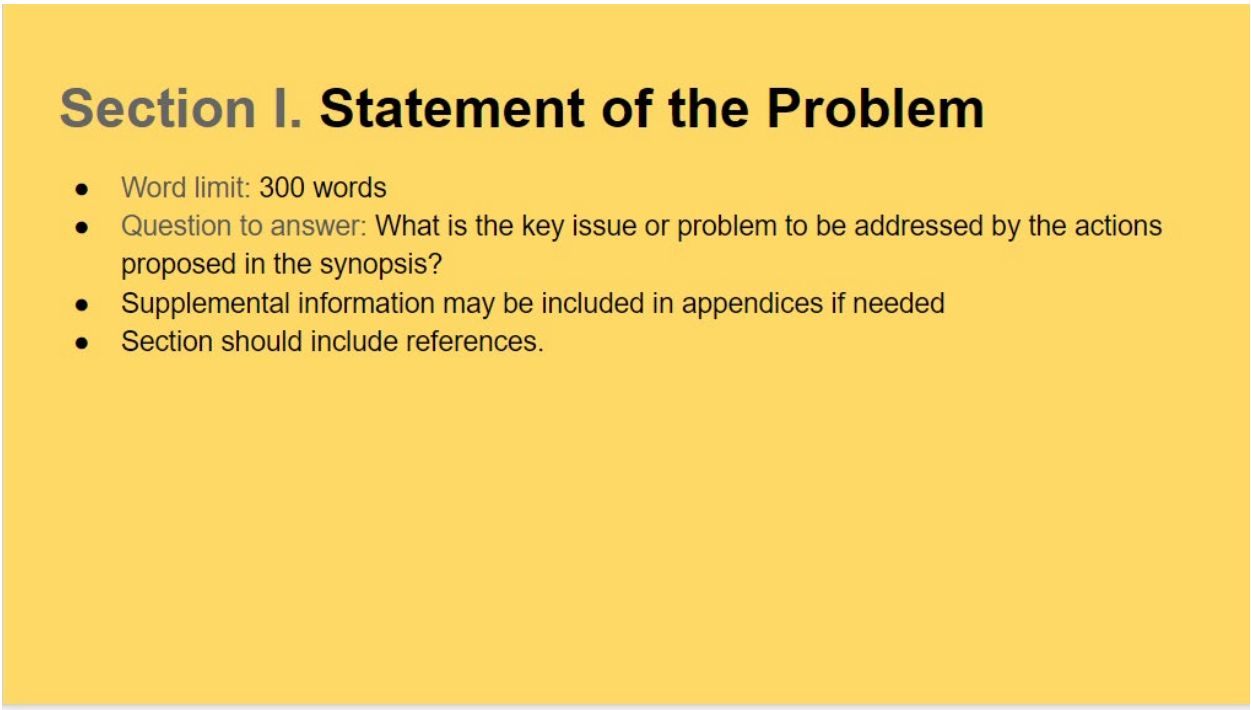
Core Working Group Meeting 3 Notes: 10/5/22

