COVID-19 IN SCOTLAND: WHAT NEXT?

A personal view

[REDACTED], University of Edinburgh, 14/07/20

KEY POINTS

1. Thanks to the progress made thus far, the public health benefit of further suppressing COVID-19 in Scotland is questionable.

2. Suppressing COVID-19 to the point of elimination would likely require lockdown to be strengthened and extended for at least another 6-12 weeks, plus the introduction of a cordon sanitaire around Scotland. These interventions would have associated harms.

3. No country in the world has yet achieved COVID-19 elimination and an elimination strategy in Scotland at this stage of the pandemic would be highly likely to fail.
4. The key strategic decision at this time is whether response capacity is sufficient to allow the effective reproduction number (Re) to rise above 1. This has far greater consequences than the differences between low, very low or zero incidence.

5. It is likely that a return to anything approaching pre-COVID-19 normality would require the capacity to Detect and Isolate (D&I) a significant fraction of infections prior to symptoms appearing.

6. D&I on a large scale would be a very challenging task, but may be a sustainable approach to keeping COVID-19 incidence in Scotland at current levels or lower for the next 12 months or more.

7. Testing on demand might achieve the necessary coverage, but take-up may be heterogeneous – this needs to be assessed.

8. Protecting the most vulnerable groups is key to minimising the long term public health impact of COVID-19.

SECTION 1: Elimination and containment

Semantics

9. ‘Elimination’ is a formal public health term that refers to zero cases for a defined period of time [https://www.cdc.gov/mmwr/preview/mmwrhtml/su48a7.htm].

10. A strategy that aims for elimination therefore must succeed in delivering zero cases for the prescribed period of time.

11. A ‘cordon sanitaire’ is a barrier to the introduction or re-introduction of infection to a region that has eliminated the infection [https://www.cdc.gov/sars/guidance/d-quarantine/lessons.html].

12. Given that the threat of COVID-19 is expected to persist indefinitely, a cordon sanitaire is an essential component of an elimination strategy.

13. ‘Containment’ refers to the prevention of community transmission [https://jamanetwork.com/journals/jama/fullarticle/2764956].

14. A strategy that aims for containment therefore must succeed in preventing community transmission but accepts that sporadic cases and localised outbreaks may occur.

Current situation

15. The public health burden of COVID-19 in Scotland in terms of hospitalisations and deaths is currently very low.

16. Numbers of reported cases are also low. Estimates of total incidence (possibly hundreds of cases per day) are higher but uncertain [SPI-M consensus statement 08/07/20].

17. The R number (case reproduction number) in Scotland is currently below 1. This means that a large scale epidemic (a second wave) is not anticipated, but localised outbreaks could still occur. The closer the R number is to 1 the more frequent, larger and longer these outbreaks will be unless rapidly controlled.

18. It is likely that only a small fraction of cases is being imported from outside Scotland and these do not currently pose an exceptional risk.

19. Nonetheless, the threat of COVID-19 from outside Scotland is likely to persist indefinitely.

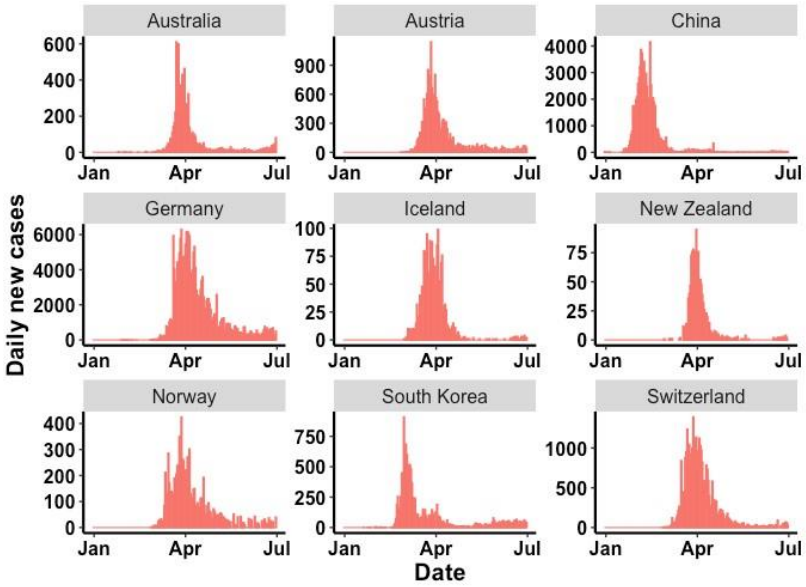
20. Current SG policy (phase 3) is for the gradual relaxation of restrictions. Any further relaxation makes elimination less achievable.

