I-MOVE-COVID-19 project

WP2 primary care meeting: Tuesday 05 May 2020

References

Author: (10)(2e) (10)(2e), (10)(2e) (10)(2e), (10)(2e)
Date: 05 May 2020 (11:00 hrs CEST)
Purpose: Minutes of the regular meeting

Attendees

	PARTICIPANTS
The Netherlands, Nivel	(10)(2e) (Work package leader)
Epiconcept	(10)(2e) (10)(2e), (10)(2e) (10)(2e), (10)(2e) (10)(2e), (10)(2e), (10)(2e), (10)(2e), (10)(2e), (10)(2e)
European Commission	(10)(2e)
ECDC	(10)(2e), (10)(2e), (10)(2e), (10)(2e), (10)(2e), (10)(2e), (10)(2e) (10)(2e) (10)(2e)
WHO-Europe	(10)(2e)
France, Sentinelles	(10)(2e)
Ireland	(10)(2e)
The Netherlands, RIVM	(10)(2e)
Portugal, INSA	(10)(2e)
Spain, ISCIII Epi	(10)(2e), (10)(2e)
Spain, ISPL Navarra	(10)(2e)
Sweden, PHA	(10)(2e) (10)(2e)
UK, PHS	(10)(2e) (10)(2e), (10)(2e), (10)(2e) (10)(2e), (10)(2e), (10)(2e)
UK, PHE	(10)(2e) (10)(2e)
UK, RCGP	(10)(2e), (10)(2e)
RECOVER	(10)(2e) (10)(2e) (10)(2e) (10)(2e)

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1. Agenda

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- AOB

2. Introductions

Welcome to all study sites, colleagues from ECDC and colleagues from WHO/EURO.

There was a welcome to Steffi Sowinski who is the H2020 project officer from the European Commission. Alike van der Velden, primary care WP lead of the H2020 RECOVER consortium, was also introduced. She outlined what they are doing in the primary care part of the RECOVER study: a registration study with GPs in 15 countries registering their consultations and patients presenting with suspected COVID-19; the second study is similar including swabs of patients seen at primary care, which will be analysed for COVID-19. Patients will be followed up for complications or management in primary care. They started their studies 3–4 weeks ago. (10)(2e) (WP2 lead) and (10)(2e) (10)(2e) (WP4) regularly join their TCs.

3. Main points

2.1. Welcome and general (administrative) issues

- Presentation by (10)(2e) (Nivel, WP2 lead) and (10)(2e) (10)(2e) (EpiConcept, Overall coordinator) outlining all admin issues (see presentation)

2.2. Looking forward: next deliverables

- The next deliverables due are
  - The WP2 protocol on the 15th of June
  - The surveillance monitoring and evaluation protocol on the 15th of July
  - The first surveillance bulletin including data from all sites on the 15th of September

2.3. Generic surveillance protocol WP2 - summary

- General points:
  - Each country already has obligation to perform surveillance and many sites are already conducting surveillance.
  - Most activities are based on I-MOVE influenza vaccine effectiveness (VE) study so we cannot leave things out of the protocol as we need to be ready when the other I-MOVE influenza activities start again
  - Some feedback from partners received: some misunderstanding about aggregate vs individual level data
    - Individual: anonymised, one record per person
    - Aggregate: counts by age, sex, number tested, number positive tested, etc.
- The aim is to collect data similar to I-MOVE influenza protocols; instead of ILI patients we broaden to suspected COVID-19 i.e. ARI (swab; collect data using a swab form/questionnaire); collect information from patients testing positive and patients testing negative
- The I-MOVE-COVID-19 WP2 individual-based surveillance is based on positive cases
- The risk factor (RF) study (WP4) uses patients testing positive and patients testing negative for a test-negative design (TND)
- If there is a COVID-19 vaccine available in future, the risk factor study would form the basis for VE study as well.
- The surveillance data can also feed into RF study.
- Alternative approaches for surveillance: as it is not always feasible to test suspected patients at this moment, ECDC recommends expanding surveillance e.g. self-swabbing, telephone consultations, participatory surveillance etc. We will discuss the feasibility of these later.

