathematical measures to indicate whether or not the two trials being assessed are similar in terms of what's going on, the statistics, and those numbers actually show that —— particularly the I—squared, the I—squared is a measure of variability between the trials, and when

there's an I—squared of 0, it means that the trials are very comparable and you would expect that you could combine them without having to make qualifications.

So it's entirely appropriate to combine those two trials, and reading about the background of the trials, one could see why they've turned out to be so comparable, because they are a similar population and it's a similar kind of intervention. So you wouldn't want to make any qualifications based on the fact that the results are a bit different. They were the same.

With very compelling results, you will get strong effect measures even with small numbers. You could get strong results even with small numbers. The first trial ever done was the James Lind trial, which had only 12 participants in, but proved pretty persuasively that the cure for scurvy was oranges and lemons. That was done in 1747. So that changed the whole understanding of scurvy and became a model for future trials. That was more by good luck than by design, but it goes to show how you can have even just a handful of people in your trial and, provided you're on the right lines in investigating what is genuine, you could get reliable results just from compiling really rather small numbers.

Q. So identifying comparators, is that an art or is it a science?

A. Perhaps a bit of both, but the key thing is that, at the outset of doing a systematic review, you identify what trials you're going to include and what nature of trials you're going to include and combine, and what ones you're not going to combine.

So if you're going to do a trial, going back to the acne example, you wouldn't combine, in this way, a trial of acne treatments where some of the trials were using oral antibiotics and some were using topically applied antibiotic cream because they're just too different. But you could well do a randomised controlled trial looking at different antibiotics, just to answer the question: does antibiotic treatment cure acne?

Q. Right.

Could we look at another example of these measures in operation.

A. Yes.

Q. This time can we look in the Graña report, and it's number 7, and at page 101 to 102, please.

A. Yes.

(Pause)

Q. Now, this is of course in relation to vaccines, and I think, looking at 101, we have figure 13, and analysis 2.1.4:

"... non—replicating viral vector vaccine. Outcome:

all—cause mortality."

And then there's a reference to Kulkarni 2021 and also to Voysey, also 2021, and data pooled from four trials.

So, first of all, can we have a little better understanding of the terminology.

A. Yes.

Q. Non—replicating viral vector vaccine, what is that?

A. Right. Well, we haven't really gone into the detail of ——

Q. We haven't.

A. —— the different sorts of vaccines that are available, but, essentially, one category of vaccine against COVID—19 has been to use a virus, a non—pathogenic virus, a virus that's harmless to humans, that will enter the body and go into cells but, while going into cells, will carry genetic instruction, but won't replicate, won't cause disease. It will just carry the genetic instruction. Various of these non—pathogenic, non—replicating viruses have been used. The word "vector" means carrier. So they're just used as a carrier.

So possibly they are actually comparing slightly different trials, but nevertheless the same sort of trial, because they're all using the same methodology.

Q. I think it's important to note, because we are taking this as an example at this stage, that the outcome that is looked at is all-cause mortality. So there isn't a suggestion of mortality being caused by the vaccine.
A. No.
Q. It is a fact of mortality --
A. Yes, precisely.
Q. -- post-vaccination?
A. That's right. Any mortality occurring during vaccination is what they are looking at, and mortality is not a subjective event; it is a terminal event, you don't dispute it. So it's quite a good outcome to look at.
Q. Now, can you just -- again, as you did with the gargling exercise -- take us through what is shown in figure 13.
A. Okay. I'll have to put my glasses on for that. I've got some reading glasses here fortunately. You might have to lend my Lord your magnifying glass.
LORD BRAILSFORD: Ah, I see.
MR GALE: Sorry.
LORD BRAILSFORD: It's all right.
A. It's disappointing that the writing is very small. If that could be corrected in the future.
Oh, no, I'm all right. You might need them.
So, yes, what has happened here is they have found

five randomised controlled trials that are all done in 2021 that are looking at this important outcome. So these are vaccines of various kinds, where the way the vaccine works, or is assumed to work, is based on a virus, a harmless virus, that is carrying a genetic code -- we can talk about that later on -- into the cells of the recipient. The whole purpose of the vaccination was -- well, part of the purpose potentially was to prevent serious COVID-19, especially serious COVID-19 and death. So they are looking at death.
So let's take the first line. Asano 2021. So -- have you got that, my Lord?
LORD BRAILSFORD: Mm-hm.
A. So they followed up the participants for 1.9 months. They gave them the vaccine, they followed them up for 1.9 months to see -- and they were looking at other parameters as well, but they were recording how many died in that period of time, and that's the name of the vaccine, ChAdOx1. It's the AstraZeneca vaccine, basically.
The group intervention 1 are the participants who received the vaccine, and intervention 2 received placebo. Placebo means probably an injection of normal saline, so there was no active constituent. I suspect that was a single-blind study, I'm not sure, but we

could look up the details if we're particularly interested.
So what happened? How many deaths were there in the vaccination arm? They were 0 out of 192. How many deaths were there in the placebo arm? Again, there were 0 out of 64.
It's interesting the two arms are different in numbers, and probably that's because the vaccination arm probably -- there were probably three arms, in fact: one with high-dose vaccine, one with low-dose vaccine and then a third arm which was placebo. So it's a three-armed trial, which is good.
Just looking across to the extreme right-hand column, you can see that there was, according to the Cochrane review authors, a well-designed trial. It was all green for the risk of bias. So there are various domains for bias, but they gave it a five-star rating in terms of study design.
So the next one down is Falsey 2021. This was a big study, and if you just go straight to the numbers, again, they had 21,587 people who were given the vaccine, probably a high-dose and a low-dose group, and 10,792 who just received placebo, they had no vaccine.
The period of follow-up was two months, and just because there were so many people, you would expect some

mortality in any event, but you might have expected there would be less mortality at this time of high COVID from the vaccine group. So let's see if that was the case.
The vaccine group, that was twice the size of the control group, had seven deaths, and the control group who just received saline had seven deaths.
Would you agree with that, my Lord?
LORD BRAILSFORD: Mm-hm.
A. So, therefore, they have calculated an effect measure, which is that little tiny square -- the square is tiny because it's just tiny transcription -- but there's a very wide confidence interval there because the numbers we are interested in, which is the deaths, are quite small. So those sort of numbers could have arisen by chance, is what we are saying here.
So because the upper end of the confidence intervals goes over the vertical line of no effect, the authors of that trial, if we actually looked at the trial, would have to say that it's suggested there were fewer deaths, but we couldn't say that with statistical certainty. Statistically, it was not significant.
But anyway, as we come to add more and more evidence, we might reach better significance.
So the next one, next study, is Kulkarni 2021. They

studied their participants for six months, which is good. I mean, really, you should study vaccine participants for a year or two, but you've got to provide interim results. They had 900 and 300, so 900 in the vaccine arm —— again, that suggests that there were two groups: a high—dose vaccine and a low or medium—dose vaccine group —— and then there were 300 in the placebo arm. They had no deaths. I'm not quite clear why that was.