21. Further relaxations are anticipated in the coming weeks/months (Phase 4). These relaxations – including the re-opening of schools – will also make elimination less achievable.

Is Scotland exceptional?

22. No country in the world has yet achieved elimination of COVID-19.

23. Countries which have controlled their epidemics successfully are all experiencing sustained epidemic tails (Figure 1).



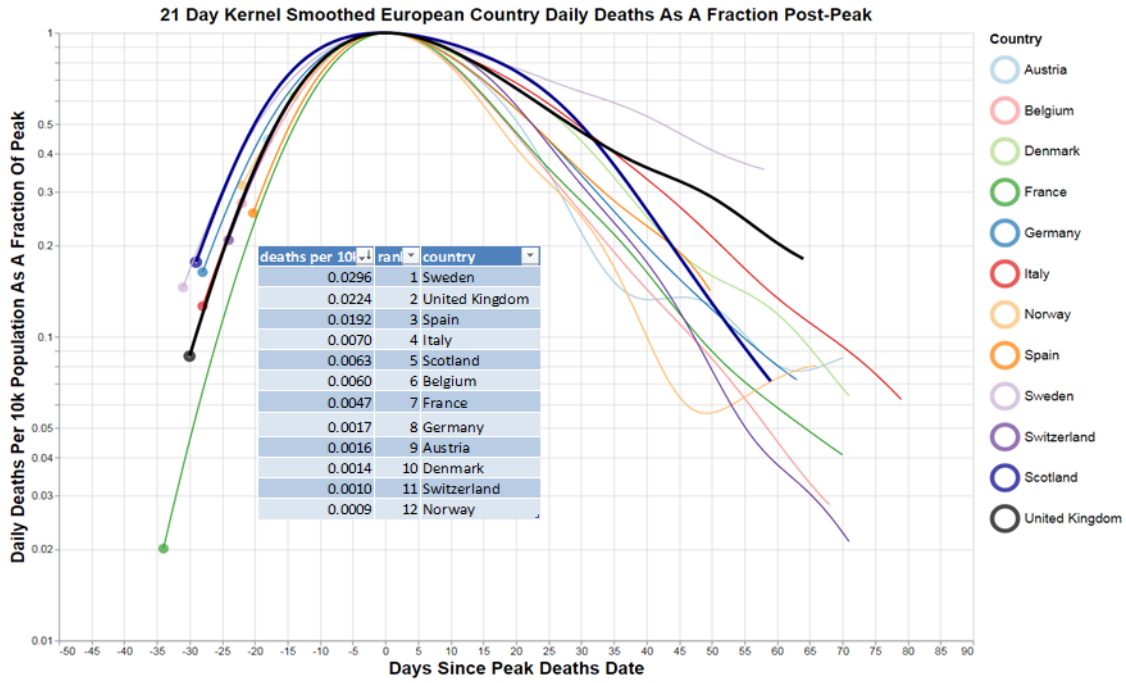
Source: European CDC (accessed 1230 30/06/2020)

Figure 1. COVID-19 epidemic curves for nine countries up to early July 2020.

24. This list includes countries that have implemented very strict lockdowns (e.g. China) and/or highly effective contact tracing and outbreak control (e.g. South Korea).