2.4. Risk factor protocol WP4 - summary

- The idea is to identify key risk and protective factors among patients presenting to primary care; the methods are very similar to I-MOVE influenza VE study.
- Having this study in place is putting in place everything we need for the VE study once a vaccine is ready.
- Data collection: similar to case-based surveillance except we collect additional variables; those testing negative will be controls, test-positives will be cases.
- Have also been approached by London School of Hygiene and Tropical Medicine and the university of Leiden regarding another kind of control selection (contact Epiconcept if interested in doing this) [Here are details on their study design proposal: http://arxiv.org/abs/2004.06033.]

- We would like to include a follow-up component as a pilot to see if a patient was subsequently hospitalised, and their outcome; we would like to pilot this, as it is not usual for I-MOVE previously.

2.5. Discussion of protocols, including feedback from every network on feasibilities for

NB: The case definition in the protocol you received says:

- Acute onset of at least one of the following symptoms: fever or cough or sore throat or shortness of breath or coryza

and

a clinician's judgment that illness might be due to a SARS-CoV-2 infection.

The "and" should be replaced by an "or":

- Acute onset of at least one of the following symptoms: fever or cough or sore throat or shortness of breath or coryza

or

a clinician's judgment that illness might be due to a SARS-CoV-2 infection.

(planned) data collection

- (10)(2e) (Nivel): The case definition is broader than ILI; the setting is same; the surveillance is all year-round not "seasonal" as for influenza. In some countries e.g. Ireland, it is not yet possible to collect this information for this protocol, but they are working on it and will hopefully be able to join in next weeks/months.
- (10)(2e) (10)(2e) (10)(2e) (10)(2e) (RECOVER): discussion of case definition in light of "a clinician's judgment that illness might be due to COVID-19", this depends on time of year; suspected cases can be different in different contexts. So now in the first wave everyone is suspect; but when the epidemic wave is over other viruses will come into play so it depends on the situation and perception of GPs based on their surveillance data etc. In Jan/Feb there will also be normal influenza. What would be a suspected COVID case then? Maybe it is better to come up with defined signs/symptoms so that you do not have to deal with these changes.
  - (10)(2e) symptoms are being collected (see next slides); on a case-based level there is always the possibility to select cases from data collected by specific symptoms. We propose a broader case definition.
- (10)(2e) (Nivel): All cases or a systematic sample of patients are tested for influenza, but we are also interested in other respiratory viruses. For samples: are some countries doing self-swabbing and point-of-care tests? Are networks doing other specimen collection? (Then we can include this in the protocol.)
  - (10)(2e) ((10)(2e) (SC): At the moment PHS cannot test samples for other viruses than SARS-CoV-19, but we are storing samples in the lab so that multiplex PCR can be done at a later stage.

- (10)(2e) (IE): Ireland is in the same situation, not currently testing but storing for batch testing at some point in the future.
- (10)(2e) (ES): at the moment in ES we are not going to test for influenza or other respiratory viruses, but we will in the future.