Then Madhi, next one down —— two more to go —— Madhi in 2021, they followed up their trial participants for two months. Again —— oh, yes, Kulkarni were using a different vector —— a different vaccine. I don't know what that is. But there we are. That could be why they had no deaths.

So Madhi had very small numbers, tiny numbers. Only 52 in —— they had two arms, only 52, and there were no deaths in the vaccine arm, one death in the placebo arm. So you can see the result. The little black dot is on the side which says "Vaccine better", but the confidence intervals are so huge, they're off the scale, because we're only talking about one finding there. But, nevertheless, that contributes to the overall finding which we are coming on to very soon.

I think we are now on Voysey. Voysey, same sort of

vaccine. 4.1—month follow—up, and ChAdOx. They had two types of control measures. One was MenACWY, that's a vaccine against meningitis. So they used a dummy vaccine, in effect, as a comparator, which isn't ideal, really. You should use a placebo in vaccine trials. You should really use saline. But anyway, they had those two different sorts of controls. They had 12,282 participants who received the vaccine, the COVID—19 vaccine, and 11,962 received the dummy vaccine or the placebo. They had two deaths out of the COVID—vaccinated ones and four out of the control group.

So, again, their results do favour —— do err on the side or they land on the side of vaccine probably —— well, you would have thought it would be better, but again, because the confidence intervals were so wide, they were very wide because of very tiny numbers, you couldn't say categorically that this was a statistically significant result.

So here we are. So now we come to, if you like, the crunch, which is: what does that mean when you add all these figures together? That's in the top blue diamond, the elongated blue diamond. Again, even though it's added the results from three trials, because two trials didn't contribute any of the data, the confidence interval still crosses the line of no effect. So even

combining those data, you cannot say —— which we would like to say —— that using this vaccine prevents deaths. You couldn't say it.

Now, it may be that no doubt there will be other trials in progress that will add to the data in due course, and then, as they add to that data, the pooled estimate of effect will get narrower as more data go into the analysis. It will get narrower, and the confidence interval will get smaller. Then, as long as it's not touching the line of no effect, you can impute a degree of confidence to that estimate of effect.

Q. Again, from your perspective, what do you take from that?

A. Well, I read the data as it's presented. I would immediately go back to the plain language summary which we can all understand, and if I do that, I think from memory the plain language summary just says we cannot with confidence say the vaccines prevent deaths. So let's do that.

Q. I think probably, before we do that, actually, Dr Croft —— we'll come to that, and if anyone wants to read it, the plain language summary is at page 55.

A. Oh, right, okay.

Q. But we'll come to that when we look at your section on vaccines.

A. Yes.

Q. I'm just using this at this stage as an example.

A. Yes. It's interesting that even though there are thousands of participants here, comparing to the gargling trials, where there weren't that many participants, but there was a very confident finding there, this really just indicates a very high level of uncertainty for this particular outcome.

Q. Yes.

I think, just for reference, if anyone is interested in it, there is a further analysis on the following page at 102, which is figure 14, analysis 2.1.5. Again, same non—replicating viral vector vaccine. The outcome that is looked at here is serious adverse events, SAEs. So one is not looking there at all—cause mortality, one is looking at serious adverse events.

We will look at this again in the context of your passage in section 4 of your report on vaccines, but it is just to give the reference to that at this stage.

A. Yes.

Q. Right.

Dr Croft, I think I can now, having done that exercise with you, move back to your report.

Can we go to part 2 of your report, beginning at page 8.

A. Yes.
Q. Now, before we do this, because you're setting out here —— and this is the longest passage within your report. It goes from page 8 to page 50—something, I can't remember the number.
A. Yes.
Q. It's the longest passage in your report. A lot of it is —— and this is not a criticism in any way —— in certain respects a series of dates and it is a narrative of what you see as significant events.
But before we do that, could we just look a little bit of background, and in particular could we look at appendix 4.
A. Yes.
Q. I'm sorry, I've got the wrong number. It's appendix 7.
A. Yes.
Q. It's at page 111 of your report. I'll be asking you to look also at appendix 8 and appendix 9.
In these appendices you give some background to previous pandemics and epidemics.
A. Yes.
Q. The first that you refer to is the immediate First World War influenza pandemic. I think it's also known as Spanish flu. I think, as we can see, perhaps it was rather something of a misnomer for it. But perhaps you

would just read through there and read through your comment on that.
A. Shall I read the part in italics as well?
Q. Everything, if you would, please, yes.
A. So appendix 7:
"The 1918—1919 influenza pandemic.
"The 1918—1919 influenza pandemic, known also as the 'Spanish flu', has been described as being among the most deadly events in recent human history. The pandemic killed between 50—100 million people. In countries such as the UK and the USA, and for reasons that have never been adequately explained, there was a high case—fatality rate at all ages, including amongst 20—40 year—old individuals."
That's an age group who are normally at low risk for severe influenza. However:
"... in some countries (e.g. in Spain itself) the influenza took the form of 'normal' seasonal flu, with average or close—to—average mortality."
So here I give my comment. I try not to interpose my comments in the main body of the report, but my report would be bland and not have much meaning unless there was some comment at some point.
Q. No, I appreciate that.
A. So I give my take on this. I made it clear this is my

comment. So I have proposed here:
"The unusually high mortality in young adults with 'Spanish flu' that occurred in some countries (e.g. UK and USA) is now thought to have been in large part due to harmful treatment protocols used in those countries [like the UK and USA]. In the early weeks ..."
Oh, here we are:
"In the early weeks of the COVID—19 pandemic the case—fatality rate was reported to be as high as 15%, causing widespread alarm. This high reported rate may likewise have been due, at least in part, to harmful treatment protocols ..."
And I give an example of some that might have been harmful instead of beneficial, for example over—enthusiastic use of intravenous fluids, nursing patients in the supine, meaning on their backs rather than on their stomachs, and the sort of treatments that are no longer routinely used for COVID management. That's just a suggestion. I have put here:
"The crude case—fatality rate for COVID—19, averaged across all age groups, is now considered to be around 0.5—1%."
I get that from —— that's in the earlier section of my report. And in Scotland I put it was only 0.29%. That was my own calculation:

"The overwhelming majority of COVID—19 deaths occur in those who are very old ..."
And that's overwhelmingly the highest risk factor. Those who are over 80 are the ones who most likely to get severe COVID and to die. Also the very sick, but that's less of a risk factor, having the pre—existing medical conditions:
"In 2020 and 2021 some commentators drew parallels between COVID—19 and the high mortality rates in young people that were reported in some countries during the [Spanish flu epidemic of 1918 to 1919]. Arguably, the drawing of these historical parallels was misleading, and [added] to the atmosphere of panic that prevailed in 2020 and 2021 —— and that hence facilitated [made easy] the introduction, in some countries, of repressive and authoritarian response measures against COVID—19 that were often harmful at a societal level, but that were declared as necessary to 'contain' SARS—CoV—2."
Within that opinion or comment I have got a scientific reference which talks about Spanish flu. Essentially, what was happening there in the UK and USA was there were massive stocks of penicillin around, because the First World War had just finished, penicillin that had been made by Bayer, a German company, had gone off patent, so it was really, really

cheap, so doctors in large cities used this new wonder drug on patients and were using it at such high doses that they were often damaging them and actually caused their death. That wasn't understood properly at the time, but it was intuitively recognised as the pandemic progressed, and in later flu epidemics aspirin doses were much lower. It's hard to prove, but it seems to be the case.

That also would explain why in Spain -- Spain hadn't been in the war and so didn't have massive stocks of aspirin -- it was just like ordinary seasonal influenza, a bit worse, but it wasn't killing young people in their tens of thousands.

Q. I think you said earlier massive stocks of penicillin ; you are actually meaning --

A. I'm so sorry, I mean aspirin. I beg your pardon.

In the United States they had this very frightening phenomenon of military barracks -- they had very large military barracks of 10,000 troops or so, and there might be hundreds of deaths per day that were going on, because the doctors were pumping the young soldiers with penicillin -- sorry, with aspirin. I'm probably confused -- my own grandfather died in the Spanish flu. He was in the merchant navy and he died in 1918. He was in Portsmouth, and I suspect he probably got the full

whack of aspirin that possibly killed him. It's a reasonable interpretation of mismanagement. Not to say -- it was probably a virulent form of influenza, but that particular influenza epidemic and no other especially affected healthy young people, and no one really knows why. But only in some countries. If it was really due to the very pathogenic nature of the pathogen, it would have been across the board, but it wasn't.

MR GALE: I think the --

LORD BRAILSFORD: But that falls into the category of informed conjecture by you.

A. Well, it's not by me, it's by other people.

LORD BRAILSFORD: By other people, yes, I beg your pardon.

A. Yes, it is. Yes. It is informed conjecture. It's based upon a reasonable scientific model.

LORD BRAILSFORD: Yes.

MR GALE: I think the paper you refer to is the paper by Dr Karen Starko.

A. Yes.

Q. And for those who want to look at it, it's document 18. The synopsis is at page 931. I don't think it's necessary to -- unless there's anything there you want to particularly take from it.

A. No, I was simply going to say this isn't central to

COVID-19, but it's an important pandemic, the worst pandemic ever that has occurred, and there may be lessons we can draw from that. I think that's one that the numbers might be overstated for various reasons that are not actually truly related to the pathogen, that is truly related to the way people responded to the pathogen, with the best of intentions, but potentially making, in the first stages, the patient worse rather than better.

Q. I think you make the point in your comments section at page 111 that:

"Arguably, the drawing of these historic parallels was misleading ..."

When one is looking at it --

A. Yes, I think so, yes.

Q. -- in the context of --

A. Yes, I think -- yes, yes.

Q. -- of COVID-19.

A. And I think I'm right in saying many commentators were saying, "Oh, we're facing the worst pandemic since the Spanish flu of 1918/1919", but that was always misleading, because 1918/1919, there were a lot of young people who were affected, and this is very unusual with flu, but there's a potential explanation for that. Starko says that the case-fatality rate in young people

was as high as 3%. That seems a tremendously high rate of death. So there's another explanation which could explain why that was.

Q. Yes.

A. Whereas in COVID it was never the case that young people were ever going to be at very high risk, because it was known from the very outset it was the very old, and that could be inferred also from the fact that the previous coronavirus epidemic, with a very similar virus, SARS -- which we might talk about shortly -- it was known from that that, although it had a high mortality rate, it was in the very old, very old, yes.

So all I'm saying is that of course one can look back in history and cite examples of very serious public health events, but the particular imputation that was being in many cases given that we were facing widespread deaths of young people in the tens of thousands, was not, in my view, appropriate on the occasions when it was used. I don't know if scientists were using it. I would hope not. But certainly media commentators were using it, and obviously it frightened people because many people still have a folk memory of the 1918/1919 Spanish flu.

Q. And I think it's right to say, doctor, that for those who suffered losses of family members and loved ones who

were in the young group, that's probably of little comfort to them.

A. Oh, I agree. Yes, certainly. Certainly, yes. Yes, indeed. I would certainly accept that, yes.

Q. Can we go on to appendix 8, please, at page 112.

A. Yes.

Q. This is your reference to the 2009/2010 swine flu epidemic. Again, this is more modern history, and probably something that we all remember to a certain extent, the H1N1, as sort of letters and numbers embossed in our memory.

But perhaps you could just read out the block section at the top and then your comment on it.

A. Yes. So the block section I have taken from a standard textbook of microbiology, the Oxford Handbook of Infectious Diseases and Microbiology, and summarises the swine flu pandemic in a few sentences:

"The H1N1 'swine flu' pandemic of 2009/2010 spread rapidly throughout the world. Rates of infection were highest in those [less than] 25 years old and, unlike seasonal flu, low in those over 65 ..."

The explanation for that might have been that the over 65s already had some pre−existing immunity to that particular virus because they'd encountered it in the 1950s, whereas the young people didn't. So the young

people were getting infected, but they weren't dying particularly, on the whole:

"Secondary attack rates were probably similar to those of seasonal flu, but rates of hospitalization and mortality were higher, especially amongst the pregnant and immunosuppressed."

Interestingly, they weren't higher amongst the very old, probably for the reason we've just suggested: that the very old had probably encountered something like this virus in their youth. But it was the pregnant and immunosuppressed who were hospitalised and who were likely to die.

So:

"Unlike the seasonal [influenza virus] H1N1 circulating at the time [this is important] [less than] 99% of pandemic [swine flu] strains were susceptible to [Tamiflu] ..."