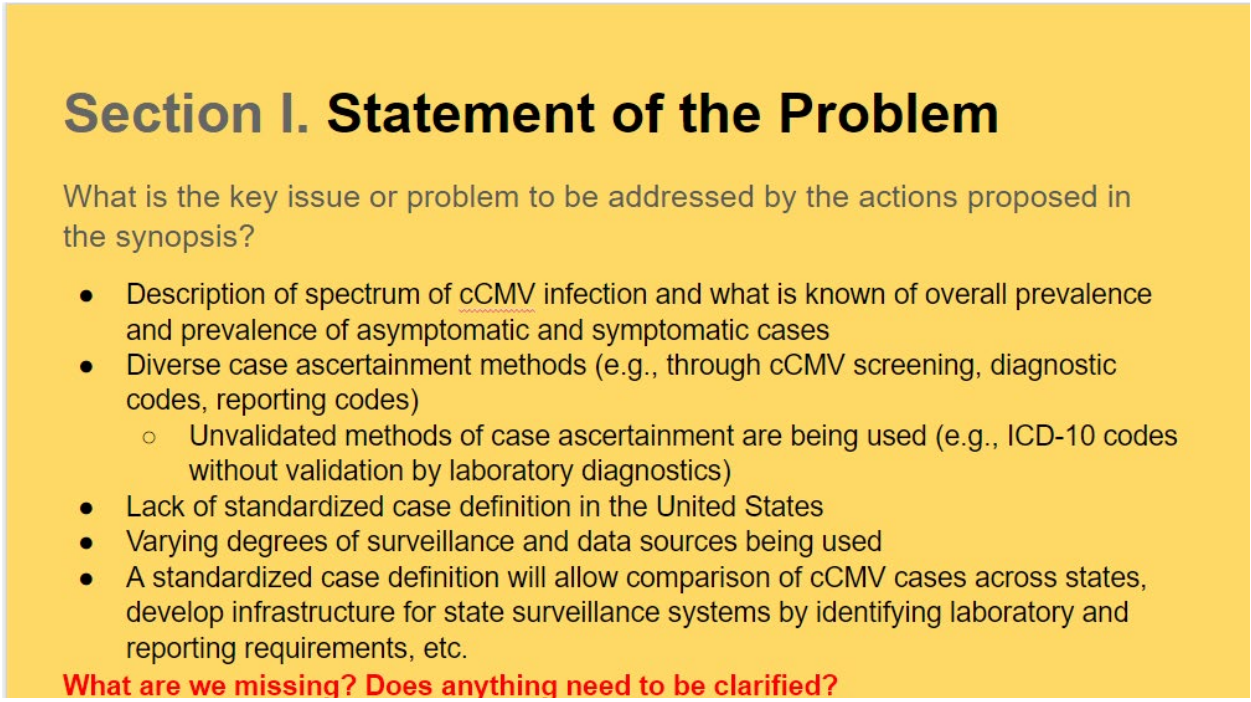
Introduction:



Stephanie: In the beginning, we shared the template on the PS that will be submitted and today we are going to talk about 1, 2, 4, and table 5. Today's goals for feedback: We want to hear from everyone (States and jurisdictions speak up, interactive discussion). Like I put in my reminder email yesterday, if you don't feel comfortable speaking up or you think of something post meeting, email me input. All of your input is welcome and needed. Our goals for today: We are going to focus on content, big picture, and larger ideas. We don't want to get lost in weeds of sentence structure, grammatical issues, wordsmithing. We are just looking at an overview of the very first draft for input on the big picture. We want to find out what's not there that should be, what is there that shouldn't be, what needs clarification, etc. Just a reminder that the PS is for CSTE. It's part of the Infectious Disease Steering committee and the title is Standardized case definition for surveillance of cCMV infection.

Section I:

Statement of the Problem:



Stephanie:

For the statement of the problem, the word limit is 300 words and we are to answer the key issue or problem to be addressed by the actions proposed in the synopsis. If needed, we can create appendices with supplemental information and this section is to include references.

So, what are the key issues to be addressed? What we have highlighted so far includes the description of spectrum of cCMV infection, overall prevalence, and prevalence of asymptomatic and symptomatic cases. It would be easier if we just took one bullet at a time. Any input, comments, or suggestions on this first bullet?

Scott Grosse (Chat): Most infected babies are asymptomatic at birth, however 10-15% of those asymptomatic babies either already have or will later develop hearing loss.11-13.

Mark Schleiss: The first bullet point is 2 different topics: The prevalence of infection (Asymptomatic/symptomatic) and a separate issue is what's the spectrum. It's minor but those are subtly different points.

Kristen: They are explained separately within the PS draft.

Scott: The issue is it's contentious –there's no clear evidence that children with asymptomatic infections have a higher rate of neuro developmental diseases than children without cCMV, but there is clear evidence for hearing loss, much of which is already present at birth.

Kristen: So, I'm understanding, there is evidence for hearing loss, but not for…

Scott: There is no consistent evidence that cognitive deficits are any more frequent in children with asymptomatic cCMV than in a general population. In other words, is there a risk of cognitive disability

due specifically to asymptomatic cCMV? That is not clearly established. Tatiana's and Gail's study found no evidence of intellectual disability in a cohort of 100 children with asymptomatic cCMV.

Gail (Chat): Other outcomes include vision loss, in addition to SNHL and developmental disabilities. in Sx cCMV.

Pablo: (Chat): It depends on how you define asymptomatic.

Kristen: That's something we're going to have to talk about more next meeting—if we could save that for later we can always go back in and update the draft once we make that decision.

Pablo: Asymptomatic and hearing loss comes up a lot from European individuals especially, so we need to be clear about that. I agree that asymptomatic kids do well.

