Florida Perinatal Quality Collaborative Webinar Series

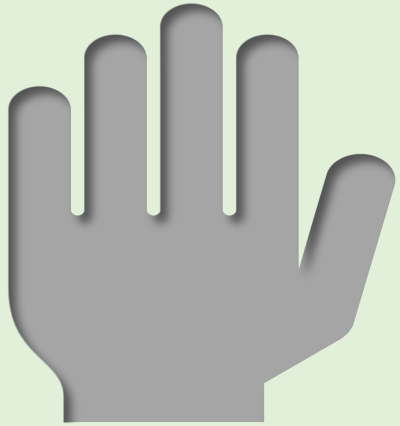
Neonatal Care During COVID-19

August 13, 2020

1:00-2:15 PM ET

Welcome!

PLEASE ENTER YOUR AUDIO PIN ON YOUR PHONE SO WE ARE ABLE TO UN-MUTE YOU FOR DISCUSSION.

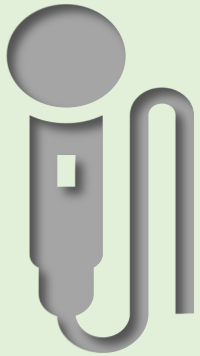


IF YOU HAVE A QUESTION, PLEASE ENTER IT IN THE QUESTION BOX OR RAISE YOUR HAND TO BE UN-MUTED.

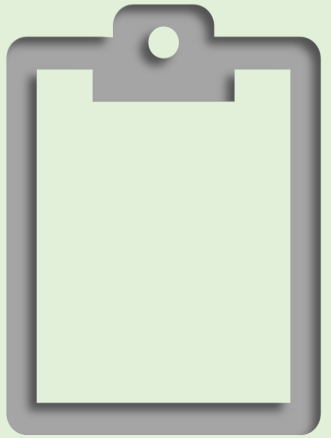
Q&A WILL BE HELD AT THE END OF THE WEBINAR!

FPQC

Welcome!



THIS WEBINAR IS BEING RECORDED.



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You can receive weekly perinatal COVID-19 resource updates by joining our mailing list!

Visit www.fpqc.org/communications

You can also visit www.fpqc.org/covid19 for COVID-19 related information!

FPQC

Neonatal Care During COVID-19
Webinar Presenters

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FPQC

Perinatal transmission and neonatal manifestations of COVID-19

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Contributors:
Gaby Cordova, MD
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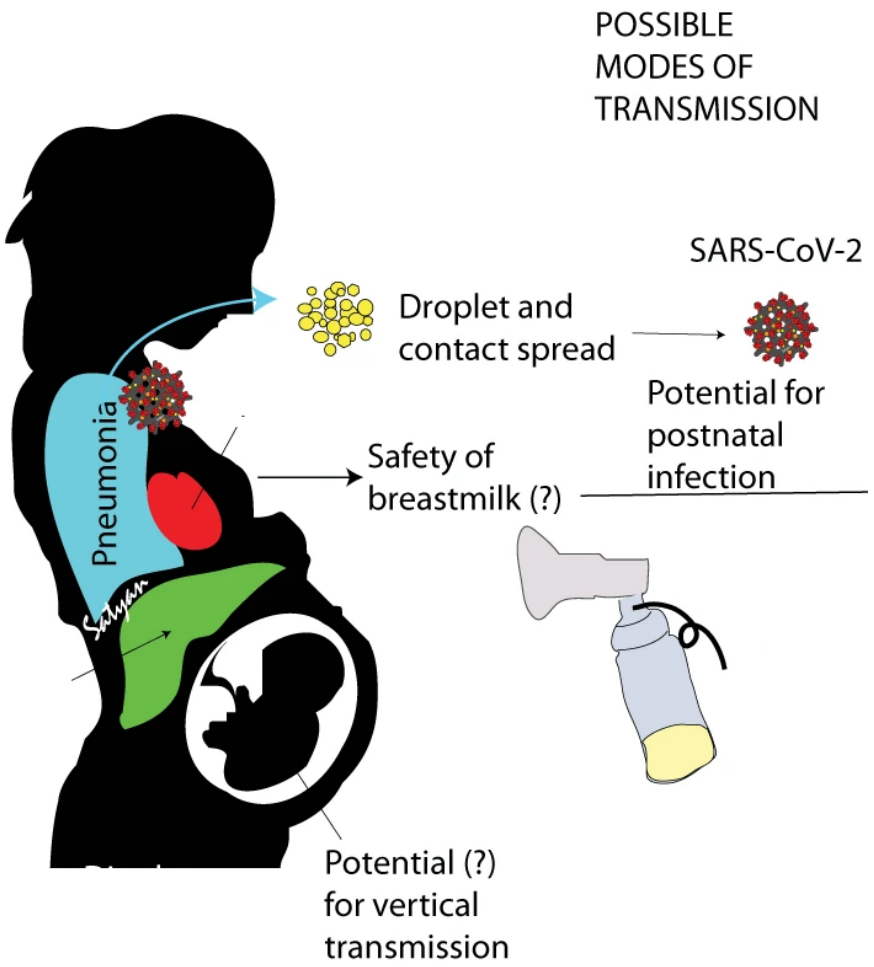
Learning Objectives

1. To categorize possible routes of perinatal acquisition of SARS-CoV-2 infection in neonates
2. To review the evidence for transplacental transmission of SARS-CoV-2
3. To identify the likelihood of postnatal acquisition of SARS-CoV-2 infection in at-risk neonates
4. To recognize possible presentations of SARS-CoV-2 infection in neonates

Neonatal Acquisition of SARS-CoV-2



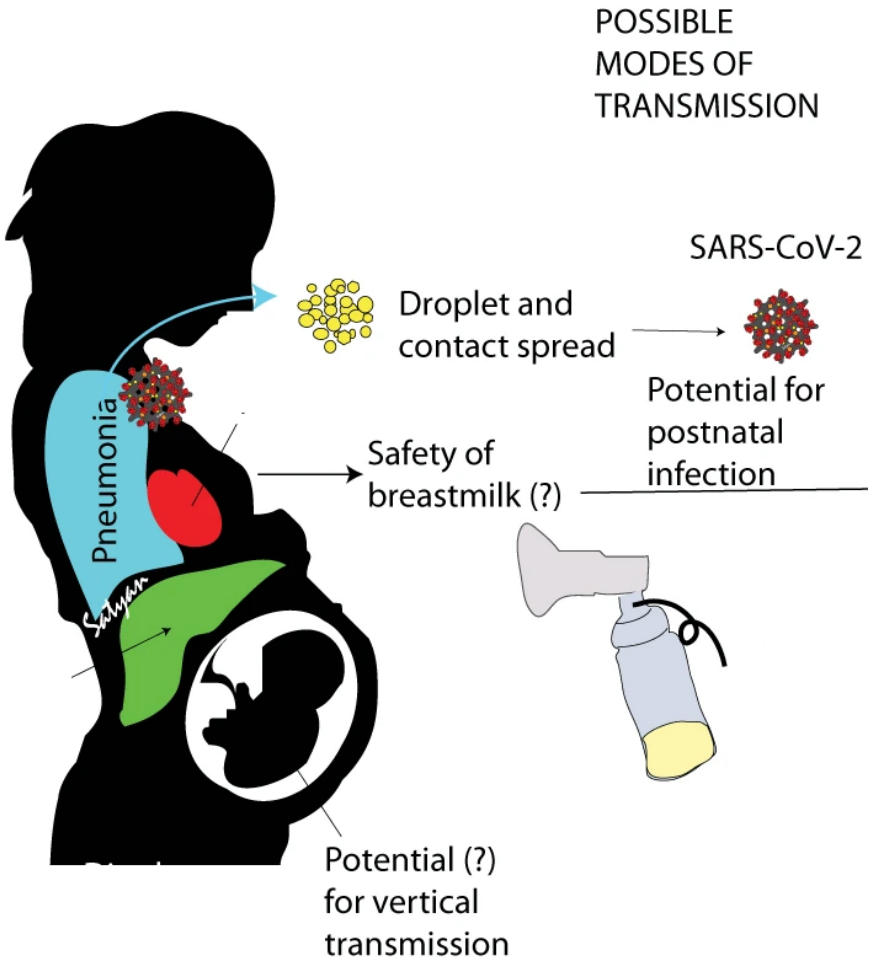
Adapted from Mimouni et al., *J Perinatology*, 2020.

Proportion of neonates testing positive is low

- 217 neonates born to SARS-CoV-2 positive moms (27 publications)
  - ***4/137 (2.9%) positive neonatal NP PCR***
    Equivocal tests in 3/137
- UK Ob Surveillance System – 194 units, 427 neonates born to SARS-CoV-2 positive moms
  - ***12/265 (5%) positive neonates***
- Spanish cohort – 82 positive mothers
  - ***5/72 (6.9%) positive neonates***
  - ***No difference in rates by delivery mode***
- National Registry for Surveillance and Epidemiology of Perinatal COVID-19 Infection (NPC-19)
  - ***43/2134 (2.0%) of infants tested were positive***

Shalish et al., *Am J Perinatology*, 2020.
Knight et al., *BMJ,* 2020.
Martinez-Perez, et al. *JAMA* 2020.
NPC-19, Accessed 8-11-20.