25. The course of Scotland's epidemic has been unexceptional among European countries (Figure 2):

    a. The initial rate of growth of the epidemic was similar across European countries
    b. The peak of the epidemic (as deaths per capita) was more variable (largely determined by the timing of lockdown) - Scotland had a close to median value
    c. The rate of decline from the peak is also variable – Scotland has a close to median value



1. European Centre for Disease Prevention and Control. (2020). *Geographical Distribution 2020 nCoV-Cases Worldwide.* https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases
2. Scottish Government. (2020). *Coronavirus (COVID-19): Trends In Daily Data.* https://www.gov.scot/publications/coronavirus-covid-19-trends-in-daily-data

Figure 2. Comparison of Scotland's COVID-19 epidemic with 11 other European countries. Smoothed epidemic curves are show relative to epidemic peak. Height of epidemic peak (deaths per capita) are also shown (inset).

A strategy that is proportionate

26. The perceived public health benefit of elimination needs to be clearly articulated so that it can be weighed against the costs.

27. Elimination is much more likely to be achieved by reverting to a strict lockdown (in contrast to the current policy of gradual relaxation).

28. The first 12 weeks of lockdown were justifiable by the imperative to reduce the huge public health burden of COVID-19. Nonetheless, lockdown itself has caused huge harm in terms of access to health services, mental health, education and jobs and livelihoods.

29. An extension and strengthening of lockdown would deliver far less public health benefit, as the COVID-19 burden is currently low. The harms that lockdown causes, however, would be the same.

30. A key consideration is the duration of an extended lockdown; this is likely to be at least 6-12 weeks (see Box 1).

31. Driving incidence to zero could be justified if it had long-term benefit, but any benefit is likely to last just a few weeks (see Box 1).

BOX 1: Duration of benefit

Given a current incidence of 10-100 new cases per day and a R value of 0.7 and assuming a generation time of 7 days it would take approximately 6-12 weeks to achieve incidence <1 new case per day.

If Re was allowed to rise back to 2.4 (see Section 2) then given an initial incidence of 1 new case per day it would take approximately 3-5 weeks to return to an incidence of 10100 new cases per day.

A strategy that is sustainable

32. If Re<1 then the public health burden can be maintained at or below the current level.

33. Maintaining Re<1 would require highly effective NPIs to be maintained for a prolonged period (see Section 2).

34. It will be essential to maintain the capacity to rapidly and effectively control any outbreak as long as COVID-19 is a threat to Scotland and Re>1, regardless of incidence.

35. It is widely accepted that global eradication of COVID-19 is not currently feasible (and may never be).

36. The public health threat of COVID-19 could be reduced by development and deployment of an effective vaccine. It is not possible at this time to say when or even whether that might happen.

Elimination versus containment

37. Elimination implies zero public health burden; containment implies some public health burden, though this is small if incidence remains around current levels.

38. Elimination would likely require extended lockdown; containment would not.

39. Elimination would require a strict cordon sanitaire around Scotland (Box 2). This implying severe travel restrictions for residents as well as visitors. Containment does not, and could replace quarantine of arrivals by testing.

40. New Zealand's elimination strategy is having severe impacts on its tourism and further education sectors [https://informedfutures.org/wpcontent/uploads/Re-engaging-NZ-with-the-world.pdf]. The same sectors are important to Scotland's economy.

BOX 2: Impact of a cordon sanitaire

A cordon sanitaire is surely among the oldest of public health intervention.

It is generally used by a population that does not have an infectious disease present to protect itself from populations where the disease is present or may be present.

The value of a cordon sanitaire depends on the epidemiological context:

1) It is most useful when the infection is absent (zero prevalence) but a single infection could spark an epidemic (Re>1).
2) It is least useful when infection is present already and a single infection could not spark a full epidemic (Re<1).

As of July 2020 Scotland is in the 2nd state.

The relative contribution of arrivals from outside depends, inter alia, on the levels of infection at the point of origin and the destination, modified by relevant individual risk factors.

