Submission to the COVID Inquiry from Ewan Birney (birney@e[redacted]

A brief overview of your qualifications, career history, professional expertise and major publications.

I am Deputy Director General of the European Molecular Biology Laboratory (EMBL), an international treaty organisation which has one of its six sites at EBI (European Bioinformatics Institute) just south of Cambridge. I am a leading genomicist, with a strong focus on human genetics, but with a broad understanding of genomics across life and a data scientist. The data science techniques I have in my own research and more broadly across the institute can be applied to many problems, with a mix of practical "data engineering" to more advanced algorithm/model driven interpretation. I have published over 200 articles, some of which have been heavily cited (https://scholar.google.com/citations?user=ftd3UB0AAAAJ&hl=en). I am a fellow of the Royal Society, the Academy of Medical Sciences and the European Molecular Biology Organisation. I am a non-executive Director of Genomics England, a wholly owned company by the Department of Health to deliver genomics for the NHS. Finally I have an extensive international network of colleagues in genomics and data science worldwide, in particular across Europe, many of whom provided formal or informal advice to their respective governments as well as analysis on the pandemic.

A list of the groups (i.e. SAGE and/or any of its sub-groups) in which you have been a participant, and the relevant time periods.

I joined on founding the International Best Practice Advisory Group (IBPAG) in April 2020, and was also on the Transmission and Ethnicity Sub groups of SAGE. I contributed by invitation to some main SAGE meetings.

An overview of your involvement with those groups between January 2020 and February 2022, including:

When and how you came to be a participant;

During April 2020 there was a new Cabinet Office/Foreign Office grouping made (I believe) from Civil servants who handled security matters. One of those people (Rob Harrison) I knew personally, and had already drawn the analogy between open source intelligence gathering and the open academic community. Rob and colleagues started the international best practice advisory group between the Cabinet Office and the Foreign Office, bringing in diverse scientists, economists, policy makers and practioners to provide advice about best practice from other countries into the UK context.

Both via this route, and due to my institute's (EMBL-EBI's) provision of fully open viral sequences (the COVID19 data platform - https://www.covid19dataportal.org/ and other tools) I was aware of many aspects of SARS CoV 2 science; this included the source apparent mutations due to sequencing errors, the broad data engineering challenge of the pandemic from test results through to viral genomics, the interaction of human genetics and ethnicity on COVID severity (a complex story) and emergence of biologically new strains of COVID. Due to this I and colleagues were involved in specific projects.

I also had numerous direct emails with Rob Harrison and some other Cabinet office teams, and would send Patrick Vallance and Chris Whitty emails, who I knew personally (Patrick better than Chris) in particularly when there was clear evidence in a foreign country which I could transmit with confidence to them.

Reciprocally I was contacted and/or informed other leading country scientists, in particular in France and my colleague, Rolf Apweiler, in Germany. I had contacts with scientists in Sweden, Austria, Japan and India. For any substantive issue of information originating from the UK system which was not clear whether it was public domain (which was rare - the UK system was good at publication at many different levels) I would check with Patrick or others.

A final point to note is that before the pandemic I was a long established consultant to a new sequencing technology company, Oxford Nanopore, and I continued to consult for them through this, in particular in the development of their LamPORE product which is an alternative to RT-PCR with far, far higher multiplexing capabilities and a different supply chain from RT-PCR. I declared this conflict interest on all forms, and would remind people of this conflict of interest when the conversation turned to these topics in meetings. Nanopore was also used for Genomic Sequencing of SARS-CoV-2 in many settings (both in the UK and worldwide).

The number of meetings you attended, and your contributions to those meetings;

The IBPAG met weekly on a Tuesday with minutes for the majority of 2020 and much of 2021, and then fell back across 2021 and early 2022. The SAGE Transmission group met somewhat less frequently but regularly.

Your role in providing research, information and advice.

The main role in IBPAG was to be a critical friend/challenge/brain trust to the IBGAP team putting together reports for Cabinet Office/Foreign Office. Some of this challenge was relatively superficial (how best to represent international comparisons) whereas others was far more profound; why did for example public health interventions in Japan to reduce transmission work so much better than in the UK? The international comparisons gave an important lens on this.

The advice/challenge here was rooted in international comparisons and there was an admirable policing of not trying to stray into analysis and "definitive" advice for UK decisions, which was the remit of SAGE (and sub groups). However, many people had overlapping roles in SPI-M settings and in other groups (myself included) so the thinking/data analysis process often informed other discussions.

Two things to stress here; Patrick and Chris, and others in SAGE had a number of deeper, broader and more diverse contacts internationally, and it was I think important to have a variety of links at a variety of levels but with clear analysis and advice going to government.

