



Contribution to the discussion of AIDS and COVID-19: A Tale of Two Pandemics and the Role of Statisticians by Ellenberg and Morris.

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3 Contribution to the discussion of AIDS and COVID-19: A Tale of Two Pandemics and the
4 Role of Statisticians by Ellenberg and Morris.
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6 Valerie Isham, 2 February 2021
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9 Ellenberg and Morris give an excellent and comprehensive discussion of the considerable
10 challenges for statisticians, working alongside scientists from many other disciplines, in their
11 quest to understand the dynamics of SARS-CoV-2, and to design and develop intervention
12 strategies that, ultimately, can bring the Covid-19 pandemic under control. In doing so, they
13 point out some of the similarities and differences between the current pandemic and that of
14 HIV/AIDS almost 40 years ago. In this contribution, I will highlight some comparisons from
15 a modelling perspective.
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19 The models used for HIV in the 1980s were broadly similar to many of those used for Covid-
20 19 today. Mechanistic deterministic or stochastic compartmental models, with varying
21 degrees of complexity but largely based on the traditional SIR form, were used for scenario
22 analyses while statistical curve fitting methods enabled short-term prediction. Longer-term
23 output based on fitted models with specific assumptions was used, then as now, to provide
24 bounds on what might occur if there were no changes in behaviour or policy. Since then,
25 computational advances have allowed the development and analysis of very much more
26 complex model structures including network and agent-based models fitted to huge data sets,
27 but then, with far fewer resources available, only simple stratified models were feasible. The
28 fitted models and their output, based on different structures and assumptions, were interpreted
29 separately: the methods of model combination and uncertainty quantification employed
30 today¹ that make due allowance for uncertainty in model structure as well as in data and
31 assumed parameter values were lacking then, and expert elicitation was informal.
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37 Mechanistic models were generally analysed by numerical solution of differential equations
38 or by using simulations, although qualitative understanding and important insights were
39 obtained algebraically. For example, simple deterministic models allowing heterogeneity of
40 the rate of effective contacts were used to show that at the beginning of the epidemic it was
41 the index of dispersion of the rates, rather than their mean, that was driving the spread². This
42 understanding informed a policy decision to target information especially towards those with
43 contact rates in the top tail of the distribution. Then, as now, in assessing behaviour changes
44 it was difficult to separate the effect of such policies from that of experiencing illness and
45 death among close friends and family.
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50 In an SIR model, the R is generally described as *removed*, rather than *recovered* as by
51 Ellenberg and Morris. As such, this class consists of those no longer contributing to the
52 transmission of infection: often those who are recovered but, depending the application, it
53 can also include those who have died or been quarantined (extra model compartments can be
54 added to distinguish these states if required). In the case of HIV, simple SIR models were
55 used from the outset, with the earliest models designating the I (infective) stage to consist of
56 those infected with HIV, who would progress to the R stage on diagnosis with full AIDS, it
57 being assumed that after diagnosis they would no longer have infectious contacts. The state-
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3 space of the simple three-stage SIR model was gradually extended to allow for population
4 heterogeneity by incorporating age structure and other factors affecting infectivity and
5 disease progression, for heterogeneity of mixing through varying contact rates among
6 different subpopulations, for variable infectivity at different stages of the infectious period,
7 and for different modes of transmission³. The unrealistic but convenient Markov assumption
8 of an exponentially distributed incubation period was sometimes avoided by using a Weibull
9 distribution with its algebraically tractable hazard function, or by adding further
10 compartments so that it was represented as a sum of independent exponential variables (the
11 method of stages). Compartmental models for Covid-19 have a similar overall form, although
12 with much larger populations at risk of infection and for which regional variation is an
13 important source of additional heterogeneity. Much finer gradations of states are now
14 computationally tractable and very detailed population structures can be assumed. In the early
15 stages of both pandemics, there was great uncertainty about mechanisms, distributions and
16 parameter values and a corresponding need for sensitivity analyses and modification of
17 assumptions as more evidence became available.