Stephanie: Part of the statement of the problem in the couple paragraphs of the draft, and why we need the case definition, we did touch on diverse case ascertainment methods—people capturing the CMV data may be capturing it in different ways. There's definitely a wide variety on how cCMV is determined in areas. We wanted to touch on and state that this is an issue and we want to see if we can standardize b/c of the variety of ways that people ascertain CMV infection. Also, there is no standardized case definition in the US and everyone is doing their own thing at the moment. The whole purpose is that if we can standardize the case definition we can compare across states and this will help develop infrastructure for surveillance to occur and reporting mechanisms to help validate case definitions. When we look at those two paragraphs, is there something other than what we hit on that we missed or that maybe is misrepresented or may not have been quite accurate?

Tory: I think one thing that is missing is why we are doing this now…we could say CMV has been a problem for a long time and more recently multiple jurisdictions are beginning some level of targeted surveillance. Now that we are doing this intentionally we need to compare rates across states.

Kristen: We tried to include that in the next section, should we include that in this section as well?

Tory: It seems like a statement of the problem and a justification, I'd lean toward someone with more experience.

Kristen: We can make a note and maybe include it both places.

Pablo: I think that's a good point and I think that our goal should be—we're identifying babies with cCMV and people have no standardization of what should be done. I think that it's not just the fact that we want to identify them but we also, as more states and babies are being identified, I think that our goal is to really provide optimal care and management for those babies. Evaluation, care management, and follow-up. I think that has to be a component of this.

Kristen: We do address that a little bit in the next section, about the importance of early identification and intervention. I agree w/ Tory that the sections are very similar and we unfortunately can't combine them but we can make that more pronounced in the next section if we need to.

Stephanie: I think that's a great comment to make sure we do highlight that, because we need to make sure these kids get the care they need by being identified early.

Kate (Chat): I think the last two bullets are really important for this. The work is happening, but the fact that we can't combine/compare is really limiting.

Suresh: The standardized case definition—the reason to have that is different than universal cCMV screening. If we want to identify all babies then universal CMV screening, but also the standardized CMV screening case definition can be useful even if there is no universal screening. They both are needed for different purposes I think.

Scott (chat): Possible wordsmithing: Most infected babies have no clinical signs at birth other than hearing loss, although 10-15% of those "asymptomatic" babies either already have or will later develop hearing loss.

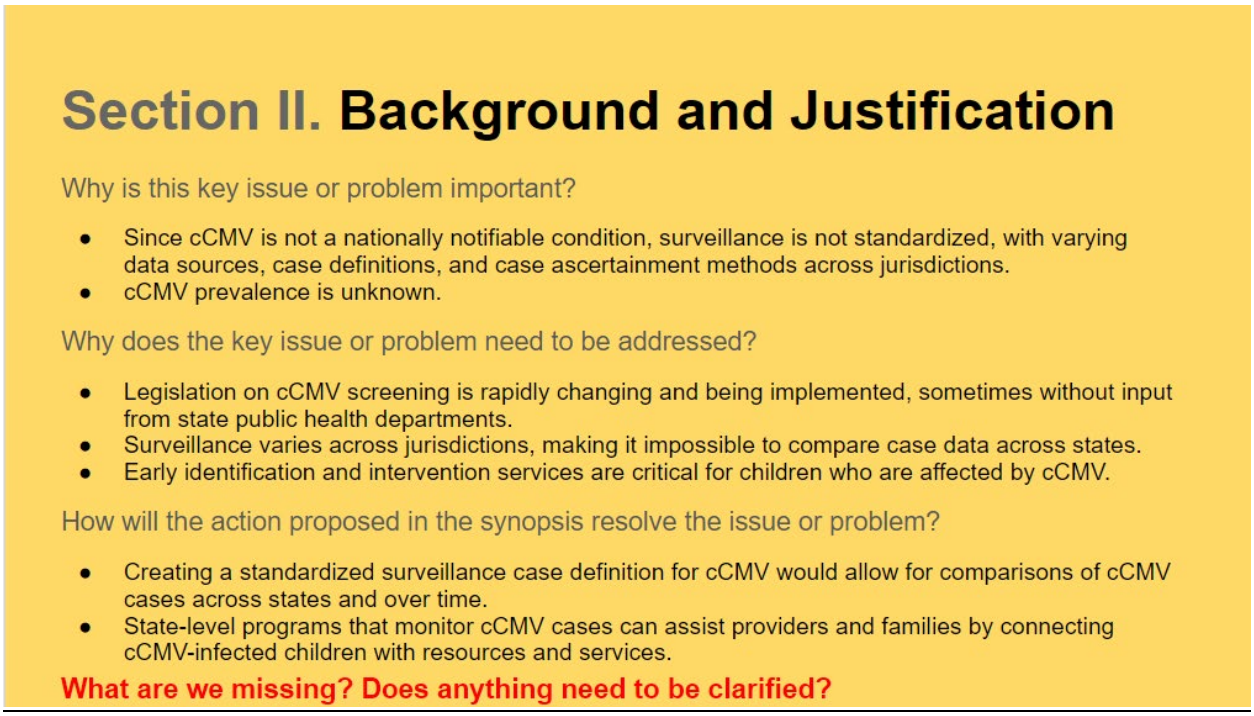
Pablo: When we're talking about the case definition, do we want to make this a surveillance case definition or diagnostic case definition? I think it would be good to do surveillance b/c I think we can gain some experience or knowledge about false positives as well.