Which is the drug that the government brought in very large quantities. It's called oseltamivir. Its trade name is Tamiflu. So the government, in response to this pandemic −− the World Health Organization declared it a pandemic −− they bought in very large stocks of an antiviral drug on the assumption that it would reduce symptoms and reduce pressures on healthcare, but basically the strain was resistant to

it, so it really had no effect, or very little effect.

Then by the following season, this new pandemic strain of the virus had become just the standard circulating influenza strain. It had merged into the background strain of influenza viruses that cause seasonal flu, and it's now considered a seasonal virus.

So it was rather alarming when it first appeared. Some people died. Some people got ill. Not that many. But that particular pandemic fizzled out. It started in about −− it was declared in the middle of the year 2009, it built up a head of steam during the autumn, and at Christmastime it just fizzled out completely. I remember working in the Surgeon General's department then. We had to implement the policies of getting vaccines out to outlying military stations, and we came back from Christmas in January and no one was talking about it anymore. It was all a bit embarrassing. It was no longer regarded as being a serious threat at all.

There was then an official inquiry, the Deirdre Hine report, which came out very quickly. She reported in July 2010. It is a very, very good report, actually, which I read just recently, and she made some very perceptive observations.

So here is my comment −− again, this is just my personal view, which I accept is my personal view, and

I have qualified at the beginning of the report that my own personal view is not necessarily or not to be taken as in any way indicative of the Inquiry's view, but I have said here:

"The above short summary of the 2009−2010 swine flu pandemic is taken from a standard textbook for medical students. The response to the pandemic by the UK government at the time (i.e. the Labour government of Gordon Brown) was unduly influenced by 'worst−case' modelling ..."

And that was something Deirdre Hine mentions in her executive summary. She said: people keep using this term, "this is a reasonable worst−case scenario". It is a reasonable worst−case scenario that millions of people are going to die in this country. She said a worst−case scenario cannot be reasonable, is I think what she's saying, and I think lawyers would understand that.

So it was:

"... influenced by 'worst−case' modelling and by alarmist predictions in the media that originated from WHO officials and UK academics who had undeclared conflicts of interest ..."

That's now well established. There was a remarkable paper by Kate Mandeville and some colleagues at the London School of Hygiene, who looked at what scientists

were telling the media, what stories they were feeding to the media. That's one of my attached papers.
Q. Just to give the reference to that, that is at pages 808 to -- it's a short paper.
A. Yes. It didn't come out until 2014, so four years after it was all over.
Q. To 814.
A. Yes, thank you. Four years after it was all over, these investigators, this is what they said. Essentially, they said:
"There is evidence of [conflict of interest] among academics providing media commentary during the early [swine flu] pandemic. [And this led to] Heightened risk assessments ..."
I'm reading from the abstract of that paper, "Conclusions":
"Heightened risk assessments, combined with advocacy for pharmaceutical products to counter this risk, may lead to increased public anxiety and demand."
And then they finish with the line:
"Academics should declare, and journalists report, relevant [conflicts of interest] for media interviews."
Q. I think, just again for the note, you are reading there at page 808 --
A. I'm reading at 808.

Q. -- from the abstract and the conclusions section.
A. Correct, yes.
Q. Thank you.
Right, if we go back to your comment.
A. Yes. So I have put here:
"... in fact the swine flu pandemic quickly reached a state of natural equilibrium by early 2010."
In fact, it was already declining by November of 2009. It already reached its peak and was waning. But anyway, by early 2010 it was all over.
So here we are:
"Important additional mistakes made in –20092010 by the UK government [it's great to be wise with hindsight] included (i) the stockpiling at great expense to the UK taxpayer of ineffective antiviral drugs (notably oseltamivir, or Tamiflu) ..."
And here I cite the editor of the British Medical Journal, Fiona Godlee, who said exactly that in 2010. She said we've spent billions on completely ineffective antiviral drugs. Other countries were not panicking to this position, but Britain was, France was. Poland wasn't, and she said this is not acceptable.
Then I put (ii), here is an additional mistake:
"... emergency-use authorisation given to inadequately-tested vaccines (notably the

GlaxoSmithKline vaccine Pandemrix, which in a significant but undisclosed number of children caused narcolepsy, a devastating and lifelong neurological disease)."
So there wasn't any vaccine around to counter this new strain of influenza, which was serious in pregnant women and those who were immunosuppressed, so the process of authorisation for vaccine-use was speeded up, and some vaccines were re-purposed from seasonal flu to be used against this new variant of flu. One of these was Pandemrix, and it had a terrible side effect in a small number of children, but it was nevertheless a significant number, some hundreds of children, who had developed this very severe neurological disease as a result of this vaccine.
Obviously, it was contested. The manufacturers contested. They said association doesn't mean proved. But it is now in the textbooks that that particular vaccine was the very unfortunate cause of this incurable condition, and the following year or maybe the year after, it was withdrawn. It was being slowly developed for use in seasonal influenza, but the manufacturer, GlaxoSmithKlein, withdrew it.
Unfortunately, the government had committed to buying large quantities of this vaccine, along with

another vaccine, which actually seems to have been quite effective, but didn't cause neurological problems, but GlaxoSmithKlein wouldn't allow a break clause, which is one of the criticisms Deirdre Hine makes in her report. So, in other words, they wouldn't say, "All right, we will take the vaccine back, now you don't want it"; they said, "No, you've got to pay for it". So that was a lesson that was identified then.
Q. Just to give the reference to the Godlee piece, that is document number 6 in the bundle, and it is at pages 48 to 49 of the bundle.
I think, as you said, Fiona Godlee was the then editor-in-chief of the BMJ; is that right?
A. She still is, yes.
Q. And still is. And this was effectively, as I understand it, as headed, an editorial article by her.
A. Yes. She's also very critical of secret emergency committees, and -- a very hard-hitting editorial and short, nice, well worth reading.
She also talks about independent experts and how hard they are to find. That's quite interesting. Experts who are involved with industry could be consulted -- she is really talking about government departments. You could consult experts on vaccines and pharmaceutical products like antivirals who are involved

with industry, but she says they should be consulted but excluded from decision-making. So there we are.

She says:

"As for the [World Health Organization], its credibility has been badly damaged."

And then she goes on to enlarge on that point.

Q. Thank you, doctor.

A. Thank you.

MR GALE: My Lord, I'm going on to appendix 9, which will maybe take a little while, perhaps more than five minutes, so perhaps it may be an opportune moment to stop.

LORD BRAILSFORD: Yes. Just choose your moment, Mr Gale.

MR GALE: I have chosen.