Neonatal Acquisition of SARS-CoV-2

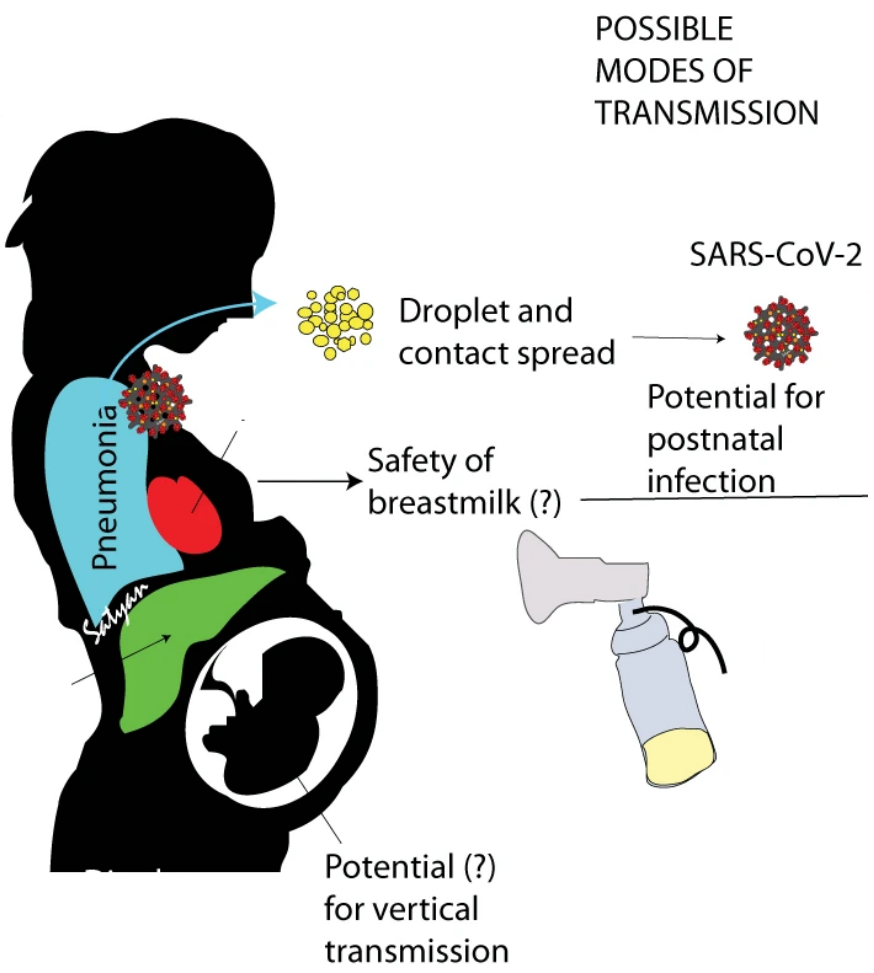


Potential Modes of Transmission

1. **Intrauterine vertical**
2. **Postnatal Droplet/Contact**
3. **Breastmilk**

Adapted from Mimouni et al., *J Perinatology*, 2020.

Neonatal Acquisition of SARS-CoV-2



Adapted from Mimouni et al., *J Perinatology*, 2020.

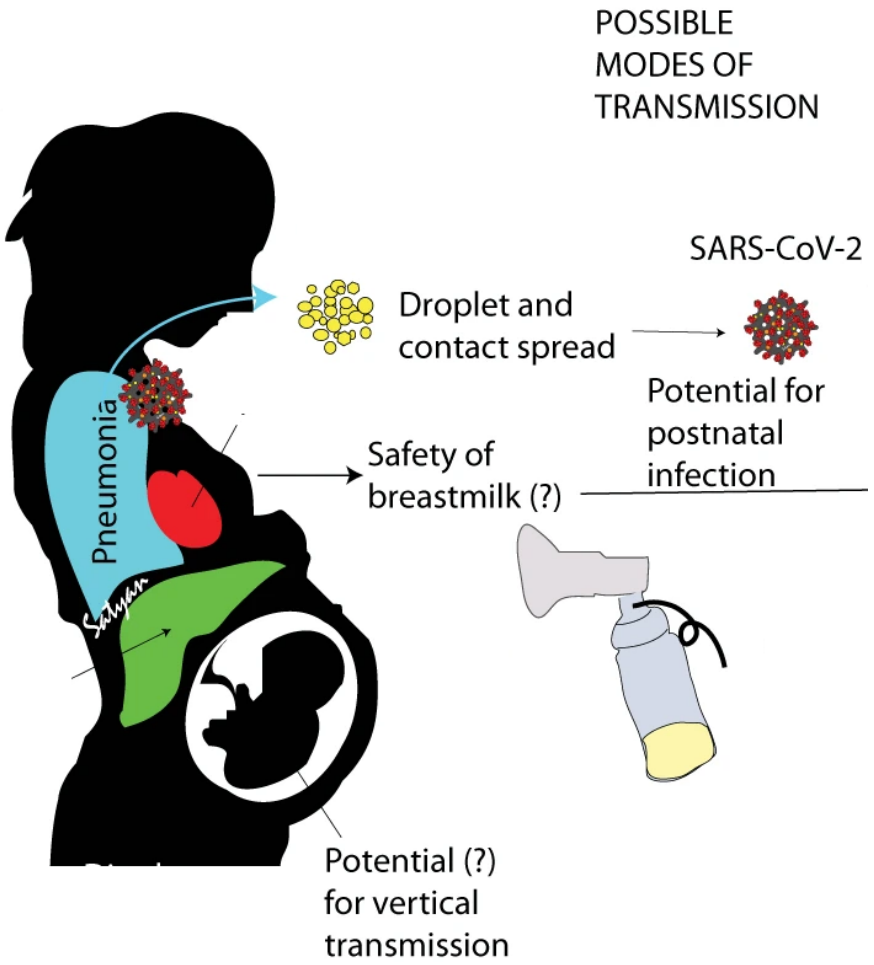
1. Intrauterine vertical

- IgM/IgG: 3/8 reported positive neonates, but *negative* PCR
  - *Does not support* intrauterine vertical transmission
- PCR of placenta, amniotic fluid, membranes:
  - French Case report: viremic mother and neonate; **acute and chronic intervillous inflammation on placental pathology with + PCR**
  - Italian case report: two placentas with +in situ hybridization for viral RNA on fetal side; infants also positive
  - Toronto case report: neonate + PCR from NP, plasma, stool; placenta with histopathologic changes (inflammation and infarction)
  - NYU case series: 3/11 positive placenta or membranes; all infants neg; *could be due to cross contamination*
- PCR of vaginal secretions – One case reported, all others neg

Evidence is inconclusive

Zeng et al., *JAMA, 2020.*
Dong et al., *JAMA, 2020.*
Xiong et al., *J Med Virology,* 2020.
Penfield et al., *Am J Perinatology, 2020.*
Kirstman et al., *CMAJ*, 2020.
Patane et al., *AJOG MFM,* 2020.
Shalish et al., *Am J Perinatology*, 2020.
Vivante, *Nature Communications*, 2020.

Neonatal Acquisition of SARS-CoV-2



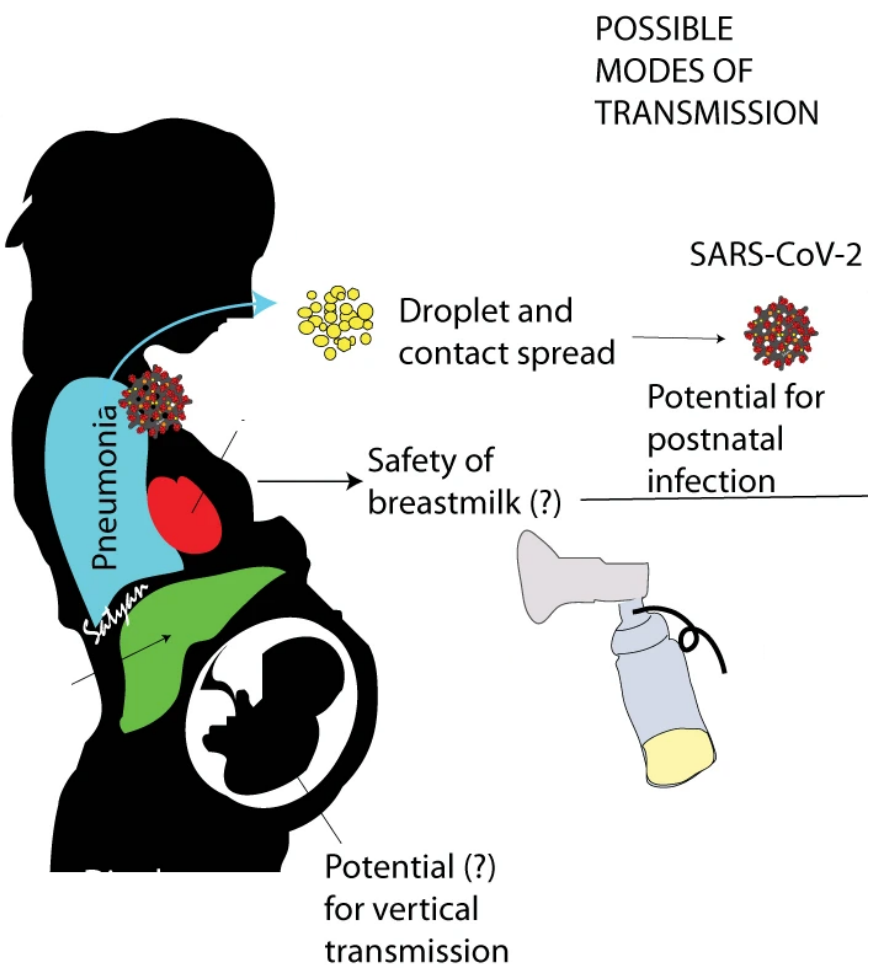
Adapted from Mimouni et al., *J Perinatology*, 2020.

2. Postnatal

- SARS-CoV-2 known to be present in aerosols, urine, fecal samples
- NY case series of 120 infants born to SARS-CoV-2+ mothers: ***all tested negative*** at 24 hr, 5-7 days (n=82), and 14 days (n=72)
  - 78% of infants were still breastfeeding at 5-7 days of life
  - Hand hygiene, maternal use of a surgical mask during breastfeeding and skin-to-skin, and use of a closed isolette when infants were not being held or fed
- AAP (updated 7/22/20), WHO, Canadian Pediatric society, Royal College of Paediatrics and Child Health (UK) now recommend rooming-in for newborns born to SARS-CoV-2+ mothers

Wang, *JAMA*, 2020.
Salvatore, *Lancet Child Adol Health*, 2020.

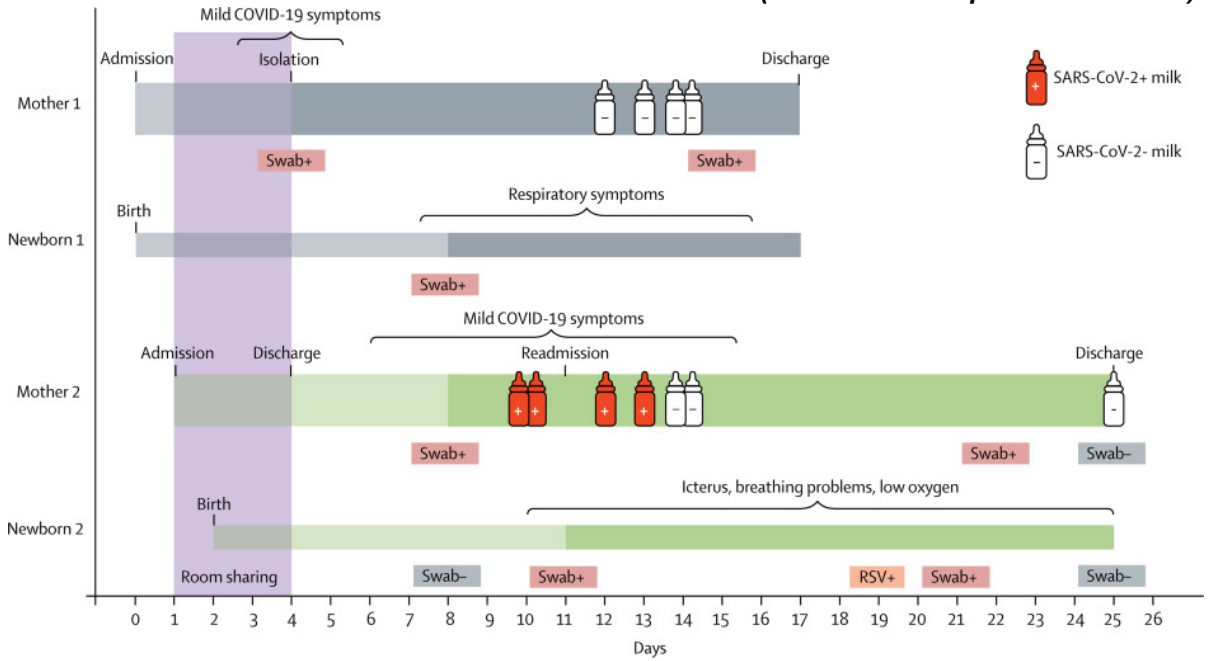
Neonatal Acquisition of SARS-CoV-2



Adapted from Mimouni et al., *J Perinatology*, 2020.