The population-level risk from arrivals is mediated by the volume of traffic. This may vastly outweigh the effect of level of infection at the point of origin (e.g. Ireland, with a low prevalence, may pose a greater population-level risk to Scotland than Brazil, with a high prevalence, because the volume of traffic from Ireland is much greater than that from Brazil).

There is a risk from returning residents as well as from visitors.

A cordon sanitaire need not involve quarantine. The use of test-on-arrival plus a follow-up test may be almost as effective, possibly as effective if compliance is higher (APHA report: International Travel Risk Assessment for COVID-19, July 2020).

41. For both elimination and containment, if Re>1 then measures must be in place to rapidly and effectively control any outbreak.

42. If Re>1 and measures are insufficient to control any outbreak then elimination should delay, but is unlikely to prevent, a major outbreak and re-introduction of lockdown.

43. If elimination were to fail then the strategy would revert to containment by default.

44. Containment has been used successfully to stabilise case numbers, e.g. Hong Kong [https://www.ijidonline.com/action/showPdf?pii=S12019712%2820%2930492-6].

45. The public health impact of COVID-19 outbreaks can be greatly reduced by protecting those most vulnerable to adverse outcomes of infection.

SECTION 2. Contribution of testing

This section considers testing for the presence of virus which requires a RT-PCR test. Testing for the presence of antibodies fulfils a different function.

The great majority of virus testing that has been carried out in Scotland to date has been either (i) to confirm infection among individuals who should already be selfisolating and, if necessary, receiving treatment or (ii) to release those self-isolating due to symptoms but do not have COVID-19 – the 'back-to-work' test.

Neither use of tests will have had much of any impact on R, incidence or the death rate because neither helps to reduce transmission rates (Annex B). A reduction in transmission can be delivered by using testing to identify and isolate individuals who do not know they are infected.

Test & Protect (T&P) reduces transmission by using positive test results to trigger attempts to quarantine contacts.

Benefits of testing to reduce transmission are contingent on a rapid turnaround: same day results will have considerably greater impact than a 48 hr delay.

The analysis below is intended to quantify the expected contribution to reducing transmission that testing individuals who do not know they are infected would need to make to prevent subsequent epidemic waves. All numerical values are illustrative only – they are not predictions.

Targeting symptomatic cases

Assume R0=**2.4** [highly optimistic; R0 estimates for Scotland range as high as 6]

Therefore, in absence of other measures, need to reduce transmission by >75% to keep Re<1.

Estimated that only **50%** transmission is from symptomatic cases [1].

Implies that even 80% effective prevention of transmission by symptomatic cases (target of T&P) would not be enough (40% reduction to Re=1.44). A more realistic **50**% effectiveness would leave more to do (25% reduction to Re=1.8).

Implies that to achieve Re<1 would need at least a further **44**% reduction in transmission rate.

At present, this reduction could only be achieved by NPIs, e.g. a continuing (partial) lockdown, use of PPE and social distancing.

The alternative route to reducing Re is by finding pre-symptomatic and asymptomatic cases.

Targeting pre-symptomatic and asymptomatic cases

It is believed that asymptomatic infections make a small contribution to Re [1], so the focus here is on pre-symptomatic infections.

Pre-symptomatic infectious period 1-3 days.
It is not clear if RT-PCR can reliably detect infection before the onset of infectiousness.

- If it can then up to 100% pre-symptomatic infectiousness can be prevented if test results are available before infectious period begins.
- If it cannot then up to 50% pre-symptomatic infectiousness can be prevented if test results are available the same day.

- In both cases 100% of symptomatic infectiousness could be prevented.

False positives

A significant problem with screening in the absence of symptoms is the number of false positives. False positives could greatly outnumber true positives if prevalence was low.

This problem could be addressed by double testing (preferably of the same sample).

Consideration would need to be given to the status of non-symptomatic individuals who test positive while a confirmatory test is awaited. However, this is essentially the same issue as the status of individuals with symptoms while test results are awaited.