- Discussion of new variables
  - Clinical signs and symptoms: have already received some comments that the list is rather long; suggested to delete coryza, loss of appetite, nausea, dermatitis - what should we leave out? Should we add? Is it too long?
    - (10)(2e) (10)(2e) (SC): we have some of these in our new form e.g. fatigue, vomiting, diarrhoea; we have self-swabbing so cannot add "anosmia" etc. as they would not know what it is, so we have instead "altered smell", etc. For other symptoms we could discuss adding them to our forms.
    - (10)(2e) (10)(2e) (SC): we are only in the second week of testing for surveillance in Scotland, so we have not had much feedback yet from patients; so we are not sure how the form is working. We have had a lot of other queries like when will we get test results. What about smoking: should we record this? We also record vaping as that is of interest in Scotland (others may wish to do this also).
    - (10)(2e) (ES): in general we are trying to keep as much as possible similar variables to influenza sentinel surveillance; in addition we have added some that are COVID-specific which are important e.g. anosmia and ageusia. We have not considered dermatitis, conjunctivitis, or dizziness, as we do not want to have a very long questionnaire; want to keep it as simple as possible. We can send you all the variables we have in ES. Most are what you have.
    - (10)(2e) (ES): we are preparing comments on protocol and questionnaire and will send them after this meeting.
    - (10)(2e) (PT): for our questionnaire we adapted the I-MOVE questionnaire and we have specific symptoms for COVID; we can share the first version of our questionnaire; we try to keep it as simple as possible. Not very easy to have all these symptoms and signs proposed in the protocol like rash and palpitations.
    - (10)(2e) (EN, RCGP): some symptoms and signs emerging are of prognostic importance e.g. chills/rigor, rash, and in particular the measurement of peripheral oxygen saturation, which is of very high prognostic value for seriousness of cases in primary care.
    - (10)(2e) (10)(2e) (SE): just rolled out an electronic form that GPs complete; with a long list of symptoms they will not like this. Can we group similar symptoms together, e.g. "GI symptoms including these…"? Otherwise they may stop as it would take too much time for them.
    - (10)(2e) (NL): the list is very long; for Dutch PC surveillance the surveillance form needs to be as short as possible for us the max is 1 page else workload too high for GPs.
    - (10)(2e) (FR): Sentinelles are already collecting diarrhoea and conjunctivitis on their swab form, which the GPs use. GPs also declare clinical cases, which includes symptoms and there anosmia and ageusia are in one question covering both. We have the possibility of matching the two

databases (virological and clinical), this works for 75% of cases; but I agree we need to keep swab form simple else a lot of missing data and may discourage GPs from recruiting patients.
    - (10)(2e) (Nivel): Agreed, maybe we can collect all of your questionnaires (those who have them) then we can see what is there and can share with those not yet prepared… and we can see what we can pool between partners.
    - (10)(2e) (ECDC): I have nothing to add; agree with what others said we should shorten to a minimum list of symptoms; I agree to have specific signs like anosmia and ageusia. Why for the case definition you do not include these very COVID-19-specific symptoms that perhaps are not part of the ARI case definition but are specific for COVID?
        - (10)(2e) (10)(2e) (Epiconcept): This is something we should discuss; the case definition is sensitive/broad at the moment.
    - (10)(2e) (WHO): is this just symptoms for one point in time or throughout the illness?
        - (10)(2e) (Nivel): Only those symptoms present at time of swabbing.
    - (10)(2e) (10)(2e) (10)(2e) (10)(2e) (RECOVER): do we include the number of days a patient is symptomatic? (Yes) And co-morbidities? (yes)
    - (10)(2e) (ECDC): for fever, do you have a definition? Also when people feel malaise, may be sub-febrile, is there value in collecting absolute temperature? (yes)
    - (10)(2e) (IE): for us the list would have to be quite short as well.
- (10)(2e) (Nivel): we will provide an updated list of symptoms for next protocol draft.
- (10)(2e) (Nivel): Pre-existing chronic conditions and vaccination: we would like to extend to pneumococcal and BCG vaccination if this is feasible and add other pre-existing conditions.
    - (10)(2e) (EN): under renal disease should we list also whether GFR and ACR tests have been done, as these have reasonably strong associations with COVID-19 with poor outcome?
    - (10)(2e) (10)(2e) (SC): for obesity, should we include height and weight so that we can define BMI and so can look at importance by range of BMI?
    - (10)(2e) (ECDC): we agree, as studies have shown different levels of BMI have impact; also do you collect whether Type 1 vs Type 2 diabetes, or is it possible to distinguish in the coding?
        - (10)(2e) ((10)(2e) : each country can decide whether they include this or not (may be different in each site).
- (10)(2e) (Nivel): Can any network do follow-up of patients? In NL it is not possible as data are anonymised
    - (10)(2e) (EN): yes we are and we are doing it; some patients consulting the GP with confirmed COVID-19 are followed-up to obtain 28-day convalescent sera, among them are also volunteers donating sera for therapeutic trials; we are also involved in household study of serology across households, which we may extend; so for us this would be possible to participate
    - (10)(2e) (FR): Sentinelles has an ongoing project not yet launched to include all swabbed patients and follow-up for 30 days and provide swabs for self-swabbing at home to see how disease will evolve; this is an ad hoc study for a few weeks; we are having difficulties already in collecting enough swabs in ARI surveillance.