3. Breast Milk

- 2 studies report + viral RNA in maternal breast milk – *unclear if this is route of transmission (versus droplet/contact)*



- Other studies report negative testing in breast milk
- One pre-published non-peer reviewed report of SARS-CoV-2 IgA reactivity in 12/15 (80%) of breast milk samples suggesting immune response in infected mothers

Shalish et al., *Am J Perinatology*, 2020.
Groβ et al., *Lancet*, 2020.
Fox et al., *medRxiv*, 2020.
Tam et al., *Clin Inf Dis.* 2020.

Neonatal epidemiology of COVID-19: China

- Chinese CDCP case series – 2135 pediatric cases Jan 16-Feb 8
  - 728 (34%) confirmed, remainder 'suspected'

TABLE 2 Different Severity of Illness by Age Group

Age Group, y[a]	Asymptomatic, *n* (%)	Mild, *n* (%)	Moderate, *n* (%)	Severe, *n* (%)	Critical, *n* (%)	Total, *n*
<1	7 (1.9)	204 (54.2)	125 (33.2)	33 (8.8)	7 (1.9)	376
1–5	15 (3.1)	245 (49.9)	195 (39.7)	34 (6.9)	2 (0.4)	491
6–10	30 (5.8)	277 (53.3)	191 (36.7)	22 (4.2)	0 (0.0)	520
11–15	27 (6.5)	198 (48.1)	170 (41.3)	14 (3.4)	3 (0.7)	412
>15	15 (4.5)	164 (49.1)	145 (43.4)	9 (2.7)	1 (0.3)	334
Total	94 (4.4)	1088 (51.0)	826 (38.7)	112 (5.3)	13 (0.6)	2133

18% of cases <1 year age

- Wuhan Children's Hospital – 171 pediatric cases Jan 28- Feb 26

Table S1. Age distribution of infected children and their respective diagnoses

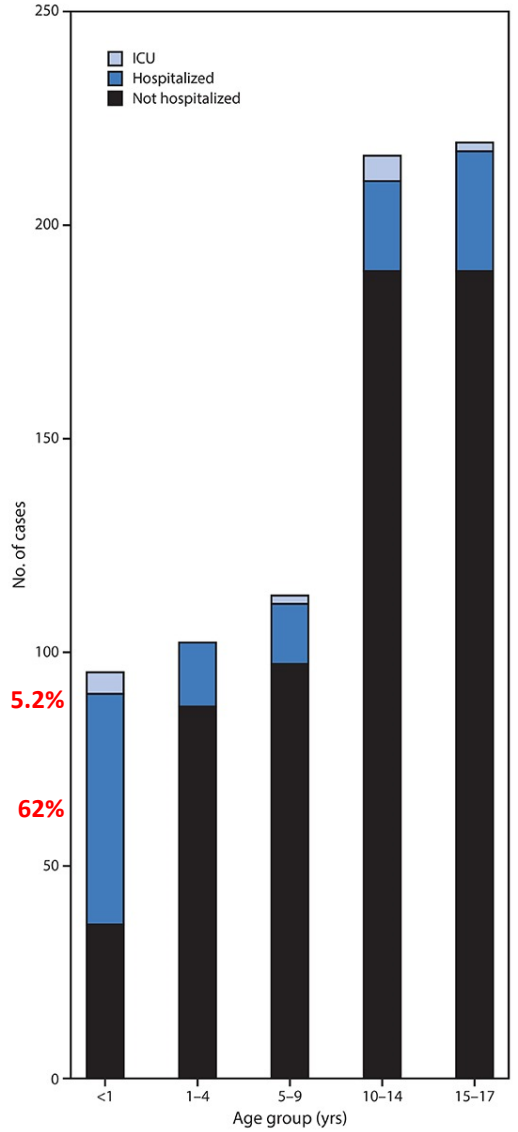
	n (%) or median (IQR)			
	All patients (n = 171)	**Asymptomatic infection (n=27)**	**Upper respiratory tract infection (n = 33)**	**Pneumonia (n =111)**
Age -years				
Median (IQR)	6.7 (2.0-9.8)	9.6 (7.6-12.6)	3.9 (1.4-8.4)	5.9 (1.2-9.3)
<1	31 (18.1)	0	6 (18.2)	25 (22.5)
1-5	40 (23.4)	1 (3.7)	12 (36.4)	27 (24.3)
6-10	58 (33.9)	14 (51.9)	10 (30.3)	34 (30.6)
11-15	42 (24.6)	12 (44.4)	5 (15.2)	25 (22.5)

One death (10 mo intussusception)

Dong et al., *Pediatrics*, 2020
Lu et al., *NEJM*, 2020

Neonatal epidemiology of COVID-19: US

- CDC series – 2572 pediatric cases (1.7%) Feb 12- April 2
  - **<u>Infants <1 yr 15% of pedi cases, 0.27% of total cases</u>** (1.2% of US pop)
  - **62% age <1 yr hospitalized**, 5/95 (5.2%) required ICU
  - **80/345 (23%) all children with at least one underlying condition**
    - 40 (11.5%) Chronic Lung Disease (including asthma)
    - 25 (7.2%) with CV disease
    - 10 (2.9%) immunosuppressed
    - *28/37 (76%) hospitalized patients w underlying condition*
- Case series of 48 PICU patients (46 PICUs), Mar 14-April 3
  - **8 (17%) < 1 year of age**
  - 40 (83%) with pre-existing medical conditions
    - 2 (4%) with CLD, 2 (4%) with congenital malformations, 19 (40%) “medically complex”
- COVID-NET: 576 hospitalized pediatric patients Mar 1- July 5
  - 108 (18.8%) 0-2 months, 20 (3.5%) 3-5 months



CDC COVID-19 Response Team. Coronavirus disease in children – United States, February 12-April 2, 2020. *MMWR,* 2020.
Shekerdemian et al., *JAMA Pediatrics, 2020.*
Kim et al, MMRW Aug 2020.

Neonatal Presentations of COVID-19

- Clinical presentations of neonates vary greatly
- Systematic review of 25 neonatal cases < 3 mo
  - Most commonly identified due to a history of maternal infection (84%)
  - 20% were asymptomatic
  - Higher proportion of neonates were severely ill compared to children older 1 mo of age (12 vs 2%)
    - DIC in two, multiorgan dysfunction in one, death in one
  - Most common clinical presentations: respiratory distress (40%), fever (32%), feeding intolerance (24%)
  - Lab findings: elevated WBC (20%), CPK (20%), liver enzymes (16%) CRP and/or procalcitonin (12%)
  - Abnormal CXR (48%)

Liguaro, *Eur J Pediatrics,* 2020.

Neonatal Presentations of COVID-19

- Neurologic Symptoms
  - Paris case series (n=5 infants < 3 mo)
    - All boys, 5/5 with fever, **4/5 neurologic symptoms**
    - All CSF PCR neg
    - All improved within 1-3 days
  - Transplacental transmission case – neonate with irritability, inflammatory findings in the cerebrospinal fluid, and white matter injury on brain MRI

Nathan et al., *Lancet,* 2020.
Vivante, *Nature Communications*, 2020.

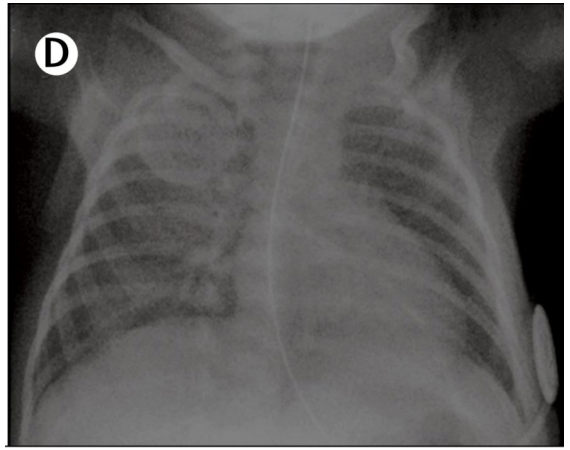
Term Severe Presentations of COVID-19

- **Italian case report**: 3d FT infant SARS-CoV-2+; mother symptomatic 2d after delivery, hypoxemia → HFNC for 2 d
  - Normal CBC and CRP, **CXR bilateral GGOs**
  - **SARS-CoV-2+ on DOL 15 and 21**
- **CHLA** case report**:** 15d FT infant SARS-CoV-2+; HFNC x1d
  - Normal labs, **CXR GGOs**
  - + NP swab at day 1 and 6, + rectal swab day 6
- **Colorado case report:** 3 FT infants 17d-33d old SARS-CoV 2+, Max 1L NC. +household contacts

Sinelli et al., *Pediatrics,* 2020
Coronado-Munoz et al., *NEJM,* 2020
Precit et al. *J Ped Inf Dis Soc.* 2020