The disadvantages of generating false positives need to be weighed against the advantages of reducing transmission.

Targeting both symptomatic and pre-symptomatic cases

Measures targeted at all symptomatic cases might achieve **25**% reduction in Re.

Measures targeted at X% pre-symptomatic cases could further reduce Re by up to X%.

If R0=**2.4** [optimistic] then, in the absence of NPIs, X would need to be **44**%. This is a very ambitious target.

If R0=3 then X would need to be 56%.

If R0=4 then X would need to be 67%.

NPIs could also be used to reduce transmission. To achieve X=0% (i.e. no need for D&I of pre-symptomatic cases) requires Re=1.33. This implies at least a **45**% reduction in R0 (from 2.4) due to sustained NPIs (e.g. face coverings and social distancing norms). It is not clear that this is achievable. The shortfall would need to be met by D&I of pre-symptomatic cases.

More detailed modelling is needed to estimate the required coverage. A possible approach would be to prioritise high risk groups and to offer testing-on-demand (see Box 3).

Testing on demand would need to be linked to specific recommendations for the circumstances were individuals should demand testing. Active efforts would need to be made to ensure that all sectors of society had equitable access to testing on demand.

Conclusion

Even under the most optimistic assumptions it may not be possible to maintain Re<1 without a combination of:

- T&P as effective as possible;
- and additional NPIs (e.g. face coverings and social distancing norms);

- ***and*** early detection of a substantial fraction of pre-symptomatic infections, possibly achieved by a combination of targeting high risk groups and testing on demand.

These conclusions are consistent with a DELVE study that indicated that for Re substantially above 1 T&P alone is far from adequate [2] and a PNAS paper that concludes that symptom-based contact tracing needs to be complemented by case isolation based on detecting pre-symptomatic cases [1].

1. https://www.pnas.org/content/pnas/early/2020/07/02/2008373117.full.pdf

2. https://rs-delve.github.io/reports/2020/05/27/test-trace-isolate.html

BOX 3: Priorities for testing

Aim: target testing capacity so as to reduce R, incidence and deaths as efficiently as possible.

Symptomatic cases are already prioritised. This may need to be supplemented by testing individuals who do not have symptoms and do not know they are infected.

Non-symptomatic individuals might be prioritised by:

1) likelihood they are infected;
2) consequences of their being infected, which reflects the number and nature of their contacts.

Health Care Workers and Care Home Workers (already prioritised) score highly on both criteria.

Other categories that might score highly on Criterion 1 include:

1) people leaving hospitals or care homes;
2) contacts of cases (already prioritised - should already be self-isolating so testing only really helps if it improves compliance); 1) people identified during an outbreak investigation;
2) people resident in known COVID-19 geographical clusters, 'hotspots'; 3) arrivals from countries with high prevalence.

Criterion 2 includes individuals in two sub-groups:

a) individuals who makes a large number of contacts, or make atypically close
contacts that increase risk of transmission;
b) individuals who will be in contact with a vulnerable person (i.e. >70 years old or with other risk factors for poor outcome).

Care-in-the-home workers score highly on both (a) and (b).

Informal carers and other 'shielders' score highly on (b).

Those regularly involved in specific activities, e.g. members of choirs, workers' dormitories etc.

More generally, both criteria may apply to many individuals transiently rather than permanently, perhaps linked to specific events, e.g. social gatherings, conferences, visits to care homes etc.

ANNEX A: R-effective (R_e)

The R number (case reproduction number) as it is used in SG strategy documents is a measured quantity.

But R can also be used as an estimate of transmission 'potential' – even in the absence of infection at the time. It is the average number of secondary cases expected from a single index case introduced into the population.

The maximum transmission potential – in the absence of prior exposure and of any countermeasures – is R_0. Otherwise it is known as R_e. R_e is less than R_0 because of any effects of immunity and measures in place that suppress transmission.

Like R, R_e is independent of prevalence, *even if prevalence is zero* (i.e. elimination). It is a measure of transmission potential. In other words, elimination (or not) has no effect on R_e.