LORD BRAILSFORD: You have chosen, okay. I thought you said in a few minutes.

Very well, we will take 15 minutes, which makes it broadly 3.10. Good.

(2.53 pm)

(A short break)

(3.15 pm)

MR GALE: Dr Croft, can we go to appendix 9, please, pages 113 to 114 of your report, where you look at previous coronavirus epidemics.

I know you're going to be referring to SARS and MERS

as we progress through section 2 of your report, but it's perhaps useful to take what we have here, and perhaps again, if you do what we've done in the past with the other appendices, could you read through the block sections and then your comment.

A. Yes.

This appendix 9 is about previous coronavirus epidemics. Until about 2000, there were four known coronaviruses, just by way of background, but it wasn't thought that they were particularly dangerous; they just caused upper respiratory tract infections and colds. But then these two novel coronaviruses came along which caused quite serious epidemics, particularly the first one, SARS, and then the second one, MERS. Of course, as we know, COVID-19 is caused by yet another novel coronavirus.

So, first of all, "Severe Acute Respiratory Syndrome (SARS) coronavirus". These are two sections, again, from a standard textbook, 2017. So this was knowledge. This is accepted knowledge. It was known at the time of the COVID-19 outbreak.

So:

"SARS was recognized in China in November 2002 and had spread to affect 29 countries across the world by February 2003."

I think there were three cases in the United Kingdom. No deaths.

"The epidemic had died out by July 2003; [in total] 8096 cases were reported, with a [case-]fatality rate of 11% (43% in those over 60 ...)"

I think that was skewed very much towards the over 70, over 80. There we are.

"Between July 2003 and May 2004, there were four small and rapidly contained outbreaks of SARS, three of which were associated with laboratory releases and the fourth thought to be due to an animal source. The cause was a novel coronavirus. Animals are thought to be the main reservoir. Transmission is by droplets and contact with contaminated surfaces – nosocomial transmission [nosocomial means hospital-associated/hospital-acquired transmission] was common in the early stages of the outbreak. The virus is present in stool and may cause diarrhoea."

Three bullet points: clinical features, diagnosis and treatment.

"▪ Clinical features – incubation is to 2-10 days. A 3- to 7-day febrile prodrome ..."

That means a pre-illness phase, when you're not feeling quite right, but you're not entirely unwell, you just don't feel right. So there's this early period of

feeling unwell.

"... notable for the absence of upper respiratory symptoms. The respiratory phase typically starts [abruptly] with a dry cough, progressing to breathlessness and progressive pulmonary infiltrates on [chest X ray].

"▪ Diagnosis – during the outbreak, [reverse transcriptase polymerase chain reaction] was performed but sensitivity appeared to be limited."

Sensitivity is more or less the ability of the test to pick up cases, and the testing was:

"... ([less than] 70% positive on NPAs [I think that means nasopharyngeal aspirates] in week 2 of illness). No systematic study was performed to validate tests. Serological testing by ELISA ..."

That means testing for antibodies, that's what serology is, ELISA is enzyme-linked immuno assays. It's a technique for estimating antibody levels:

"... at 3 weeks appeared most sensitive."

This is important, I think:

"▪ Treatment – no specific therapy. Care is supportive. Patient isolation and infection control precautions were key to the control of the ... outbreak. This was ... facilitated by the long prodrome [so cases could] be identified early and isolated before they

became infectious."

So that's all very relevant, I think, my Lord, because when SARS−CoV−2 came along, the virus was very similar to the SARS virus. Quite a lot of work had been done on it. 79.5% similarity to −− and very many of the features of SARS−CoV−2 had already been seen in SARS, which, as you have just read, died out.

So Middle East Respiratory Syndrome. That was rather different, although still a coronavirus. It's a virus that is closely related to several bat coronaviruses. This was identified in 2012 from a man admitted to hospital in Saudi Arabia who had pneumonia and renal failure. About the same time, an identical virus was identified in Qatar, in a patient with similar features who had been to Saudi Arabia. Then there were cases all round the Middle East and five other countries from patients who had returned from the Middle East, and UK, France, Italy and Tunisia reported limited human−to−human transmission to close contacts of the index cases. This had a very high case−fatality rate of 60%. I don't know why −− I don't think anybody knows why that was. But luckily didn't spread.

"▪ Clinical features − incubation period of around 5 days (but [less than] 10 days). Symptoms ranged from none (positive [reverse transcriptase polymerase chain

reaction] tests were found is several asymptomatic close contacts) ..."

So, in other words, they had the infection but they had no symptoms.

"... mild respiratory illness, to severe pneumonia requiring ventilation or extracorporeal membrane oxygenation [at the most extreme end]. Other symptoms: pericarditis [inflammation of the pericardium of the heart], renal failure, DIC [disseminated intravascular coagulopathy, which is a clotting disorder], and diarrhoea. Those with underlying medical problems seem at greater risk of severe disease.

"▪ Diagnosis − [reverse transcriptase polymerase chain reaction] testing of lower respiratory tract specimens is most sensitive."

We all know PCR testing is probably best.

"Testing multiple specimens at different times from different sites increases the likelihood of detecting virus. Guidance should be sought from national public health authorities regarding who to test, based on contemporary epidemiology.

"▪ [Again] Treatment is supportive, and infection control paramount."

Q. Before you go on to your comment section, doctor, a couple of points.

In relation to SARS, I think you say that animals are thought to be the main reservoir.

A. Yes.

Q. Can you explain that, please?

A. That will be explained later on if we go to that particular point of my part 2.

Q. Right.

A. But the coronavirus is 79.9 −− sorry, the virus here was −− actually, I'm not quite sure what animals it was thought to have come from. I can't be certain. But it could well have been bats as well. Please accept my apologies on that.

Q. No, no, we will come back to that if needs be.

A. Sure.

Q. There are two references in both SARS and MERS to "Care is supportive".

A. Yes.

Q. What is that meant to signify?

A. What that is meant to signify is that during these emergencies −− and the first one was an emergency especially in China, the second one was an emergency in the Middle East −− there would have been attempts to use antiviral drugs and extreme or, should we say, what could be called aggressive medical interventions to save the patients who were getting unwell, but they weren't

successful.

So, essentially, the accepted wisdom as regards these two viruses −− which are still around, but they are not causing problems −− is if you get a patient with them, just nurse them with ordinary nursing care. Don't try anything fancy, it is going to make them worse, just to put it into very simplistic terms. But that's what supportive care means: it means give them oral fluids, give them painkillers, simple painkillers, but don't sort of get out your antiviral drugs from the cupboard, just because they are there to see if it's going to help, because it probably won't, and may make them worse.