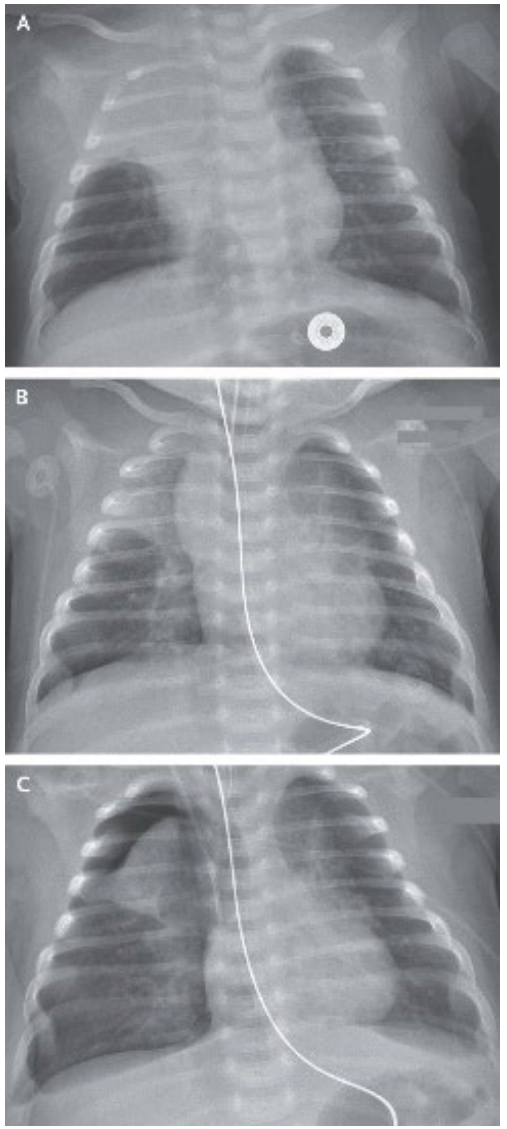
Preterm Presentations of COVID-19

- UK case series (n=8 infants <1yr)
  - **1 premature** – 5d ex 34wker, mom COVID+; CPAP x 3d
    - Presented with **hypothermia, apnea, lethargy, jaundice, decr PO**
    - Normal CBC and CRP; CXR with GGOs; Echo with ASD



- Belgium case report: 1 week ex26wk SARS-CoV-2+; mother +COVID
  - **No change in baseline respiratory support**, but CXR with b/l streaky infiltrates

- TX case report: 3 week old ex 36 weeker, URI sx and poor feeding
  - **Hypoxemia requiring intubation x 5d**; **PTX**
  - Hydroxychloroquine + Azythromycin
  - Household contact with symptoms



Ng et al., *Pediatr Inf Dis Journal*, 2020
Piersigilli et al., *Lancet Child Adol Health,* 2020.
White et al. *Neonatology*. 2020

Multisystem Inflammatory Syndrome in Children (MIS-C)

Kawasaki-Disease like presentation associated with COVID-19 with cardiac injury and myocarditis **– not yet reported in neonates**

New Inflammatory Condition in Children Probably Linked to Coronavirus, Study Finds

Researchers compared 10 cases in Italy with previous cases of a similar childhood illness, Kawasaki disease. The rate of the new cases was much higher, and the conditions were more serious.

- Youngest reported patient 1 year of age
- Age older than Kawasaki disease (mean 7.5-11)
- Myocardial involvement, shock, rash, GI symptoms; respiratory symptoms in minority
- 70-80% IgG+ but PCR negative

Verdoni et al, Lancet May 2020
Belhadjer et al, Circulation 2020
Levin, COCA Call 5/19/20
Schneider, COCA Call 5/19/20

Summary

- Neonates appear to be at higher risk than pediatric population for severe disease, but overall underrepresented in severity compared to adult disease
  - Rates of postnatal transmission, with proper precautions, seems low
  - Unclear evidence re: vertical transmission
- Presentations vary widely from asymptomatic to respiratory failure, with very little mortality seen
- Little data among high-risk infants, including preterm infants

Florida Perinatal Quality Collaborative
Webinar

Neonatal Care During COVID-19

August 13, 2020

AAP Guidance on Management of Infants Born to Mothers with COVID-19

Karen M. Puopolo MD, PhD

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Conflict of Interest Disclosure

- **In the past 12 months I, Karen M. Puopolo, MD, PhD, had NO financial relationships with the manufacturer of any commercial product and/or provider of any commercial service**
  - **I do not intend to discuss any unapproved/investigative use of a commercial product/device in my presentation**
- **I received no compensation for this presentation nor for my work contributing to AAP Neonatal COVID Guidance**
  - **I receive research support from the National Institutes of Health and the Centers for Disease Control and Prevention**

COVID-19 and Newborn Health

- ***Numerous management issues arise when women have confirmed or suspected COVID-19 at the time of delivery***
  - **Can SARS-CoV-2, the virus causing COVID-19, be vertically transmitted from a mother to her newborn before birth, or during the birth process?**
  - **What is the best way to minimize the risk of horizontal transmission of SARS-CoV-2 infection from mother to newborn?**
  - **Do newborns get sick from SARS-CoV-2?**
  - **Should we test the newborn to determine if the infant has acquired the virus?**
  - **Can mothers with COVID-19 breastfeed?**
  - **What should we do after the newborn goes home?**

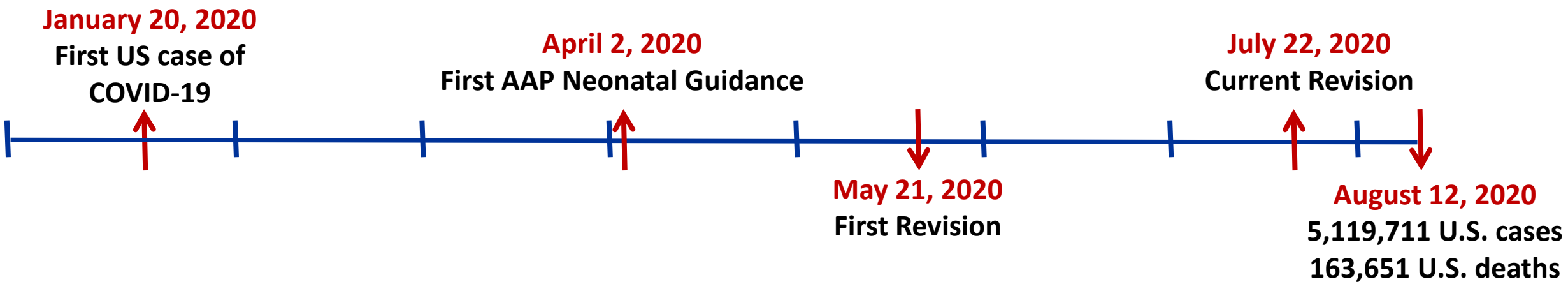
COVID-19 and Newborn Hospital Management

- **What personal protective equipment should be used to care for the infant born to a mother with COVID-19?**
    - **In the Delivery Room**
    - **In the NICU**
    - **In the Well Nursery/Postpartum setting**
- **Can parents with COVID-19 visit their newborn if the infant requires neonatal intensive care?**

March 2020: Need for Neonatal Guidance

- Although evidence was accumulating to inform adult care, relatively few data were available to guide neonatal care when mothers have COVID-19
  - Yet neonatal clinicians were faced with this scenario on a daily basis
- AAP convened a writing group to develop guidance based on:
  - Published reports addressing pregnant women with COVID-19 and information on neonatal and infant outcomes
  - Evolving understanding of how the SARS-CoV-2 virus is transmitted person-to-person and how long infected persons remain infectious
  - Guidance provided by CDC

Evolution of AAP Guidance



- **Mark Hudak**
  Section on Neonatal-Perinatal Medicine
- **David Kimberlin**
  Committee on Infectious Diseases
- **Jim Cummings**
  Committee on Fetus and Newborn

- **Arun Gupta**
  Section on Hospital Medicine
- **Karen Puopolo**
  Committee on Fetus and Newborn
- **Anne Edwards**
  AAP Board Leadership

Sunnah Kim and Jim Couto, AAP Staff

Guidance and Evidence

- When we started in mid-March 2020, we had little evidence regarding pregnant women and newborns, but did know that:
  - This virus is very contagious
  - This virus was killing a lot of humans
  - If mother had onset of illness near the time of delivery, newborn is unlikely to have maternally-derived, transplacentally-acquired protective antibody

COVID-19 and Neonatal Medicine

- **Can SARS-CoV-2 be vertically transmitted from a mother to her newborn before birth, or during the birth process?**
- **What is the best way to minimize the risk of horizontal transmission of SARS-CoV-2 infection from mother to newborn?**
- **Do newborns get sick from SARS-CoV-2?**
- **Should we test the newborn to determine if the infant has acquired the virus?**
- **What should we do after the newborn goes home?**

- **Vertical transmission is not common with most studies showing 0-2% of infants test positive for SARS-CoV-2 within 24 hours of birth (placental studies ongoing)**

COVID-19 and Neonatal Medicine

- **Can SARS-CoV-2 be vertically transmitted from a mother to her newborn before birth, or during the birth process?**
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- **Do newborns get sick from SARS-CoV-2?**
- **Should we test the newborn to determine if the infant has acquired the virus?**
- **What should we do after the newborn goes home?**

- **Infection control and prevention practices (hand hygiene, masks and distancing between care) can prevent mother-infant transmission without requiring physical separation**

COVID-19 and Neonatal Medicine

- **Can SARS-CoV-2 be vertically transmitted from a mother to her newborn before birth, or during the birth process?**
- **What is the best way to minimize the risk of horizontal transmission of SARS-CoV-2 infection from mother to newborn?**
- **Do newborns get sick from SARS-CoV-2?**
- **Should we test the newborn to determine if the infant has acquired the virus?**
- **What should we do after the newborn goes home?**

- **Newborns and young infants can get sick from SARS-CoV-2 but only rarely critically ill**

COVID-19 and Neonatal Medicine

- **Can SARS-CoV-2 be vertically transmitted from a mother to her newborn before birth, or during the birth process?**
- **What is the best way to minimize the risk of horizontal transmission of SARS-CoV-2 infection from mother to newborn?**
- **Do newborns get sick from SARS-CoV-2?**
- **Should we test the newborn to determine if the infant has acquired the virus?**
- **What should we do after the newborn goes home?**

- **Currently testing is helping us understand perinatal/pediatric viral transmission**

COVID-19 and Neonatal Medicine

- **Can SARS-CoV-2 be vertically transmitted from a mother to her newborn before birth, or during the birth process?**
- **What is the best way to minimize the risk of horizontal transmission of SARS-CoV-2 infection from mother to newborn?**
- **Do newborns get sick from SARS-CoV-2?**
- **Should we test the newborn to determine if the infant has acquired the virus?**
- **What should we do after the newborn goes home?**

- **Use time- and symptom-based criteria for discontinuing precautions in most cases**

Neonatal Provider PPE

What personal protective equipment should be used to care for the infant born to a mother with COVID-19?