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24 Ellenberg and Morris describe the many problems associated with data for Covid-19. For
25 HIV, initially, data were very limited. The time scales and courses of the two infections are
26 very different, but the lack of data on asymptomatic infections with Covid-19 in some sense
27 parallels that on early infections with HIV where there was a long and largely asymptomatic
28 incubation period before AIDS symptoms developed. The primary data were of AIDS
29 diagnoses and, except for transfusion recipients, times of infections could generally not be
30 pinpointed. In the same way that data on the outbreak of Covid-19 on the Diamond Princess
31 cruise ship provided early information on Covid-19 transmission, so these transfusion data
32 provided information on the distribution of the incubation period between infection with HIV
33 and diagnosis with full AIDS (albeit that distribution might not be the same for those infected
34 by other means). Convolution of the estimated distribution of the incubation period with the
35 unknown HIV incidence curve would give an estimate of the incidence of AIDS diagnoses
36 and so, in reverse, deconvolution using data on AIDS incidence allowed the back-calculation
37 of the incidence of HIV infections up until the current time; similar methods are used with
38 Covid-19 to infer infections from case data. Finally, forward convolution could be used to
39 predict the numbers of future AIDS cases³⁻⁶. These predictions would not include anyone not
40 yet infected, but given the length of the incubation period, should not seriously underestimate
41 the true values in the short-term.

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48 Non-pharmaceutical interventions (NPIs) were used from the outset to control HIV, as they
49 are now for Covid-19. One of the most important uses of model scenarios is in helping to
50 develop and assess possible strategies for the use of NPIs, as well as to compare vaccination
51 regimes, to inform government policies worldwide. The state spaces of compartmental
52 models can easily be extended to include vaccinated individuals, although assumptions must
53 be made about the appropriate (time-dependent) levels of protection from disease and
54 reduction in transmission that vaccination confers. However, incorporating NPIs in such
55 models is often challenging, as many are not well set-up properly to incorporate highly local
56 or individual measures. While, to an extent, simple scaling parameters can be introduced to
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3 allow for the reduction in effective contacts resulting from NPIs such as mask wearing or
4 social distancing, track-and-trace measures are most easily incorporated in highly detailed
5 agent-based models. Modelling behavioural responses and compliance with interventions
6 and, also, allowing for possible feedback from individual experiences of the course of the
7 pandemic itself, present further challenges. Once control measures are decided upon, the
8 models can be used to suggest what data should be collected to assess their effects, and a
9 particular problem, given the incredibly rapid evolution of the pandemic, is how to use
10 observed data to disentangle the effects of different interventions applied simultaneously or in
11 overlapping time periods, or to different populations.
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16 As well as the much more rapid spread of infection, and the very much greater computing
17 power now available, there are other significant differences between Covid-19 and
18 HIV/AIDS. The speed at which the Covid-19 epidemic is spreading through the global
19 population means that epidemic modellers and statisticians are working under much greater
20 time pressure to provide model output and updates to inform official policy. However, the
21 need to ensure that the many assumptions, caveats and accompanying estimates of
22 uncertainty are carefully communicated to (and understood by) policy makers remains
23 unchanged. The modelling and statistical communities working on Covid-19 are orders of
24 magnitude bigger than the handful of those working on HIV/AIDS 40 years ago. Building
25 from that base, and by gaining experience in the intervening years through tackling the
26 frequent human and animal epidemics occurring round the world, there is now a substantial
27 network of researchers with good multidisciplinary and international links able to bring their
28 skills to bear on the pandemic. Much more can be done very quickly: there are many new
29 sources of data to be understood and assimilated, following the huge advances in genome
30 sequencing and phylogenetics, and in just a year several vaccines for SARS-Cov-2 have been
31 developed, tested and rolled-out around the world. On the other hand, effective treatments are
32 still in the early stages of identification and development. In contrast, there have been very
33 considerable advances in antiviral prophylactics and treatments for HIV infection over the
34 last 40 years, but there is still no vaccine.
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42 For the future, further pandemics are inevitable; since 2014, five Public Health Emergencies
43 of International Concern have been declared, four due to viruses of zoonotic origin⁷. Given
44 the wide-ranging and serious effects of pandemics such as Covid-19 on individuals and
45 nations, planning and preparedness are essential and present many challenges for modellers⁸.
46 Not least among these is a need to widen the interdisciplinary network of modellers yet
47 further by including social scientists and economists, with the aim of combining behavioural,
48 economic and epidemic models to provide a transparent methodology for assessing together
49 the health and economic effects of pandemics.
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