Kristen: This is only for surveillance, we will include language that says it shouldn't influence diagnosis, treatment. A lot of times these cases won't be identified until cases occur.

Pablo: I think that should be put in the front then.

Kristen: We will include a statement about that. I think it goes in a later section after the case classification section but we will make sure it's included.

Section II:



Section II. Background and Justification

Why is this key issue or problem important?

- Since cCMV is not a nationally notifiable condition, surveillance is not standardized, with varying data sources, case definitions, and case ascertainment methods across jurisdictions.
- cCMV prevalence is unknown.

Why does the key issue or problem need to be addressed?

- Legislation on cCMV screening is rapidly changing and being implemented, sometimes without input from state public health departments.
- Surveillance varies across jurisdictions, making it impossible to compare case data across states.
- Early identification and intervention services are critical for children who are affected by cCMV.

How will the action proposed in the synopsis resolve the issue or problem?

- Creating a standardized surveillance case definition for cCMV would allow for comparisons of cCMV cases across states and over time.
- State-level programs that monitor cCMV cases can assist providers and families by connecting cCMV-infected children with resources and services.

What are we missing? Does anything need to be clarified?

Stephanie: This is a 500-word limit, and it's the background and justification section. We are supposed to answer why this key issue or problem is important, why does it need to be addressed, and how will the action proposed in the synopsis resolve the issue or problem. We can create appendices and references

should be included. The highlights, Kristen summarized from the bullets: Why is it important? Since cCMV is not nationally notifiable, the surveillance is not standardized, and there are varying data sources and case ascertainment methods used and diff. case ascertainment methods across jurisdictions. That's one thing we highlighted in the very first paragraph. We also wanted to touch on the true prevalence being unknown b/c universal screening hasn't been conducted nationally. We truly don't know the prevalence and being able to do public health surveillance can help us guess-timate it more closely. When we're looking at section 2, is there anything else we should address that states why this is important in addition to those two bullets?

Tory had mentioned answering the question of *why now* can also be important to do in this section.

Kim: In the second paragraph, it starts off by saying "Formalized cCMV surveillance is also rapidly changing" But it goes on to talk about cCMV screening not surveillance. The lead sentence speaks to surveillance but the rest of the paragraph to screening. Also, I want to make sure we are saying universal cCMV screening of newborns vs. universal newborn screening to make the distinction of cCMV screening not happening through the newborn screening programs. I understand the point we're trying to make but it's the need for surveillance is increasing because of the increase in screening of newborns.

Tatiana: That's a good comment and hopefully we can figure out a sentence to make a transition. The screening and surveillance programs are kind of siloed and perhaps with cCMV surveillance and screening we will able to fill in and bridge the gap.

Kim: But if only if the state newborn screening program is doing the screening. It may be the state doing the screening. We need to be general enough regarding the screening that takes place but also the connection about the screening that's happening and the need for surveillance along with that.

Scott (chat): The Joint Committee on Infant Hearing recommends "all infants who test positive on a neonatal screen for CMV require periodic monitoring by audiology to identify changes in hearing thresholds, with the provision of appropriate amplification and early intervention as indicated." Follow-up should begin "no later than 3 months of age."

Tory: One other thing that I thought of that kind of fits in the last paragraph, sort of related to educational campaigns. One thing that we have to do is to apply the case definition to outcomes, because that's lacking right now. We also say that a case definition would allow us to analyze trends by geography and demographics—I wonder if that's really accurate. In this scenario we are recommending a case definition but not nationwide surveillance.