Delivery Room

- gown and gloves
- either an N95 respiratory mask and eye protection goggles or an air-purifying respirator that provides eye protection
- protects against both maternal virus aerosols and potential newborn virus aerosols that resuscitation procedures

NICU and Well Nursery

- Dependent on aerosol-generating respiratory support or not
- If yes => same as DR
- If no => use standard mask*

https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control.html

*May use N95 if in same room as sick mother

Data from Chinese Experience

- **Chinese case series of 2143 pediatric patients (731 with test-confirmed infection) found that infants <12 months of age *can* suffer severe illness**
- **Chinese case reports demonstrated that newborns *can* test positive for SARS-CoV-2 and develop illness**
  - **4 reports with total 17 COVID pregnant women found no newborn infection**
  - **2 reports with total 34 COVID pregnant women found newborn infection in 4/34**
- ***Infants universally separated from mother at birth and cared for with isolation for 14 days***

Chen, et al. *Lancet* 2020; Liu, et al. *Preprints* 2020; Wang X, et al. *Clin Infect Dis*. 2020; Wang S, *Clin Infect Dis*. 2020; Zeng, L. *JAMA Pediatr* 2020; Zhu, H. *Transl Pediatr*. 2020

Maternal Newborn Care

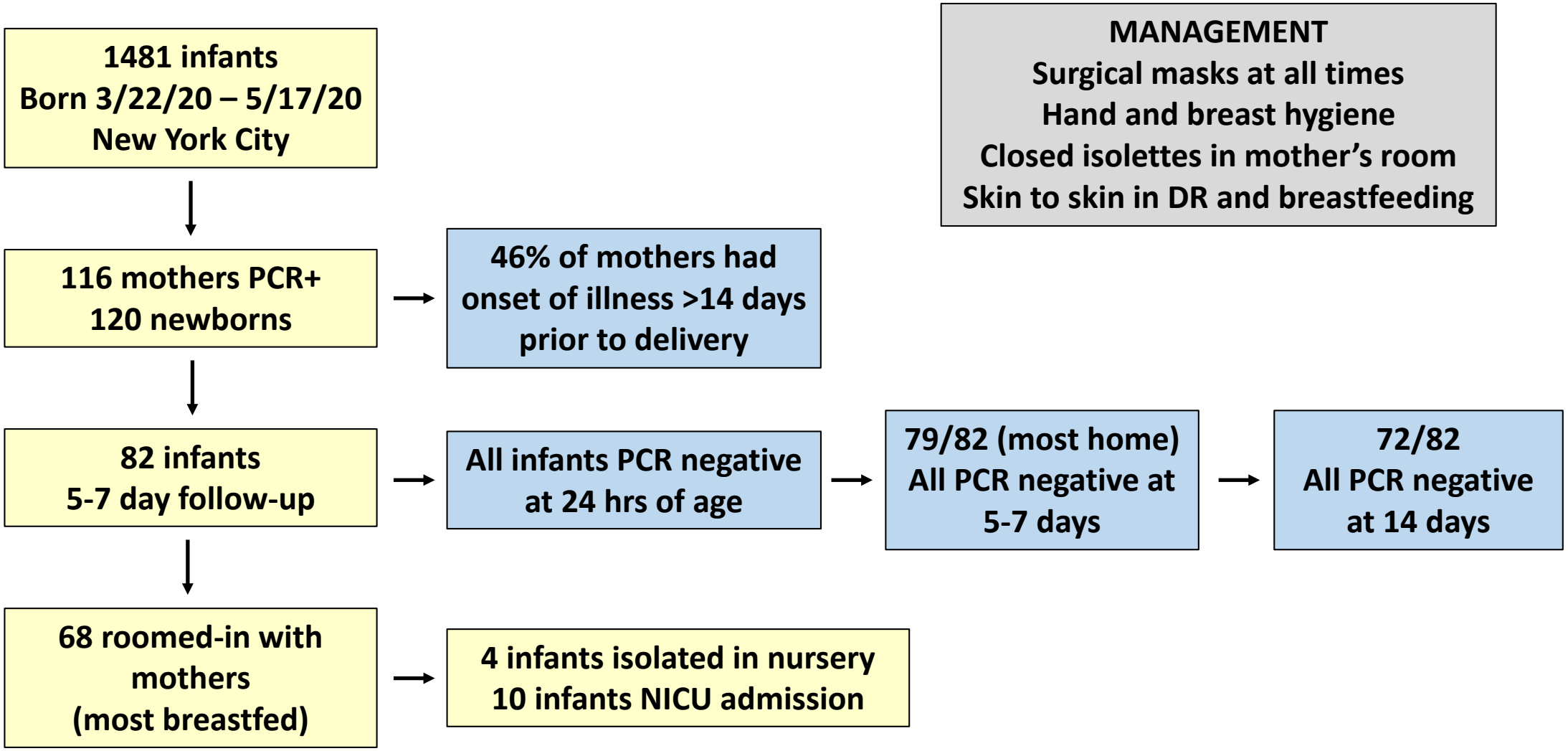
What is the best way to minimize the risk of horizontal transmission of SARS-CoV-2 infection from mother to newborn?

- Other serious respiratory diseases occurring at birth managed with maternal-infant separation
  - Varicella
  - Tuberculosis
  - H1N1 influenza

- *Initial guidance recommended physical separation at birth until mother during the birth hospitalization*
- Provide time for maternal recovery and decreasing infectiousness

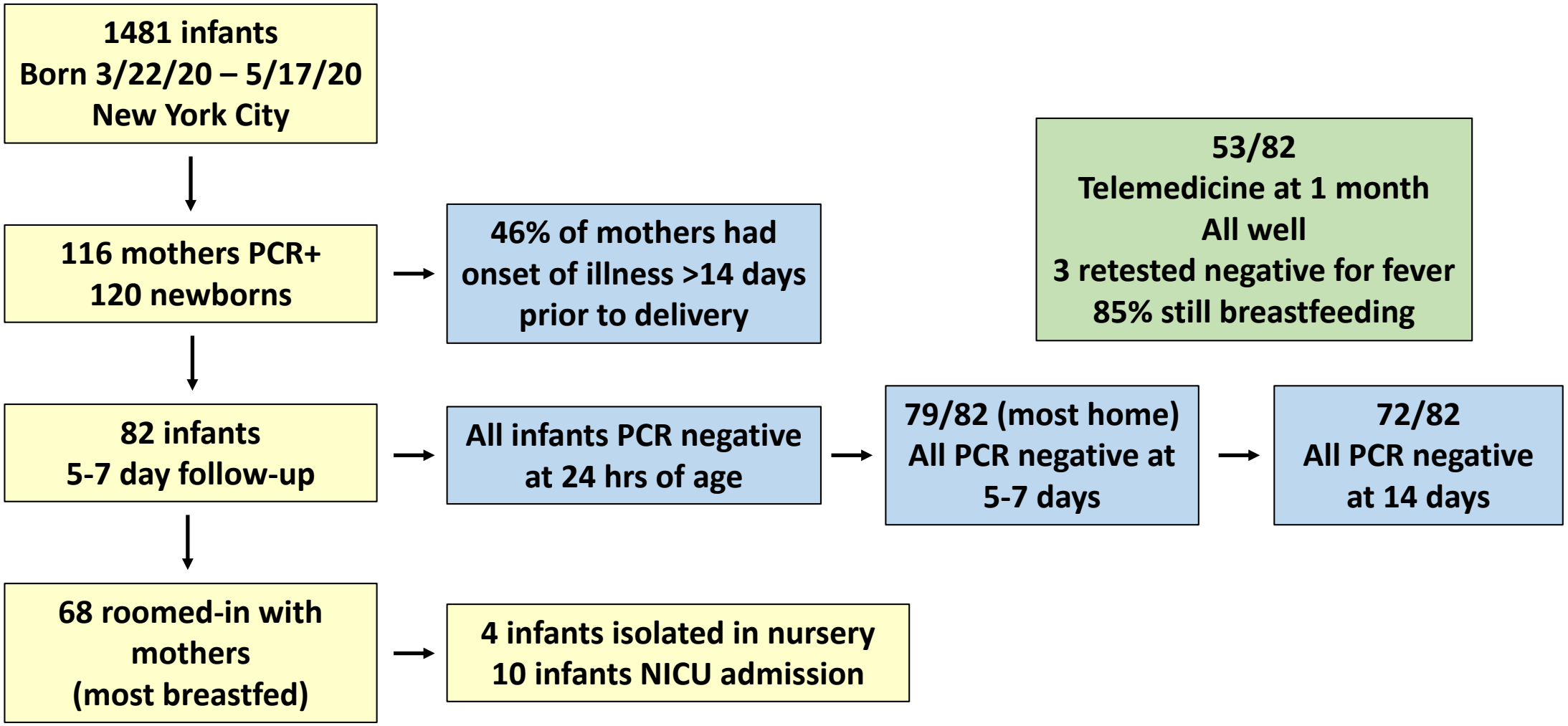
AAP Red Book; CDC guidance.

Data from New York Experience



Salvatore CM, et al. *Lancet Child Adolesc Health*. 2020

Data from New York Experience



Salvatore CM, et al. *Lancet Child Adolesc Health*. 2020

Maternal Newborn Care

What is the best way to minimize the risk of horizontal transmission of SARS-CoV-2 infection from mother to newborn?

- Evidence to date suggests that the risk of horizontal transmission during the birth hospitalization is low when precautions are taken
  - appears to be not greater with rooming-in
- Women positive by universal obstetric NP-PCR screening on admission may not be contagious
- *Mothers and newborns may room-in according to usual center practice*
  - *Use masks, hand hygiene and appropriate distance*
- Consider separation if mother too ill to care for infant
- If using isolette, provide education to prevent infant falls

Why Would We Be Worried About Breast Milk?

- *AAP strongly advises breastfeeding*
  - Very few instances where breastfeeding prohibited
- Some viruses readily infect infants from maternal milk
  - HIV
    - current guidance varies
  - HTLV-1
  - Ebola virus
  - CMV
    - BF may be form of “natural immunization”

What Have We Learned About Breast Milk?

- **Initial Studies mostly did not detect SARS-CoV-2 in breast milk**
  - **10 studies from China**
  - **Milk samples from 28 women**
  - ***Only one tested positive for SARS-CoV-2 by RT-PCR***
    - **Milk obtained on day 1 after birth; repeat samples negative**
- **One study measured IgG and IgM in breast milk**
  - **Mother and 13-month old infant both developed symptomatic COVID-19**
  - ***SARS-CoV-2 IgG detected in milk on Day 8 and Day 24 after onset of maternal illness***
  - **IgG also detected in maternal and infant serum**

Lackey KA, et al. Preprint. *medRxiv*. 2020; Yu, Y., et al. (2020). Preprint. *Research Square*. 2020

Breastfeeding

Should infected mothers breastfeed their infants?