Secondly the UK system had an admirable commitment and realisation of (a) data and analysis publication (for me the benchmark here has to be other countries) (b) a "single source of truth" and "single consolidated advice/options" mindset which was true at the very least for the infection and health aspects and (c) a clear view that the route to influence the scientific advice lead through SAGE and represented by Patrick+Chris at the end of the day. I considered my role to be part of that scheme.

A summary of any documents to which you contributed for the purpose of advising SAGE and/or its related subgroups on the Covid-19 pandemic. Please include links to those documents where possible.

There are two scientific publications which I was co-author on which represented some of the more in depth analytical aspects of advice I was involved in. There are often documents with the components of this as advice nearer the time but it is quite complex to pick apart where those documents are (expect to say in SAGE publications)

https://europepmc.org/article/MED/34649268

Infection tracking/modelling in the UK split by variant, which was excellent work from the analytics at EMBL-EBI from Harald Vohringer and Mortiz Gerstung using the simply excellent broad and deep sequencing from the COG consortium. This paper (which spans the rise and fall of Alpha and the rise and fall of Delta) was published far later than the analysis that fed through into the system; the first of which was December 2020 around Alpha. Figure 3 I think is particularly important as it shows two things. Firstly in Figure 3(c) that (counterintuitively to most commentators) the Tiering system in the autumn of 2020 was close to effective for *non alpha* (ie, original Wuhan) variants, with Tiers 3 and 4 estimated to have R at or below 1 - however, this scheme could not hold Alpha. Secondly a version of Figure 3e was one of the key figures in realising that Alpha could not be held by the previous ways of preventing transmission in very early Jan 2021.

One should carefully consider the counterfactual of what would have happened if infection data (RT-PCR) and sequencing data (COG) was not being collected and analysed at pace. Almost certainly the rise of Alpha would have gone unnoticed for a longer time in the background of reasonably large infection; by the time the downstream consequences on hospitals admissions occured it would have been perhaps even worse than March 2020, closer to perhaps to the northern Italian situation.

All credit here should go to COG-genomics and Harald and Moritz; I was one of the routes for this analysis to be understood by the system.

This second paper was the culmination of the observation that in particular in Japan, but also other places such as Germany, South Korea and Taiwan, a fundamentally higher level of transmission suppression could be achieved for a given level of broad societal controls (lockdown rules). The Japanese experience here is particularly informative, as they were informed by the transmission patterns of SARS-CoV-1 and implemented very early on a specific form of backtracing, which is a well established intervention for infectious disease in particular where there is a single geographic site of infection (eg, an infected water system) or a long incubation period (eg, TB). The goal is to identify the point of infection from infected individuals, and then identify other people who are infected but often unaware from this point of infection in the past. It is to be contrasted to forward tracing which is to find the people which a currently infected person could have infected. Many countries, the UK included, performed back tracing, but mainly to inform risk assessment of types of places for transmission. A few countries, notably Japan and Germany performed back tracing *and* acted on it within a time window for that infection train. Only in Summer of 2021 did this happen for a brief time in England, and this scientific work was part of the evidence to show it would be effective.

https://europepmc.org/article/PPR/PPR369557

A summary of any articles you have written, interviews and/or evidence you have given regarding the work of the above-mentioned groups and/or the UK's response to the Covid-19 pandemic. Please include links to those documents where possible.

Although this seems very modern, I made a point of providing my thoughts on the pandemic in long(ish) twitter threads. This was partly a way to make sure my thoughts were publicly available; the other aspect was that it allowed people in other countries to tap into my perspective from afar. I know that these twitter threads were useful, mainly beyond the UK. Here is one example.

https://twitter.com/ewanbirney/status/1451945802646138887?s=20&t=w43xb_m_nrlrED6CL1Ce2g

Your views as to whether the work of the above-mentioned groups in responding to the Covid-19 pandemic (or the UK's response more generally) succeeded in its aims. This may include, but is not limited to, your views on:

a. The composition of the groups and/or their diversity of expertise;
b. The way in which the groups were commissioned to work on the relevant issues;
c. The resources and support that were available;
d. The advice given and/or recommendations that were made;
e. The extent to which the groups worked effectively together;
f. The extent to which applicable structures and policies were utilised and/or complied with and their effectiveness.

Your views as to any lessons that can be learned from the UK's response to the Covid-19 pandemic, in particular relating to the work of the above-mentioned groups. Please describe any changes that have already been made, and set out any recommendations for further changes that you think the Inquiry should consider making.