- (10)(2e) (10)(2e), (10)(2e) (SC): we can follow electronically using CHI numbers, can link through a Scottish study which recently been reactivated and expanded to include 1.2M people in Scotland; by electronic linkage we can make the most of this cohort
- (10)(2e) (10)(2e): the idea for the moment is to ask no questions other than whether patient was hospitalised (and if the patient died).
- (10)(2e) (IE): we would have this information but, similar to NL, we cannot identify patients so cannot link; but we can look at datasets and see if perhaps could link a proportion of them.
- (10)(2e) (10)(2e) (Epiconcept): those interested in taking part in this study - even if only partially feasible, could send me an email? This is not part of WP2 but WP4 so there is some additional budget associated with it.

- (10)(2e) (Nivel): for frequency of data delivery to Epiconcept and issues for data sharing: we aim for a monthly basis for individual data (data entry form available). Data transfer will be as for I-MOVE. Is this frequency feasible? What about data sharing?
  - (10)(2e) (10)(2e) and (10)(2e) (10)(2e) (Epiconcept): We want to avoid double reporting
  - (10)(2e) (ECDC): this would be very useful to have these data but we do not want double-reporting and would like to reduce the load as much as possible; depending on data flow to Epiconcept etc. If we know what is already being reported we can take this into account. For case-based data, we can organise through TESSy or otherwise to ensure no double-reporting with I-MOVE data (we can discuss to make sure of this). The timelines of weekly (aggregate) and monthly (case-based) are perfect, but we understand people are very busy so may not be possible.
  - (10)(2e) (Nivel): send us your suggestions by email and any worries about overlap, and what you think is feasible etc. and we will prepare the next draft.
  - (10)(2e) (10)(2e) (SC): we are trying to prepare for the information governance and data sharing; when is your expected first dataset? Is there a deliverable for data?
    - (10)(2e) (Nivel): unsure; common surveillance report is due in September, including pooled data.
    - (10)(2e) (10)(2e) (Epiconcept): the sooner the better within what is feasible; our deliverable is to summarise everything in September but if we can have data before this, it would be great.
    - (10)(2e) (10)(2e) (Epiconcept): also important to note regarding the surveillance report - the three deliverables are quite spaced out but it would be nice to have more frequent surveillance available. Many of you are already reporting your surveillance for your network, we don't want to duplicate. So we need to decide what we report - do we refer to your website, paste your report or summarise everything? Also does it make sense to pool at this level, how much heterogeneity is there in the systems? But it would be useful to have data as frequent as possible with surveillance reports.
    - (10)(2e) (Nivel): if there are great differences between countries it would be important to see this; if a country is using the I-MOVE protocol it would be easier to share/pool - all suggestions are welcome. We have to be careful that data are anonymised.