- **Initial reports suggested it was unlikely that SARS-CoV-2 would be transmitted by breastmilk**
- **Initial guidance focused on transmission from maternal respiratory secretions during direct breastfeeding**

- ***Infected mothers initially counseled to express breast milk (after appropriate breast and hand hygiene) and this milk may be fed to the infant by uninfected caregivers***
- **Counsel driven by perceived need for physical separation**

Further SARS-CoV-2 Detection in Breastmilk

Reference (Site)	Clinical Details	SARS-CoV-2 Detected in Milk
Tam, et al. *Clin Infect Dis* 2020 (Australia)	Mother and 8-month old infant with symptomatic COVID-19	Day 5 and 15 after symptom onset
Bastug A, et al. *Breastfeed Med*. 2020 (Turkey)	Asymptomatic mother at birth; infant later with asymptomatic infection	Colostrum on Day 1; milk on Day 3 and Day 4 after birth
Groß R, et al. *Lancet*. 2020 (Germany)	Symptomatic mother and infant	Days 10, 12 and 13 after birth

Breastfeeding

Should infected mothers breastfeed their infants?

- **AAP strongly supports breastfeeding as the best choice for infant feeding**
- **Although studies now detect SARS-CoV-2 nucleic acid in breast milk, it is not yet known whether viable, infectious virus is secreted in breast milk, nor is it yet established whether protective antibody is found in breast milk**

- ***Mothers should perform hand hygiene before breastfeeding and wear a mask during breastfeeding***

Post-hospital discharge, prioritize pediatric office visits and telemedicine to support COVID-impacted (and not impacted) breastfeeding mothers and infants

Duration of Precautions

When is it safe for mothers to dispense with mask?

When is it safe for mothers to enter the NICU?

- **Initial guidance driven by uncertainty around the duration of viral shedding and the relationship of PCR-based detection of nucleic acid to shedding of infectious virus**
- **Assumed PCR positive = Contagious**

- ***For newborn home discharge***
  - **Resolution of fever without the use of antipyretics for at least 72 hours *and***
  - **Improvement in respiratory symptoms *and***
  - **>7 days passed since onset of symptoms *or***
  - **negative PCR results from at least two consecutive NP swabs ≥24 hours apart**
- ***For maternal NICU presence***
  - **All of above PLUS negative PCR results from at least two consecutive NP swabs ≥24 hours apart**

Duration of Precautions

When is it safe for mothers to dispense with mask?

When is it safe for mothers to enter the NICU?

- **Concentrations of SARS-CoV-2 RNA in upper respiratory specimens declines after onset of symptoms**
- **Contagious virus also declines after onset of symptoms**
  - ***Cannot assume PCR positive = Contagious***
  - **Recovered patients can remain PCR+ for up to 12 weeks**

- ***For newborn home discharge***
  - **Resolution of fever without the use of antipyretics for at least 24 hours *and***
  - **Improvement in symptoms *and***
  - **>10 days passed since onset of symptoms**
- ***For maternal NICU presence***
  - **Resolution of fever without the use of antipyretics for at least 24 hours *and***
  - **Improvement in symptoms *and***
  - ***>14-20 days passed since onset of symptoms***

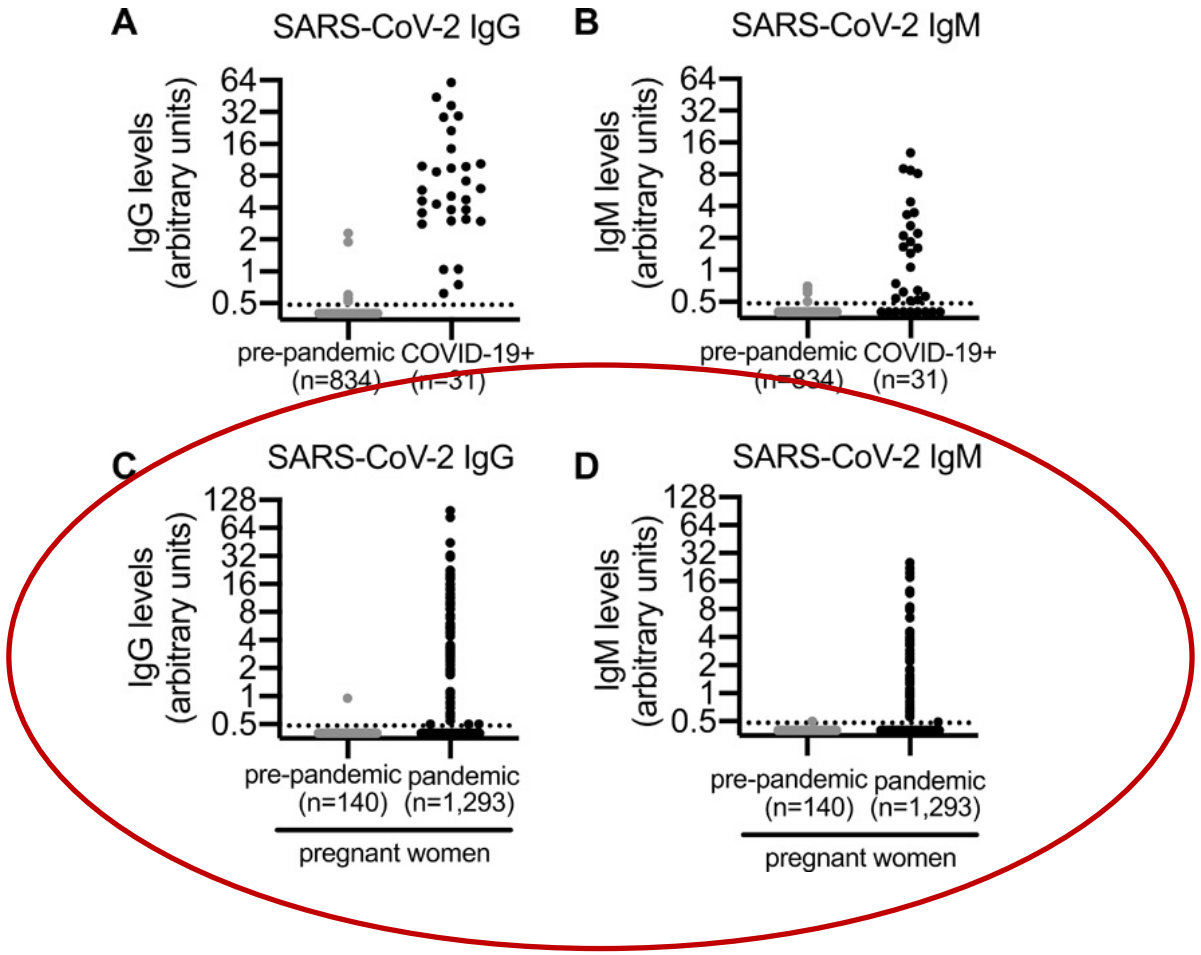
https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html

Rationale for Conservative NICU Guidance

- **Vulnerable health of NICU infants of whom some are functionally immunosuppressed**
- **Open-bay structure of many NICUs**
- **Concerns around protecting personnel who support the critical infrastructure of NICUs**
- ***Prohibiting parent presence is a terrible step***
    - **Centers may choose to set guidelines most appropriate for their local structure and context of care**

SARS-CoV-2 Antibody Levels in Parturient Women in Philadelphia

- **Discarded sera from 1293 pregnant women admitted to two Penn birth hospitals from April to June 2020**
- **ELISA assay targeting SARS-CoV-2 spike protein receptor binding domain with <1% false-positive rate**
- ***6.2% of parturient women with IgG and/or IgM at time of delivery***



Flannery et al. *Sci. Immunol*. 2020

Relationship of NP-PCR Testing and SARS-CoV-2 Antibody

Serology Timing	NP Tested	Seropositive
Before NP Test	17	10 (59)
0-7 days after NP test	26	15 (58)
7-13 days	5	5 (100)
14-20	2	2 (100)
≥ 21 days	14	14 (100)
Total	64	46 (72)

- How does antibody correlate with immunity?
- What is the timing of maternal infection and transplacental antibody transfer?
- ***Maternal/newborn care will be optimally informed when we understand <u>WHEN/IF</u> it can be safely assumed that newborn has acquired maternally-derived, protective SARS-CoV-2 antibody***

Flannery, et al. *Sci Immunol* 2020

AAP Section on Neonatal-Perinatal Medicine (SONPM) COVID-19 Perinatal Case Registry

- **SONPM is inviting every hospital that takes care of infants to participate in a National Perinatal COVID-19 (NPC-19) Registry by submitting de-identified maternal and neonatal data as it pertains to perinatal COVID-19**
- **See registration information at SONPM website at https://services.aap.org/en/community/aap-sections/sonpm/**
- **Currently, 246 centers are fully registered with IRB approval (!!)**

AAP Guidance

- **Committee on Fetus and Newborn; Committee on Infectious Diseases; Section on Neonatal-Perinatal Medicine. “FAQs: Management of Infants Born to Mothers with Suspected or Confirmed COVID-19”**
  - https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/faqs-management-of-infants-born-to-covid-19-mothers/
- **Section on Breastfeeding. “Breastfeeding Guidance Post Hospital Discharge for Mothers or Infants with Suspected or Confirmed SARS-CoV-2 Infection”**
  - https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/breastfeeding-guidance-post-hospital-discharge/

Questions and Comments Most Welcome!

- **Email:** Karen.Puopolo@pennmedicine.upenn.edu
- **Email:** puopolok@email.chop.edu

National Registry for Surveillance and Epidemiology of Perinatal COVID-19 Infection (NPC-19)

AAP Section on Neonatal-Perinatal Medicine

Mark Hudak MD, Chair, SONPM

Raison d'être for NPC-19

- By early March, potential impact of SARS-CoV-2 on hospital obstetric and newborn services became clear
- AAP posted initial management guidance in early April 2020 (in absence of robust national perinatal data) as a "dynamic" document
- AAP recognized need to revise guidance as evidence developed

Specific Questions

- Is there evidence for transplacental transmission?
- What is the likelihood that an infant will acquire infection with SARS-CoV-2 in the hospital after birth?
- Would a strategy of temporary infant separation reduce the risk of perinatal transmission?
- What are the clinical signs in infants who acquire infection?
- What is the continuing risk after discharge?