A crucial policy question is what value of Re we are aiming at. There are three options: $R_e < 1$, $1 < R_e < R_0$ or $R_e = R_0$. These have very different implications both for what countermeasures are kept in place and for what response capacity would be needed in the case of outbreaks.

> $R_e < 1$ is the current situation. It implies i) little risk of a major outbreak though continued concern about clusters and high-risk settings and ii) sufficient lockdown measures still in place so that a new epidemic is not possible. This situation could maintain low levels of infection at a low level but with no return to anything like business as usual until other solutions (such as an effective vaccine) become available.
>
> $1 < R_e < R_0$ implies that single cases could spark off major outbreaks or even another epidemic (though not as explosive as the 1st wave). This corresponds to a combination of (likely partial) lifting of lockdown measures and or permanent measures in place to reduce transmission (e.g. social distancing practices; wearing of face coverings).
>
> $R_e = R_0$ was the situation in February. It implies i) a return to a pre-COVID-19 normality and ii) a risk of a fast-developing epidemic. This corresponds to a containment strategy with 'business as usual' otherwise.

The crucial distinction is between $R_e > 1$ and $R_e < 1$. Any strategy that allows $R_e > 1$ would have to be linked to a standing capacity to respond rapidly and effectively to new outbreaks, which would have the potential to become epidemics. That capacity would be needed for as long as there is any risk of COVID-19 being present or introduced into Scotland, i.e. indefinitely.

ANNEX B: Roles of testing

How rapid virus testing contributes to suppressing transmission of COVID-19

- **Testing is an essential tool** for delivering some but not all strategies for suppressing transmission. Testing to suppress transmission is about detecting unrecognised cases of infection (**false negatives**) who can then be isolated.

- A major potential benefit of testing is the detection of infection during the **pre-symptomatic phase** (24-48 hrs). To realise this benefit test results must be available rapidly (same day) and/or be sufficiently sensitive to detect infection early in the incubation period.

- Other uses of testing are very important in their own right but do not directly contribute to suppressing transmissions:
    - Testing to confirm suspected cases already being managed as infected does not suppress transmission further
    - Testing to identify **false positives** (based on symptoms) – the 'back to work' test – does not suppress transmission at all

- **Testing**, in itself, **is not a "strategy"** for COVID-19 control.

- Different uses may require massively different numbers of tests per day (see Table).

- **A headline count of the number of tests per day is almost meaningless** in terms of its contribution to epidemic management. What matters is the strategy the testing helps to deliver.

- **Speed is as important as scale**. Strategies to suppress transmission benefit from being linked to much more rapid testing.

TABLE. Main functions of testing, comparing strategies contributing to suppressing transmission (yellow) or having other functions (grey).

Activity	Can this be done on symptoms alone?	Benefits of 24-48hr testing?	Additional benefits of same day testing?	Additional benefits of antibody testing?	**Maximum** no. people in Scotland **per day** for whom useful to do rapid testing for virus
Social distancing	N/A	NO	NO	NO	N/A
Surveillance	N/A	YES	NO	YES	Population sample 100's
Clinical diagnosis	YES	YES	YES	N/A	ARI patients 1,000's
Return to work (false +ves)	NO	YES	YES	NO	(Key) workers with symptoms 1,000's
Contact tracing (at current levels of infection)	YES	YES	YES	NO	Contacts (x15-30) of everyone with symptoms or testing +ve 10,000's
Shielding	YES	YES	YES	YES	HWC, care home workers, carers, household members 100,000's
Self-isolation/quarantine	YES	YES	YES	NO	Everyone 1,000,000's

All activities would benefit if virus testing were available at the necessary scale.

However, all activities (except surveillance) would benefit even more if virus testing were also rapid.

To be effective, activities aimed at suppressing transmission are likely to require very large numbers of tests on a very regular (e.g. daily) basis.

There are very significant cost implications of large-scale daily testing.