Mark: Thinking of the primary focus of this working group, you can't begin to think of surveillance and trends until you agree on what a case is. If you can't agree on that, everything else downstream becomes difficult to analyze.

Stephanie: This is the first necessary step to allow us to conduct public health surveillance.

Tory: Maybe we need to explicitly state that somewhere.

Scott: I don't think surveillance has the same focus on making sure each individual case is ascertained. The goal of surveillance is to understand population prevalence and trends, so surveillance case definitions may be more noisy than a scientific case definition and that's okay. I'm thinking of the CDC's autism program which several years ago streamlined the case definition to no longer require a clinical

assessment but used healthcare data to classify and could be done more inexpensively and quickly. A surveillance case definition might not be the same as a clinical case.

Pablo: Yes, but this is more surveillance.

Stephanie: If we go back to our slide, we talk about what Tory mentioned - there is movement going on with increased screening by jurisdiction. State level programs can assist by providing resources and screening. The case definition can help with provider and family education, so that is what we were also trying to hit on. Is there something that needs to be clarified in paragraph 4?

Scott: This is the CDC study that compared two case definitions for surveillance of autism spectrum disorder in school-age children. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9022042/.

Suresh: A couple comments in the second paragraph, you mention diagnostic odyssey, but I also think if there is no timely diagnosis you cannot prove hearing loss to be CMV related, so you don't have a diagnosis even after going through a diagnostic odyssey. And then, the beginning of the 3rd paragraph, it says 5-10% cases of hearing loss are caused by cCMV, I mean there are differing numbers over there, for example the review paper by Cynthia Morton in the NEJ in 2016 suggest 20% at birth and 25% at 4 years of age is related to CMV.

Stephanie: The reference is lower, but that's a great point that we missed that. We can put the range.

Tory sent in chat an excerpt from an AGS position statement to use as an example (Which Kristen wrote 😊*).*

Stephanie: Email cmv@utah.gov any additional comments.

Suresh: In the last paragraph, you mentioned measures related to COVID-19 pandemic, but maybe make it clearer and more specific because not everything related to COVID-19 precautions would affect CMV prevalence. The sentence says "While the measures were adopted to prevent the spread of SARS COV 2 they likely reduce the spread of cCMV" –be more specific.

Mark: The problem is it's hard to be specific because I don't think we know, I agree social distancing wasn't the key issue but was it hand hygiene, reduced group daycare.

Suresh: Daycare, handwashing, and the face masking, probably not contact with saliva. But I usually would say there's a lot of supportive data but no definitive evidence.

Mark: We don't know the mechanisms, I agree. Keeping hands out of nose and mouth is probably more important for CMV and that's why masks are relevant, but I don't think we know the exact reason—I think handwashing and decreased use of group daycare.

Kristen: Do you think this section should include this part of COVID or should we use this real estate to describe how CMV is transmitted or tie it back to COVID and CMV may have similar transmission routes in some cases?

Mark: I think if the overarching goal is to develop a case definition, one would argue background information isn't relevant for this task so we could keep it to a minimum.

Tory: I also wondered why we talked about COVID there but I think we follow-up with a point that we can't learn things like this if we don't have standardized case definition. It's just an example of an area that could be benefitted by a standardized case definition.

Pablo: I would stay away from COVID, I wouldn't go there—this is completely a separate issue.

Kristen: In my experience working on PS, a lot of the executive board and state epis are interested in position statements that implement surveillance or case definitions that you can do something about so we can focus on how this would influence prevention methods through education. Maybe we can switch out COVID to talk briefly about how CMV is transmitted and how having a standardized case definition can help us with case count and focus on prevention.

Suresh: I think that's a great point, agree.

Tory: From a newborn screening perspective, I'm hoping a case definition can help us determine whether population-based screening using a newborn screening program is useful—are we identifying cases we can do something about or are we not? We will have data to see if newborn screening is doing what we think it's doing.

Stephanie: What would be a good sentence to capture what we said? It doesn't have to be perfect, but just the gist?