Q. Is that viewed as being almost what one might term palliative care?

A. Yes. Yes. Yes. Although palliative care has connotations that the person is going to die, supportive care has connotations the person is going to recover. They're more likely to recover. So therefore −−

Q. Yes, I wanted to make that distinction, yes.

A. Indeed, yes.

Q. Right.

If you go on to your comment section, doctor, please.

A. Thank you, yes. Again, my Lord, these are my

interpretations because the data is very bland.
So I have put:
"The above short summaries of ... SARS and MERS ... epidemics ..."
Interestingly, WHO never designated them as pandemics. They could have been, but they weren't. They are taken from standard textbooks for medical students. This knowledge was available when COVID-19 started in March 2020, and like the swine flu pandemic of 2009 to 2010 the MERS pandemic of 2012 proved to be self-limiting, although there still are sporadic cases. So MERS seems to be over -- seems to be over as a kind of major public health threat, but SARS is somewhat different:
"The 2002-2003 SARS epidemic ... first recognised in China ... then spread to 28 other countries [so it was widespread] was also self-limiting, since most [of those] countries did not adopt emergency measures against SARS [particularly] and yet the epidemic died out."
I'm sorry, there's a typographical error there. The epidemic died out by July 2003. So whereas in all other countries -- so we had SARS in this country, and we didn't go into emergency state. There were prudent measures taken, but in China, by contrast, they went

into full lockdown mode. This is when lockdown was invented, and I call them a series of repressive and authoritarian measures, including lockdowns, meaning closures of schools, workplaces, entertainment venues and stay at home orders.
And then social distancing was imposed in China, enforced spatial separation of at least 1 metre between those infected and those not infected, and they had border closures and compulsory face mask wearing. They are all mandated by the Communist Party of China. So I've written:
"These extreme government-mandated measures were afterwards judged by the Chinese government - but without any scientific evidence [any rigorous scientific evidence] to support this judgment - to have resulted in the 'containment' of the SARS epidemic."
And they used exactly the same package of measures when COVID-19 came along because in their view they'd worked. But in fact they had the worst experience of SARS of any country. So a contrary view would be that their extreme package of measures made what should have -- an epidemic that should have reached natural equilibrium quickly, it actually prolonged it.
Q. Would that be possibly through containment of individuals in close proximity to each other?

A. Well, yes, indeed. So if people were being contained in their flats during the winter in conditions where a virus that wasn't that transmissible would easily infect the other person in the same apartment, then that would provide a micro-focus of infection that would perpetuate the infection, whereas if they'd been allowed to go about their ordinary business, it may not have occurred to the same degree.
Q. Yes.
A. So:
"In respect to SARS, China was the worst-affected country ... by a wide margin."
And especially, as I repeat, in the very old, the over 80s, they were the group that were really very much at risk of death:
"Since secondary attack rates of coronavirus within households are high, the 'containment' measures against SARS ..."
I put "containment" in inverted commas because this is one of Deirdre Hine's points, that you cannot contain these respiratory transmitted viruses. You can slow their spread, but the idea that you can contain them isn't possible with that sort of transmission.
Q. Just remind us who Deirdre Hine is.
A. I beg your pardon. Deirdre Hine was appointed to -- she

was chair, like Lord Brailsford, of the official inquiry after the swine flu epidemic and she wrote her inquiry report in July 2010. And she doesn't like the phrase "reasonable worst-case scenarios". She says it's a contradiction in terms and engenders unreasonable panic. And she doesn't like the phrase "containment". She doesn't like the concept of containment, even though they were talking all the time then about containing swine flu.
So:
"The 'containment' measures against SARS that were adopted by the Communist Party of China may have made the SARS experience worse, not better -- for example, by creating hundreds of new foci for the ready acquisition of SARS in people's homes. Notwithstanding these uncertainties, [exactly] the same 2002/2003 package of repressive and authoritarian 'containment' measures, (and with the additional new measure of population-wide electronic surveillance of citizens' movements) was adopted by the Communist Party of China in 2019-2020, at the [very] start of the COVID-19 pandemic."
They adopted the same measures in January 2020:
"In early 2020, with high COVID-19 case numbers occurring in most countries -- including China itself -- the Chinese model of coronavirus 'containment' was

adopted by many other governments, including the UK and the Scottish governments. In Scotland, two population−wide electronic surveillance schemes on the Chinese model were procured; these were (i) Test and Protect, procured by the Scottish Government in May 2020, and (ii) Protect Scotland, procured ... in September 2020."

I don't know much about them, but I got that data from the timeline that's on the website.

In England the measure that was adopted there was procured in 2020 by the then Secretary of State for Health, Matt Hancock, called Track and Trace. I do know that that was hugely expensive and that it was not at all effective.

So I end up by saying that there's no evidence of these −− of any effectiveness of these population−wide electronic surveillance schemes, as far as I know, in [sic] helping to spread SARS−CoV−2 infection.

Q. Right. We will come back to some of that as we progress on, particularly in section 3, but if we now go back to your statement, please, at section 2.

A. Yes.

Q. I think it's page 8. Yes, page 8, "The COVID−19 pandemic".

Now, again, Dr Croft, if you would read through

that, and I think fortunately I probably don't have to interrupt you very often on this because I think it is largely factual.

A. Yes.

Q. So if you would start reading at 2.1 and continue.

A. Yes, thank you. So 2.1:

"What is COVID−19?"

COVID−19 is a syndrome, and that's the jargon term meaning a multisystem illness, caused by a virus which we now know as SARS−CoV−2, and in the UK it's a statutorily notifiable disease, meaning that if doctors diagnose or suspect it, they have to report to the local authority:

"COVID−19 has a varying presentation ranging from asymptomatic or insignificant to respiratory distress and death. The death is milder in children, with the greatest risk of severe illness and death in those aged 85 years and older.

"SARS−CoV−2 was responsible for a global pandemic in 2020−2023."

The pandemic has now been declared over:

"The pandemic has been associated with severe negative impact in most countries, with decreases in gross domestic product and an increase in inequalities among lower socio−economic groups."

Quite a strong statement. I have taken it from a standard textbook. Everything here is from standard medical textbooks. I consider it would be not contested, my Lord.

Then the last paragraph here, which is interesting:

"A subset of individuals ..."

Oh, I beg your pardon. That's the wrong way round:

"A subset of individuals [with SARS−CoV−2 infection] have progressed to a recurring pattern of physical and cognitive symptoms known as long COVID. The public health measures used to manage the pandemic have also led to social isolation with adverse mental health consequences."