- (10)(2e) (Nivel): the last issue to address is where testing of patients is not feasible, are alternative approaches available for you? i.e. should we include any other areas, what are your thoughts?
    - (10)(2e) (PT): we will include dedicated centres and Influenzanet (adapted to COVID-19), so we have participatory surveillance.
    - (10)(2e) (NL): participatory surveillance is possible for NL. We are part of Influenzanet.
    - (10)(2e) (NL): and surveillance based on (telephone) consultation data is in use, for COVID-19, ARI and other outcomes.
    - (10)(2e) (10)(2e) (SE): in Sweden we already have phone consultation running. But this will stop during influenza season. We also have a cohort with self-reported symptoms each week. Difficult to disentangle what is what.
    - (10)(2e) (10)(2e) (SC): in Scotland, we have dedicated COVID-19 centres. We are trying to get info from triage centres. In terms of participatory surveillance: there are a few apps around but we do not have access to these data yet.
    - (10)(2e) (FR): in France we collect data on incidence of ARI consultations. COVID surveillance is based on ARI surveillance in France. It would be difficult to change especially during influenza season. We are also part of Influenzanet.
    - (10)(2e) (ES): in Spain we are planning to use ARI definition for COVID surveillance; we are going to use weekly ARI consultations (normal GP or phone consultations) using sentinel GPs in some regions, in others sentinel-dedicated COVID-19 surveillance, depending on region. At first we will try to test every suspected COVID-19 case and if not feasible will try to implement systematic swabbing of suspected cases same as we do for influenza surveillance. We are now setting this all up and at the moment do not have all of the completed information.
    - (10)(2e) (IE): all of our GPs have phone consultations now and refer COVID-19 to dedicated testing centres; what we are trying to do is identify which patients are from sentinel GP network and which from other GPs. The plan is to have both of these datasets but it is a work in progress.
- (10)(2e) (ECDC): is there a plan/timeline for genetic analysis and sequencing? We can support sequencing through a contract. Is there a central lab for I-MOVE? Note that we can help to fund this; we can do as for I-MOVE in TESSy where we collect the GISAID number etc. and indicate sequences coming from cases included in I-MOVE.
    - (10)(2e) (10)(2e) (Epiconcept): Part of our proposal is to include clade-specific information and to describe over time and also to look at RFs for clade; we have not yet discussed timelines; maybe we can ask this now: whether people are sequencing and what delays are expected?
    - (10)(2e) (10)(2e) (Epiconcept): the genetic aspect of the surveillance is coordinated by Paco Pozo and (10)(2e) from the National Reference Centre in Spain but they have asked us to wait a few weeks before they can organise this; there is no central lab as many countries have the capacity.
    - (10)(2e) (10)(2e) (SE): we are running this and have already uploaded 90 samples to GISAID, we will continue doing this; once you have established the WGS platform it is easy to keep going.
    - (10)(2e) (10)(2e) (SC): for Scotland we now have about 1000 samples across the country being sequenced as part of a UK project; it would be very useful for us to

have a protocol or sampling frame as we could then request that these samples are of interest and then we can provide you this information.

- (10)(2e) (10)(2e) (Epiconcept): we propose to do very similar to influenza; those who can sequence all samples are very welcome to do all; in the I-MOVE influenza VE study what happens is that among the viruses a random sample is selected for sequencing, so that it is representative
- (10)(2e) (10)(2e) (Epiconcept): we need to have a meeting asap when Paco Pozo/Inmaculada Casas Flecha, once they have the time, to discuss the lab aspects; we will include ECDC.

- We look forward to all suggestions and comments by email to Mariette, Esther or Marta; we will produce the next protocol draft addressing the most commonly raised issues; those interested in the RF study please also send an email to us.

4. Action points

	Action	Responsible (deadline)
1	Send comments and suggestions on items discussed in today's meeting to Nivel/Epiconcept	All sites (by 12 May)
2	Let Nivel/Epiconcept know if your site can participate in the aggregated surveillance, the case-based surveillance, both or neither at this current point in time.	All sites (by 12 May)
3	Prepare next draft of surveillance protocol	Nivel and Epiconcept (18 May)
4	Prepare next draft of RF protocol	Epiconcept (18 May)
5	Send email to Esther if interested in participating in RF study	All interested sites (12 May)
6	Arrange meeting to discuss laboratory aspects	Epiconcept (meeting before 20 May)
7	Contact Epiconcept if interested in using another (not TND) style of control selection for RF study (http://arxiv.org/abs/2004.06033.)	Relevant sites (18 May)
8	Send to Nivel/Epiconcept existing questionnaires or protocols (country-specific)	All sites (12 May)

5. Annex 1: presentation from the meeting