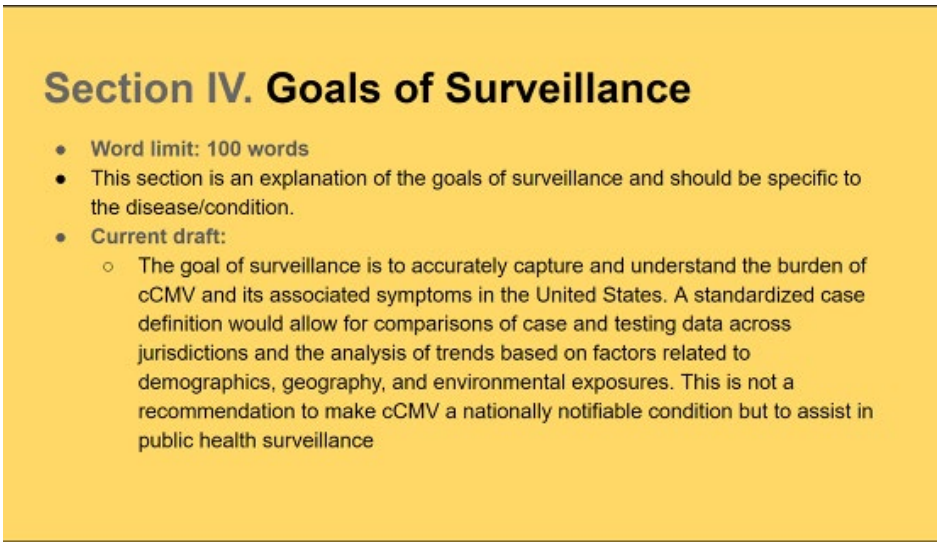
Tory: A standardized case definition would allow jurisdictions to evaluate whether…I'd have to come back to this.

Stephanie: If you have time to think about it, please feel free to send it our way - you're giving us such good input.

Sondra (Chat): "A standardized case definition will help jurisdictions screening for CMV compare performance metrics and outcomes to help evaluate the benefits of universal screening." Something like that Tory?

Section IV:

Stephanie: This is a little section with the goals of surveillance—a short and sweet synopsis of our goal and we are supposed to explain the goal, it should be specific to cCMV, and the current draft b/c it's such a small section we do have it on the slide:



That was 71 words—we have 29 left.

Kristen: We can also add something about this being a surveillance case definition and not for clinical use, we can draw from language from AGS PS.

Tory: I would think about adding in understanding the burden of cCMV and its association of symptoms, also outcomes, and something about morbidity and mortality?

Suresh: You could say just the disease burden. So, if we're going to have a statement about the fact that this is for surveillance and not clinical diagnosis, do we need to have the last sentence about this not being a nationally notifiable condition sentence?

Kristen: This is more for the audience that will be reading this…you usually have PS to make a condition nationally notifiable. I think it should still be there but we can shorten it, it's important everyone knows that it's not nationally notifiable that we're trying.

Pablo: I know we're not doing wordsmithing, but when you start out with the goal of surveillance then it's a very general statement and the goal of surveillance is not to capture and understand the burden of cCMV, it's of any disease…I think rewording would be helpful. I also wonder if we should include that this is not a goal of nationally notifiable condition? I would like it to be positive rather than it's not and maybe elsewhere say that it's not the goal to be a nationally notifiable condition—I think we should be as positive as possible. It might lead to making it a nationally notifiable condition, who knows. I think it just needs some rewording…

Scott (Chat): In place of benefits, substitute outcomes.

Pablo: The goal of surveillance for cCMV and then honing on what it is…

Stephanie: Is there any input? It currently says "the goal of surveillance of cCMV is to accurately capture and understand its burden and associated symptoms".

Pablo: I wouldn't say accurately because this is surveillance, to be accurate you need to be diagnostic.

Scott (Chat): Also, it is not clear how surveillance data would allow programs to assess outcomes of newborn screening beyond number of cases identified. If that is a goal, that would need to be explained. I agree, take out "Accurately".

Kristen: I liked Tory's suggestion of changing symptoms to outcomes or morbidity and mortality.

Stephanie: In the next section where we say how the case definition would allow us to do these things…comparing case and testing data, etc.—did we hit the mark on that or would you suggest something else?

Scott (chat): Symptoms refer to clinical signs present at birth, very different from outcomes, which refer to sequelae or complications.

Tory: I was sort of unclear of what we meant by testing data—I think case data or data would work.

Kristen: Let's say data.

Pablo (Chat): Outcomes is better - agree.

Table V:

Table V. Recommended sources of data and extent of coverage for ascertainment of cases of cCMV

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites*
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies, poison centers), specify: **hospitals**	X	
Death certificates	X	
Hospital discharge or outpatient records	X	
Data from electronic medical records	X	
Telephone survey		
School-based survey		
Other, specify: **Autopsy reports, Birth Certificates, Birth Defect Registries, EHDI Information Systems, available NICU data, maternal health records**	X	

2022 Template

- What sources of data are needed for case ascertainment?
  - Consider the following for each data source: sensitivity/completeness, PPV, timeliness, inclusion of unique cases, information value
  - Description of surveillance methods for each data source will be described in Section V.