Q. Right. Having said I wasn't going to interrupt you, I now contradict myself and do so.

Two things I would like just to clarify.

A. Yes.

Q. The first sentence on 2.1, you refer to a multisystem illness?

A. Oh, yes, yes.

Q. Again, that may be probably self−evident, but can you just explain what that is?

A. By multisystem is meant many body systems. So it's an illness that could affect the brain, the lungs, the heart, the kidneys, the liver, the lymph nodes. Just

pretty much any system in the body could potentially be caused by SARS. Although we have tended to regard it as a respiratory illness, there are people who are quite ill but their lungs are fine. So there are many dimensions to this illness.

Q. Right. And in the third paragraph on that page you make reference to severe and negative impacts in most countries ––

A. Yes.

Q. –– with decreases in GDP and an increase in inequalities among lower socio−economic groups. And then you also go on in the next paragraph to say:

"The public health measures used to manage the pandemic have also led to social isolation with severe mental health consequences."

A. Yes.

Q. Now, can I just understand –– put yourself, Dr Croft, in the situation of someone with your public health and epidemiological background who is asked to advise either a public body such as a government or a public body such as an authority ––

A. Yes.

Q. –– or a commercial organisation, or a local authority ––

A. Yes.

Q. –– about restrictive measures that may be thought of

being considered so as to combat COVID-19?
A. Yes.
Q. Within your area of expertise, would you feel it appropriate for you to highlight what you might envisage to be the negative aspects of restrictions such as you've identified here?
A. I would expect to -- well, I would look at economists, to give detail on the economic damage that says -- that was caused, and mental health experts to talk about the adverse mental health consequences.
What I'm really doing here is in a way providing what appears to be incontestable knowledge that such consequences did occur.
Q. Well, we've got that, I suppose, with the benefit of hindsight.
A. We have, yes.
Q. But at the time of formulating restrictions, would you issue, as it were, a warning in relation to these issues?
A. Yes. I have worked in policy making to an extent and when I was doing it we would normally make a recommendation and there what we call an impact statement. There might be some other jargon. The impact of this policy would be blah blah blah, and so therefore there would be a recognition that every policy

decision would have some kind of knock-on effect that would often be undesirable.
So in making any policy decisions which might or not be taken up, I would expect there to have been something like an impact statement that this will have the following potential consequences in these areas of society, because these were measures that were affecting the public at large. They weren't individual measures.
Q. So, again from the perspective -- from your perspective as a public health practitioner and consultant or specialist, if you were considering with policy makers matters such as isolation of elderly people in care homes, would you again, as that policy was being considered, think it appropriate to issue some form of caution, if I can put it that way, about the potentially adverse consequences of that?
A. I would expect it to form part of the decision-making process. But whether or not the government went so far as to put out a health warning, so to speak, that incidentally we're now going to see many more cases of mental illness and social isolation, would just depend on the context. I -- that would just really be a matter of how expedient it was thought to be.
It's similar to -- going back to -- going to the general practitioner, the general practitioner would

say: try these pills and I have to tell that you there are some side effects associated with them. So it would -- or they can necessarily assume that because there's a package insert telling about the side effects, that would be part and parcel of the contract between yourself and the general practitioner.
But all public -- all decisions that affect the public health have consequences beyond the immediate ones and they need to be taken into account.
Q. And within your discipline of being a public health practitioner, would you feel both competent and confident in at least alerting a decision-maker, or potential decision-maker, to these potentially deleterious effects?
A. Yes, although it may not be the case that the exact detail of the deleterious effects might fall outside my immediate competence. So if they were economic or educational, for example. But I would have to at least alert the decision-maker that there would be consequences of that nature. Sometimes they would be self-evident, but they might need to be spelt out, that more factors need to be taken into account than just the medical benefit to be derived.
Q. So, for example, do you find it in any way surprising that social isolation had adverse mental health

consequences?
A. I think that would be a foreseeable and regrettable consequence of the social isolation, the mental health sequelae.
Q. Yes.
A. We are social animals and we have to associate with other people, and when we can't we suffer consequences.
Q. Yes. Can we go on to section 2.2 at page 9, please. Again, if you just read on.
A. Yes. So here we talk about viruses:
"What are viruses?"
"Viruses are small (20-150 nm) protein packages. They are much smaller than other infectious agents.
"Viruses have a central nucleic acid core (genome) surrounded by a protective coat (capsid) that is antigenically unique for a particular virus. The virus genome consists of either DNA (i.e. deoxyribonucleic acid) or RNA (i.e. ribonucleic acid), but not both."
So it's one or the other.
Q. Right. Can I just stop you there, doctor. It might be helpful, although it's coming subsequently in your report, if you refer to the figure --
A. Yes.
Q. -- on page 14 under the heading 2.5.
A. Yes.

Q. "What characterises SARS−CoV−2?" It's perhaps useful if you can describe what is a virus under reference to that figure.
A. Yes. Shall I explain some of those terms?
Q. It would be helpful, I think, yes.
A. Thanks. I'll come back to that as and when.
So just −− there's a lot of jargon, but I think we need to understand it because when we come to the papers, the investigators use these terms.
So the genome means the entirety of the genetic instruction of an organism. It's what it is that makes the organism what it is, and we each have a genome. The capsid a protective coat. So we go on to say the virus genome consists of DNA −− that's explained there −− RNA, ribonucleic acid, but not both.
So DNA and RNA are nucleic acids. They are classed as nucleic acids, and nucleic acids consist of many nucleotides that are joined together, bonded together, and a nucleotide is a sugar and a phosphate base −− this biochemistry −− and then a sugar and phosphate element with a nitrogenous base attached to it. And the nitrogenous base may be −− in the case of DNA it's guanine, adenine, cytosine or thiamine. In the case of RNA the nitrogenous base might be guanine, adenine, cytosine or uracil. So they use four of those bases and

that gives it its particular characteristic. The bases can change round, and that's part of the process of mutation that RNA and DNA can undergo.
Q. Yes.
A. So I don't think we can really −− so looking at the figure, so there's −− on page 14 of my report, there's the virus that causes COVID−19. It's called SARS−CoV−2 and the RNA is in the middle of the virus there, and that's the genetic constituent of the virus. The viral genome is that totality of viral RNA that's in the middle of the virus there.
In humans the genome is contained within the nucleus of the cell. We are probably coming on to that later, but viruses don't have a nucleus as such. So the RNA −− the genome is sort of scattered around within the middle portion of the virus.
Have we said −− oh, yes, the next paragraph down. So you can see the envelope round the RNA virus will go to −− that comes in the next paragraph on page 2.2.
The envelope −− so some viruses, for example, coronaviruses, have an outer envelope which consists of lipid, that's fat, and protein. And this is important because envelope viruses can't survive as well in the environment. So they can −− they have to get quickly from one infected person to the next, and so they're