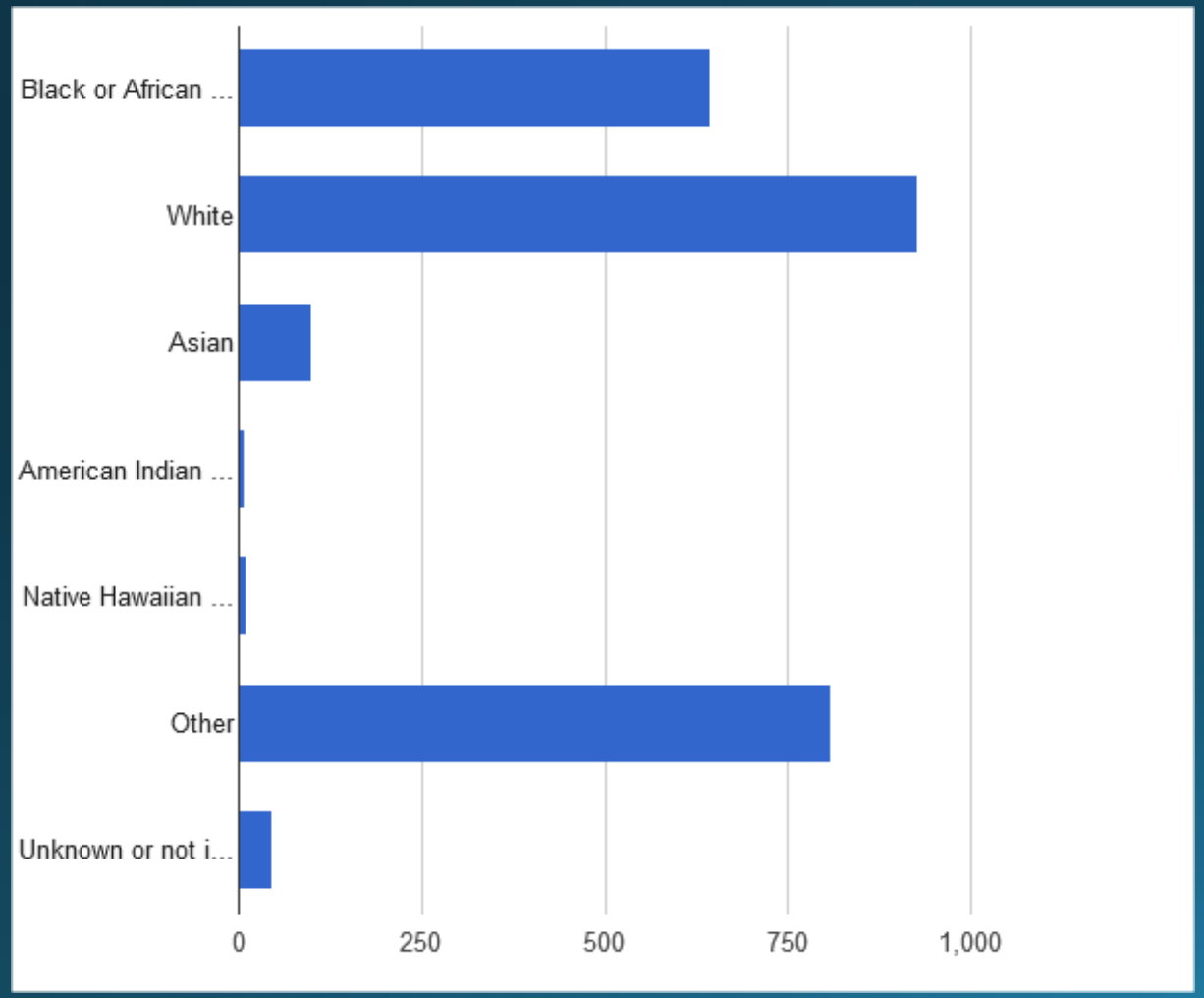
Process

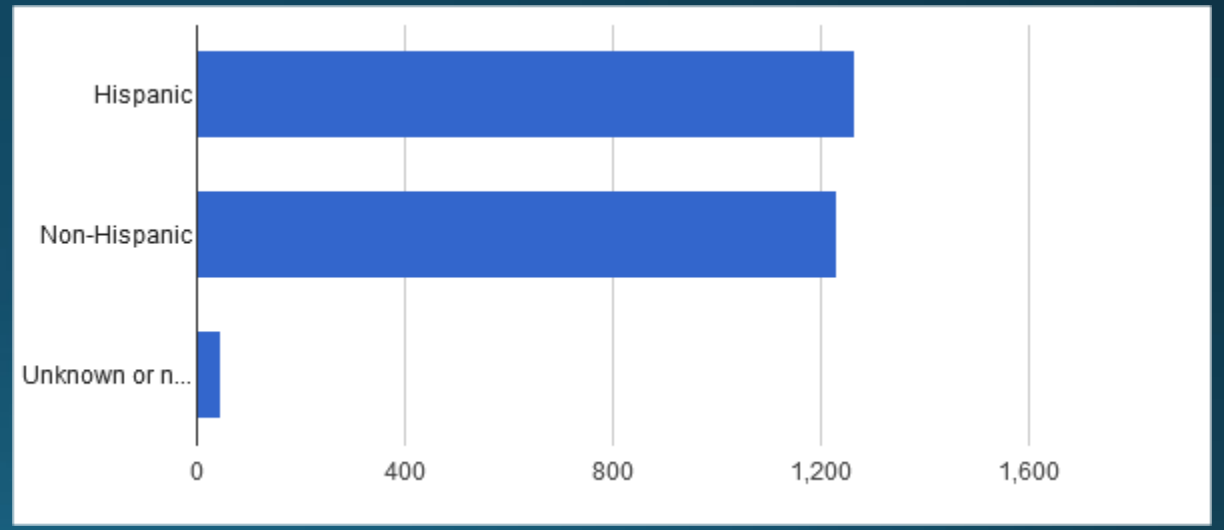
- Wide consultation with a variety of experts from VON, MedNAX, UPenn, and international colleagues (Ju-Lee Oei in Australia and Jayanta Banerjee in UK)
- UF IRB approved in late March
- Rapid "active COVID" registry opportunity made known to centers in early April through SONPM, VON, and MedNAX
- Adaptive revision of data elements occurred over two months
- Addition of a "Resolved COVID" arm in late May
- Desire to expand to obtain phone follow-up after 1 month

Progress

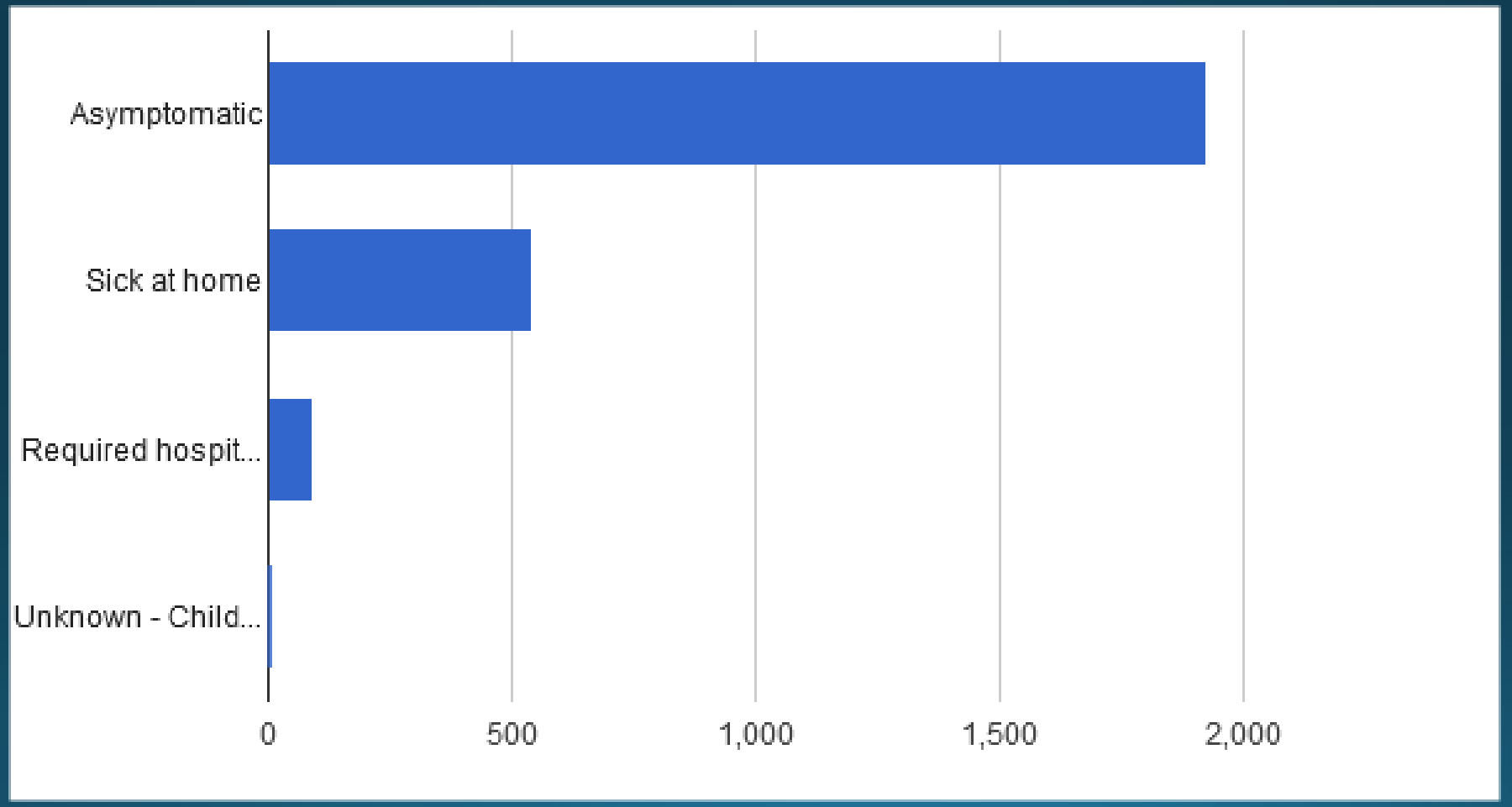
- Initially slow (through April 30: 103 dyads)
- Accelerated through May (572), June (1,370), July (2,296)
- Currently:
  - 2,574 dyads in active COVID-19
  - 157 dyads in resolved COVID-19
  - 248 activated centers (45 states and the District of Columbia); capturing about 17.5% of all US births