Are any other data sources used by your jurisdiction?

*Not applicable to cCMV

Stephanie: This is table V. Kristen, do you want to review this one?

Kristen: This is a little bit complicated. Table 5 is within section V and it talks about sources of data that are used for case reporting and ascertainment. We are trying to include all data sources that a jurisdiction would receive - either an alert such as ELR with a + CMV test that would trigger an investigation of a CMV case. Or, in other cases, if it's case ascertainment—say every quarter or so if a HD pulls cases of CMV, what source or indicator would be used for this case ascertainment? Using the surveillance assessment that we just performed and was published this week, that's where I gathered

these data sources from. For the jurisdictions on the calls or the SMEs, if you're aware of any other data sources that are used for reporting for case ascertainment please let us know so we can include it. The blue indicates anything that we had to specify—either not included or we had to specify. Also, while we're talking about this, we have to consider how good these data sources are because in section V we have to talk about methods that are used when using this data source as well as sensitivity and completeness of data, positive predictive value, timeliness, ability to identify unique cases. All that being said, is there anything missing that should be included?

Paul: There's nothing missing at first glance but there is a fair amount of overlap in these, they aren't mutually exclusive sources. You probably want to think about whether you want to identify mutually exclusive or non-mutually exclusive sources.

Kristen: I don't think it will be mutually exclusive—different jurisdictions use different sources for case notification, during our assessment we heard some of the birth defect registries are where CMV cases are identified. That's why there are different ones, even though they aren't mutually exclusive.

Paul: Birth defect registries don't generate their own data.

Kristen: Right, but HD won't look at original data sources and will look at birth registry checkbox…this is trying to identify the first level of notification to the HD.

Sondra: I wonder if it's worth expanding on school-based survey—dept. of education expanded?

Kristen: We don't have school-based survey checked off as a source - does MN use it to identify CMV cases?

Sondra: We use that for surveillance purposes to see how cases are doing.

Kristen: Is that used for measuring an intervention, you wouldn't identify new cases?

Sondra: Right.

Kristen: I'm going to make a note of that because I'm not sure…

Kim (chat): infectious disease reporting systems?

Kristen: Is that different than data from EMR or hospital records or clinician reporting?

Kim: It would be related to what you said about BD registry where registries get their information from hospital records and clinicians and so does our ID data system. With COVID, we are going to our ID registry for information about COVID cases.

Kristen: So, it's a unique data source? [Yes].

Stephanie: That's a good point b/c we have cCMV reporting in our communicable disease rule which I think would be the equivalent of an ID registry. In our communicable disease rule, cCMV testing gets reported to the state so that's a great point.

Tory: All of this is confusing because it depends on what perspective you're thinking about—like the infectious disease reporting system probably gets their information from clinical reporting and lab reporting. Like was already stated, the birth defects system gets their information from the same place.

Should we only be listing the ultimate source of the data and not the system that is being used to get the data?

Paul: That would be my preference. I think you want to look at the primary source, b/c when I look at data from EMR or hospital discharge or hospital records, it's a matter of what type of record and I think more specificity is needed here and that's the issue with BD registries. Data are only as good as the sources they have, and for a CMV checkbox without prenatal data, I'm not sure I would trust it and a lot of surveillance systems don't have access to prenatal data.

Kristen: I included the full instructions for this section in the chat and hopefully that explains what should be included in this section.

Paul: I'll look, but we are mixing primary data sources with BD registry but that's a mechanism not a data source?

Kristen: We need to focus on what's triggering the investigation or how the HD Is notified of a potential case of CMV. It doesn't always go back to the original data source b/c that's not how the HD would find out about it.

Paul: I think you need to be clear about what you're trying to define here for the user.

Kristen: We will go more into that in the actual section and we will include additional info and appendices if we need to. Hopefully when we write that out it will be clearer but before I started writing that section I want to make sure I'm including all the different possible data sources?

Meghan (chat): Possibly Early Intervention referrals?

Kristen: Is that different than the EHDI information sections?

Meghan: It would be if they didn't have hearing loss picked up or if they weren't picked up associated w/ hearing loss at birth. It depends on the state but many states don't capture CMV within their EHDI data—I don't think we do in MI yet.