spread by respiratory, sexual or blood−borne routes.
Non−enveloped viruses survive better in the environment and they are predominantly transmitted by faecal−oral route or respiratory routes.
So coronaviruses then are enveloped and they can't survive as well in the environment.
Q. Yes.
A. That has implications for ventilation of rooms and being out of doors. The viruses just don't survive very long outdoors, and they survive for better periods indoors, and in contained −− contained environments:
"Some viruses contain enzymes."
We're back to section 2.2. So HIV, human immunodeficiency virus, contains an enzyme called reverse transcriptase. Then we talk about viruses being grouped into orders, families, subfamilies and genera. There's a lot of, shall we say, uncertainty about how to group viruses. At the moment only about half of viruses have actually been properly classified and the classification may change.
Viruses have colonised most life forms, including bacteria, plants, insects and animals, but viruses are not alive. They are metabolically inert. So they're metabolically not metabolising. So they have to live intracellularly within the cells of their hosts. And

they can't replicate independently. So if there's virus on the surface, it can't produce more viruses. It has to get into a host, a living host, in order to replicate.
So what they do is they subvert host cellular processes in order to synthesise their nucleic acids.
Q. Right. I think you are going to have to explain that.
A. I'm so sorry. It's an exact quote from −− so what this means is that they get into the cell. Cells do know how to produce new cells. Viruses can't really do it. So they have to take over the cells' replicating functions in order to synthesise their nucleic acid so as to create more RNA copies of themselves or DNA copies of themselves, and then they multiply within the cells and then they burst out of the cells into the extracellular environment and penetrate new cells, and then the same process repeats itself.
So there's a sort of −− there's a time element involved in viral infection. They can do this pretty quickly, but a virus won't infect you one day and −− won't infect you and then kill you an hour later because it needs time to get into the cells, replicate, get into more cells, replicate, get into more cells.
Q. Yes.
A. But because they're in the cells −− this is, I'm sorry,

ex tempore, but because they're in the cells, you can't treat viruses with antibiotics in the way that you can treat bacteria that are generally extracellular. You could possibly use antiviral drugs that interfere with some of those replicating strategies, but generally viruses don't respond to antibiotics, and this has important treatment implications.

So we are saying now that whereas bacteria may have several thousand genes, and a gene is the basic unit of heredity, a gene is defined as a small section of -- in humans a gene is a small section of DNA. We've said DNA is deoxyribonucleic acid, and a gene is a little section of DNA that codes for a particular protein. The proteins are the substances in our body that actually do things rather than just being inert like fats and sugars. Proteins do things. And there are 20,000 proteins in our body. Many of them we don't really know what they do, but some of them have clearly defined functions like haemoglobin, which carries oxygen from the lungs to the tissues as a protein. So what a gene does, it will instruct the body to produce a particular protein.

So viruses -- viruses have the ability to produce more than one protein from the same gene by means of what's known as RNA splicing or frameshifting.

The protein -- yes.

(Pause)

Yes -- okay. I'm just seeing if any of that needs explanation.

(Pause)

Yes. I have put a little note about proteins. Proteins are also known as polypeptides. Some of the papers we refer to call them polypeptides. They are complex molecules made up of chains of amino acids.

Amino acids are the basic building blocks of proteins. There are 22 of them that we require to build protein. Some of them we derive from food. We break down food, animal proteins and vegetable proteins, and re-use those amino acids to make our own proteins, and some of them we can synthesise ourselves.

So, just to continue:

"Viruses evolve rapidly due to the high number of genome duplications undergone in short spaces of time."

So because they have subverted the cellular replicative processes they are rapidly multiplying. That's the whole purpose of their existence. And in doing so, because those bases that I was talking about the cytosine, adenine and -- sorry, guanine, adenine, cytosine, uracil that are in RNA viruses, because the way the bases may get rearranged, there may be

mutations, changes in the virus structure as it's replicating.

So therefore genetic sequencing of isolated viruses is important to identify new mutations and variants, and experience has shown that most viruses, if they produce copies of themselves that aren't exactly like themselves, those copies probably won't be as efficient as the parents, but occasionally the new -- the new variant, the new strain may be especially pathogenic or it may be less pathogenic than the parent strain.

Q. I think this is probably the first time that you've mentioned variants, and I think --

A. Yes.

Q. -- this is one of the things that we will come on to, because I think we are all familiar with the various variants that there were, the Delta, the Omicron, etc.

A. Yes.

Q. Can you just indicate how significant would the variant have to be in order to constitute, as it were, a new variant?

A. This -- yes, that's true. This is -- there's a committee that actually decides whether this new form of virus is a new variant or a subtype. So that's defined by virological experts. They use certain criteria as to whether what has been seen is like --

entirely new or just relatively new. That's my best understanding of the situation.

So it isn't something that's intuitive. It has to be discussed and thought about and then pronounced upon.

Q. And this -- the identification of a new mutation or variant is dependent on the genetic sequencing?

A. Yes, exactly, exactly. So viruses can -- can't be seen with light microscopes. They can be identified through electron microscopes, and their genetic sequence can be established. The order in which the molecules are arranged is all important to what it is that the virus can do, and in special research laboratories the viruses can be, if you like, numerated in great detail, and those who are expert in this field will think, oh, that's interesting, that sequence of bases is different to the sequence that we would normally expect from this virus. And this could be -- we could be looking at an entirely new variant or strain of the virus.

Q. If you go on at the bottom of page 10, doctor.

A. Thank you.

Q. I think to a certain extent this is something you've already said, that effectively they're parasites.

A. Yes, they're parasites. They need the internal environment of a host cell in order to create new virus particles. The infectious virus particles are called

virions. Periodically, maybe every few hours or every few days, new virions are discharged to the exterior of the infected cell, and so therefore the cycle of viral infection is perpetuated.

MR GALE: Right.

That's probably a point to stop, my Lord. The next section is slightly lengthy.

LORD BRAILSFORD: No, no, not at all. Very good.

Well, thank you, Dr Croft.

A. Thank you.

LORD BRAILSFORD: Thank you, everyone else. We will adjourn now until 10 o'clock tomorrow morning.

Thank you very much indeed.

(3.58 pm)

(The hearing adjourned until Thursday, 27 July 2023 at 10.00 am)

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