This is a wonderfully open-ended question, and I will endeavour to answer it as best as I can. Firstly, and obviously, this is just one view and certainly one will need multiple views from multiple people (the whole point of an enquiry). Although this has framed the question in a narrow way about how advice worked, I'd like to put the framing from my own perspective - firstly a comparative international perspective; secondly unpicking the difference between strategy/policy and operations, third a note about not strategically bridging infection through health to economics and finally the advice systems present in the UK (English) system over the pandemic.

Comparative International Perspective

A striking difference between scientific research and even its neighbouring practical utilisation in healthcare (whether infectious disease healthcare here or in other areas, eg, genomics) is that scientific research is instinctively international whereas many other aspects of society are very constrained by national systems and often struggle to get a perspective beyond national borders. This is important to place the UK's overall outcome in COVID in an international context, and then, in my view, be shameless in aiming to understand what things worked better elsewhere, why they worked better, and how that better delivery can work inside the UK. It is worth noting of course this process is reciprocal; many countries can learn from what worked well in the UK.

At an overall level UK came out as a reasonably standard large European country through COVID. I would claim Denmark as a far better (but smaller) country; Germany had a simply excellent start and much of its transmission suppression policy and operations worked well (more on this below) but was sorely let down by a strong vaccine hesitancy / political anti-vax at the end. France, perhaps the country with the strongest analogies with the UK, or more specifically England - highly centralised (inside England) I think performed somewhat better overall but it was a close run thing, with both systems making clear errors in hindsight.

This overall 10,000 foot high view I think hides a very bimodal response from the UK (again, predominantly English) system - some areas of complete world leading response, in particular in data collection, aggregation and openness (there were wry comments from German advisors that they just had to wait until things happened in England and Denmark before they could work out what was going on), the in-house vaccine development and vaccine roll out was excellent (and not something I was directly involved in, but clearly showed up in the data that I analysed or was involved in). In contrast there were some glaring mistakes and oversights in hindsight; the chronic dithering in March 2020 was one; the sending the elderly potentially infected in hospital back to care homes another; September-November 2020 a third. Some of these I have insight into, the early ones I don't though I urge the committee to carefully sort through systematic issues that lead to poor decisions and not the blame assignment to individuals which I doubt will be useful for future pandemic / crisis planning. This bimodal response/delivery can be contrasted to the French where there was less variance in both sides on the response.

I was not close to SAGE or decision makers in early March 2020, but a key aspect of that time is working out why the UK system apparently made many rushed (perhaps panicked) decisions in a short period of time despite having flagged the problem early on and having excellent analysis groups. I am sure the perspective "inside" the machine is quite different from the outside, but it is notable that France and Germany both made better decisions and also with less apparent panic. Unpicking this with clarity and understanding where there were structural components to fix will be a key point to learn from for the UK system.

Expanding from this example, I personally think that some level of systematic international response, almost as a grid of "event" and "response" across perhaps 10 different countries (say; England, Germany, France, Sweden, Spain, Italy as core "large European culture" countries; Japan, South Korea as open Asian societies, Denmark and Israel as two small countries with varied response and US probably) would provide great insight and allow people to see the art of the possible. Crudely if no country was able to achieve a particular "optimal" response then it is unlikely that the UK could have. Here it will also be easier to see where the UK system was effective as well.

Strategy/Policy vs Operational

From the start of the pandemic it was clear that there were very practical different operational level delivery of public health, infection characterisation and transmission control between countries. This is most clear cut when one considers Germany vs Italy - two places with early seeding from China, and yet suppressed in Germany and not in Italy (with disastrous results in early March 2020); Germany remains one of the best European countries for operational suppression of transmission certainly across 2020, leading to waves happening later in Germany in this year. There are also big and clear differences to the open Asian countries of Tawain, South Korea and Japan (I can't comment / use China's experience well for all sorts of reasons - the earliest events; closed system; poor data access and poor reporting). Focusing back on Germany, Germany's ability to suppress transmission using public health means was clearly far more effective than, say, Italy's, Spain's and the UK's

Some of this is structural - in the case of Germany, the distributed and private nature of their testing labs allowed them to scale up testing simply by providing reimbursement and free PCR designs. Another structural example is the allowed use of mobile phone mast tracking in South Korea. But much of this is also operational details - how, in fine detail, does public health infection tracking work in Germany and Japan. Over the pandemic there was one operational detail which I personally took all the way through - backtracing with action, described above - which is a self identified key aspect of the Japanese response and is implicitly present in the German system (which I describe as "total tracking"). It was a source of frustration that it took myself and other colleagues over 1 year to get the English system to get their head around it, though really the question here is having a public health system with enough capacity to deliver and innovate/adapt at the same time.

Drawing from this observation, I also note a huge tendency in many places, UK included, to focus on strategic, structural and policy debates, partly because they are easier to understand and partly because they often align with outside of crisis politics (big centre vs small etc) and partly because the response on operational effectiveness is to say "the best possible please".