Stephanie: That's correct. cCMV is a qualifying condition for early intervention in UT and so I know other states also have that as the case. If cCMV is a qualifying condition, they would know…

Meghan: Congenital infections is one of the examples provided in the federal IDEA (?) but of course it's up to states to determine. I'm just throwing that out there as another possible source, I don't know how that happens in real life.

Kristen: I made a note of that, thank you Meghan.

Tory: Section V says surveillance should use the recommended data sources…are we recommending that you should use all these data sources or is it not that prescriptive?

Kristen: That kind of contradicts what it says in the instructions to identify the sources of data needed for case ascertainment. Later on, it says if case finding is based on using multiple data sources describe the trade offs between them. I'll ask Meredith about that because that's aggressive language…

Tory: Yeah, they're not all needed…

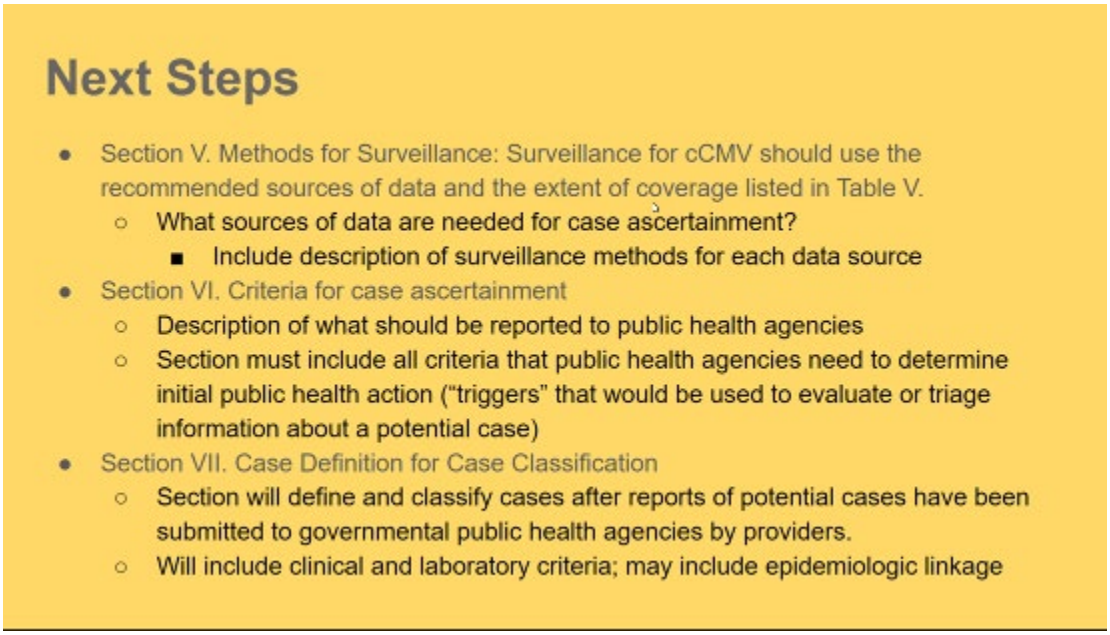
Scott (Chat): Few states have routine access to EMR data.

Kristen: I'm going to put the link for the new publication, so I think that'll help. That's the publication on the surveillance assessment we conducted with 13 jurisdictions. Kate included the Zika position statement which we used to gather information.

Kate (Chat): Just FYI - it may help to look at how other congenital infections complete this table? Zika for example https://cdn.ymaws.com/www.cste.org/resource/resmgr/2016PS/16_ID_01_edited7.29.pdf

Next Steps:

Stephanie: Feel free to continue to think on this and send us your input. We are going to refine the sections and the table that we have worked on today, and the next big sections that we will be tackling are: Section 5 that goes along with table 5, section VI and the criteria for case ascertainment, where we'll get into what should be reported to public health agencies and the criteria that will trigger a notification into the public health agencies. Then section VII is the case definition for the case classification, where we know there will be quite a bit of discussion and input and brainstorming and thinking. This is where we are going to identify and classify cases and we know there will be a lot of discussion on nomenclature, classification, etc.



Attendees:

Stephanie McVicar - UT EH...

Kelley Raines (CDC)

Kristen Nichols Heitman# ...

Suresh Boppana

Ashrita Rau (she/her# CDC)

Tatiana Lanzieri

Kate Woodworth (CDC)# s...

Gail Demmler Harrison MD

pablo sanchez

Kimberly Noble Piper (she/...

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