During the crisis I also noticed that much of the scientific expertise was drawn towards these bigger picture questions and ultimately SAGE. I think this is inevitable and mirrored in other countries, but I felt that were always missing good, broad science delivery inside of organisations which could hear and ingest the arguments. Thinking about this carefully, I don't

think “scientists as external consultants” work well for delivery organisations because delivery is different beast and very details/logistics/operations driven; rather these organisations need to have “in house science groups” which understand the science and can bulk up in a crisis. Of course some of this existed in PHE and other organisations, but I felt we missed having a science cadre across the key delivery organisations.

Operational effectiveness is obviously important in delivery but it is also gives more time and space for strategy/policy decision makers, and more confidence to the strategy that it can be executed. Having good operational effectiveness is a no-brainer - noone is going to debate the benefits or not, but it is the hard yards of public health here to create and of course there is a link to straightforward business of funding. In many ways this is now the HSA improvement mindset (and I have huge respect of PHE colleagues and HSA now) but this is key to get at a high level “in peacetime” (ie, no pandemic) and can scale up when a pandemic happens.

Infection/Health/Economics models

One large scale lacuna worldwide was the lack of end-to-end frameworks/models that spanned infection (SIR models etc) through to health (Hospital capacity modelling, ICU capacity etc) through to economy (impact of different measures). There was the ability to bridge from infection to health models, though knowing at least the existence of the very data driven NHS capacity models present in the pandemic we could have probably linked these even better. It is frustrating because the respective academic fields of infection epidemiology, health economics/health operations and economics cost benefit analysis actually have many methodological similarities and surprising synergies. Having thought about this quite a bit, I don’t think a joint model would have necessarily changed much - once we knew a vaccine was feasible (say, June/July 2022 it was clear it there was some reasonable probability something would work) then enough suppression for control was the right policy until you knew how much the vaccine would change things (as it happened; an awful lot). A key aspect of this is the healthcare capacity present at any particular time. However, a joint model would have clarified thinking and given more confidence to economic/treasury policy people that broadly the right strategy would be followed; this in turn would likely have made early and sharp suppression decisions in the autumn of 2020 clearer that this was the right approach.

The structural fix here I think is quite simple; explicitly fund end-to-end infection/other health events/crisis modelling with economics at a macro level as an academic multi-disciplinary area. It’s frustrating we didn’t have this in 2020; no reason we can’t in the future.

The other aspect of economics is that there is a good argument that the interaction between the research economics through to synthesised advice to policy makes in the Bank of England Interest Rate committee and the Office for Budget Responsibility have a good understanding of how to synthesise diverse inputs and then present to policy/decision makers. These structures are well understood by actors who consume advice. There is something to learn from economics here in this interface of advice into the system.

Advice

Broadly I think the advice from the UK system was good to excellent. It excelled at data aggregation and timely analysis in a way most other large countries could not get close to (in fact I don't know a better country). This is different than saying whether the advice was acted on appropriately. This is absolutely demonstrable for genomic sequencing, but in fact the RT-PCR positive data was just as important and just as important it was aggregated and analysed by a variety of people.

I think SPI-M did really well. Graham Medley was an extremely good chair of a complex area. However, I think the presentation of the advice/synthesis into the system could have been improved with more of the aspects of OBR / Bank of England.

SAGE overall was good. It was a brains trust I feel for Patrick and Chris and they used it this way; the fact that there were two people to absorb this information and transmit it into central government I think was good. I know people could see the points where there was potential "advice positioning" - ie, when the advisors couch the outcomes in a slanted way, but actually the vast majority of the time this was following the correct "Reasonable Worse Case Scenario" mantra, which is wise. For example, the reasonable worse case scenario on the rise of Omicron was pretty bad, even if the outcome was (due to biological properties of the virus variant) some way better. I think complaints of slanted advice are broadly overblown (though not zero). Certainly it was not obviously different in France and Germany from my perspective.

To answer the questions specifically.

a. The composition of the groups and/or their diversity of expertise;

Good. I liked the practitioner perspective in IBPAG.

b. The way in which the groups were commissioned to work on the relevant issues;

Broadly good, though I think we could get stuck on some things. We needed to kill some irrelevant discussion

c. The resources and support that were available;

Good.

d. The advice given and/or recommendations that were made;

I think overall good with options. There will be some picking over the bones here but I urge the committee to benchmark globally not to perfection.

e. The extent to which the groups worked effectively together;

This was very good.

f. The extent to which applicable structures and policies were utilised and/or complied with and their effectiveness.

Please note the above section on operations.