Maternal Race and Ethnicity

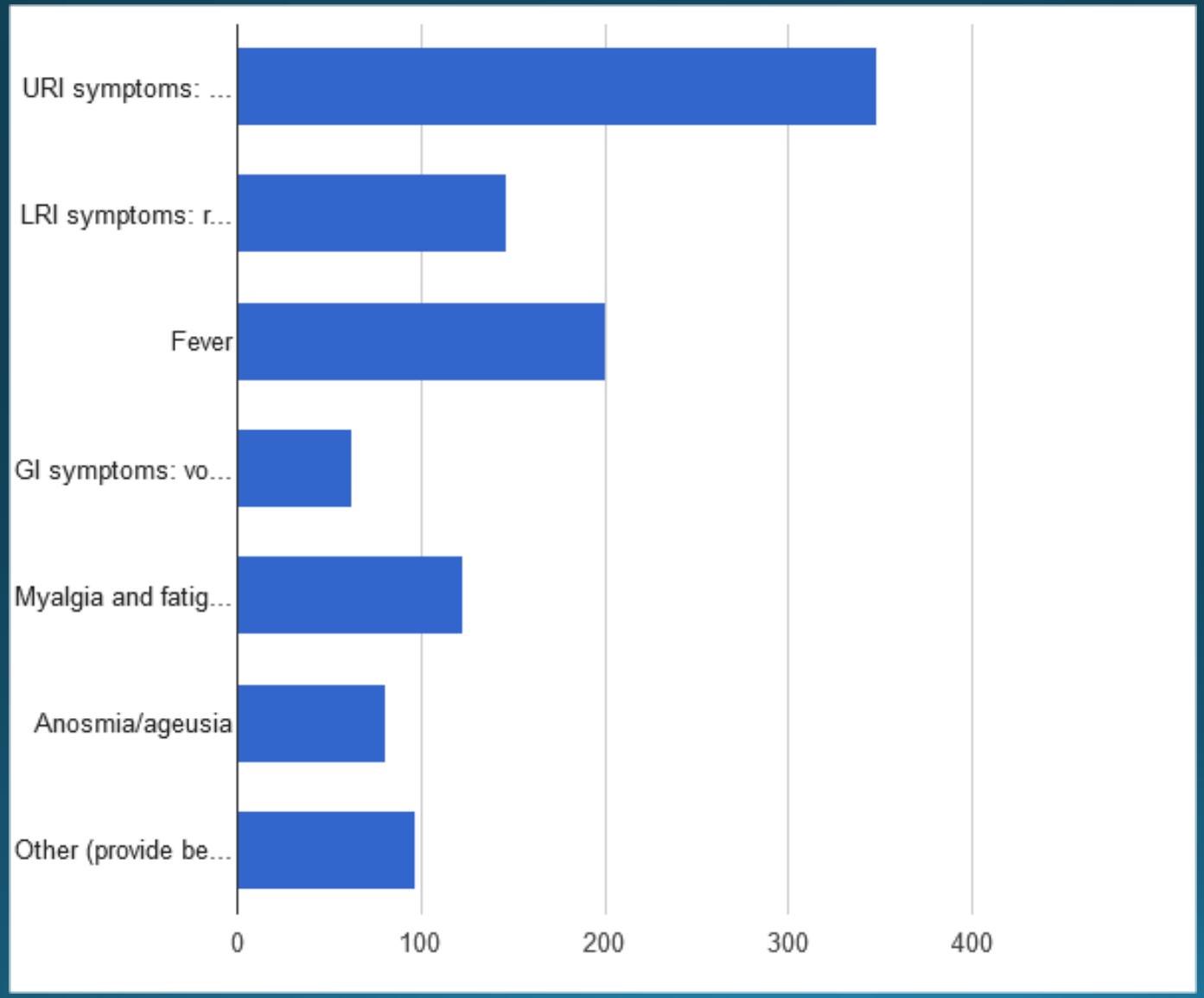




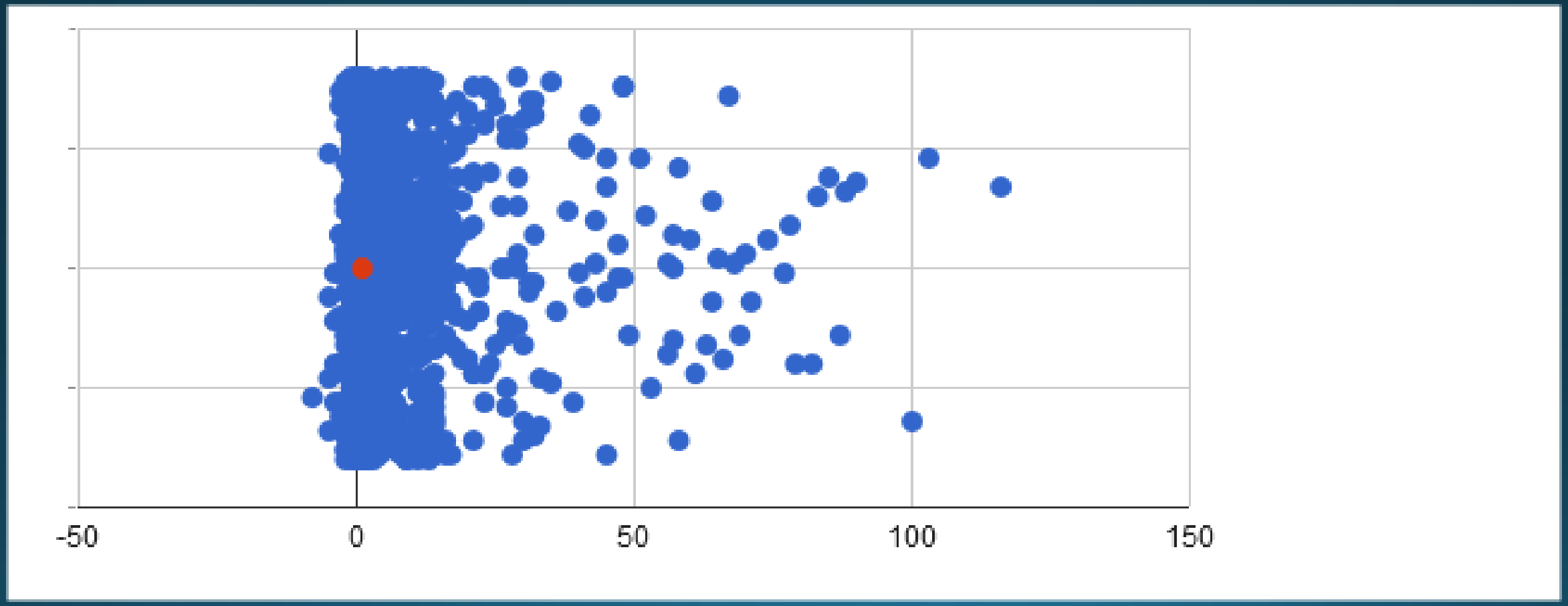
Maternal Status on Admission



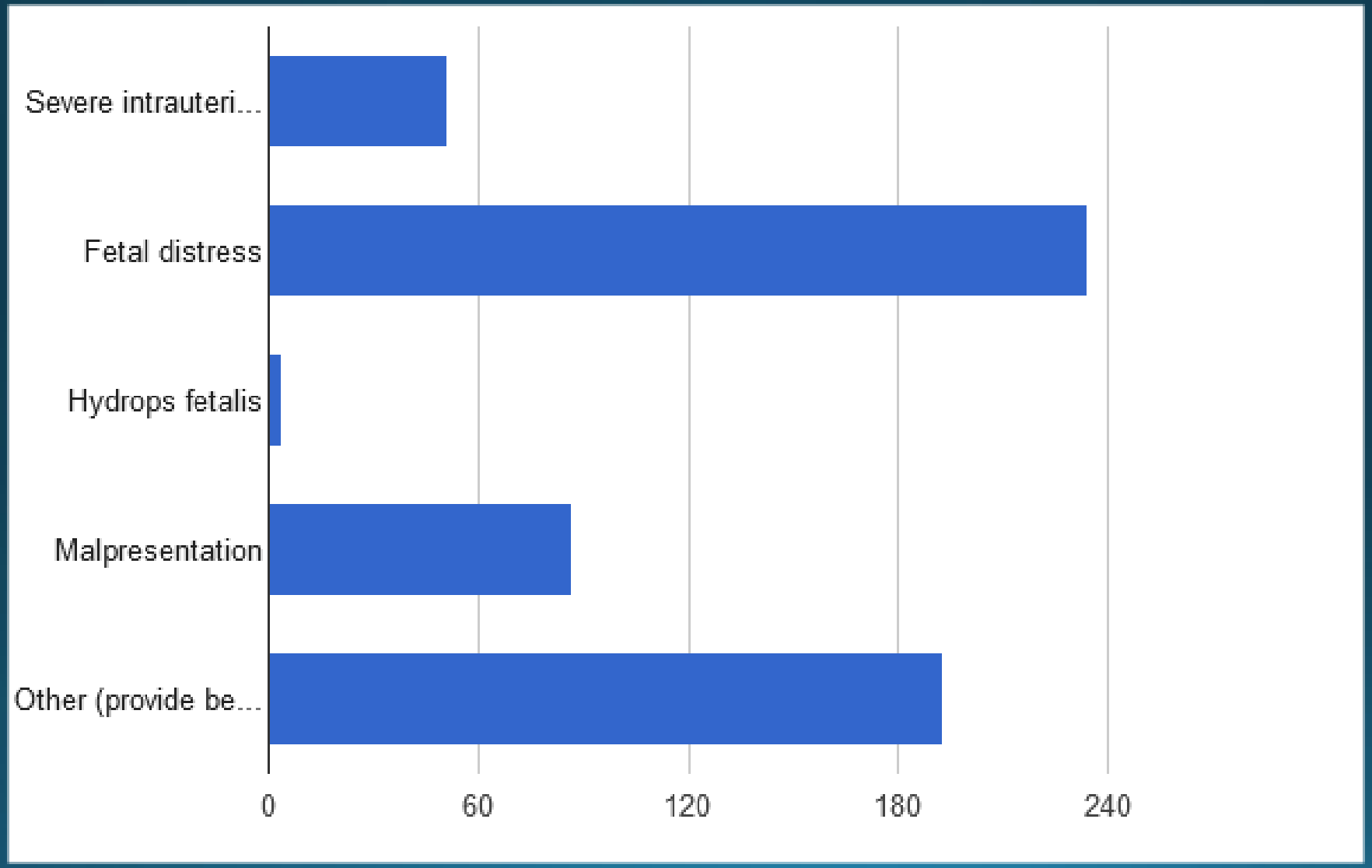
Maternal Symptoms of COVID-19



First Positive Maternal SARS-CoV-2 Test Number of Days Before Delivery



Fetal Indications for Delivery



Infants Tested in Hospital

- 2,111 infants tested
- 43 positive in hospital, another 4 positive after discharge
  - Colonization (4 day 1, 1 day 2): 5
  - First test negative: 17
  - First +/- later tests positive: 21
- Transplacental rate?
- Perinatal rate?

PCR + vs. PCR – Infants: Mothers

Maternal Characteristic	Infants with + PCR in hospital (n=43)	Infants with – PCR in hospital (n=2068)
Non-white (%)	64.2	63.2
Hispanic (%)	63.4	49.5
LOS (days)	5.2	3.6
Died (%)	0	0.2
Sick at home/hospitalized for COVID-19 (%)	33.3	25.8
C-section delivery ($)	57.1	38.7

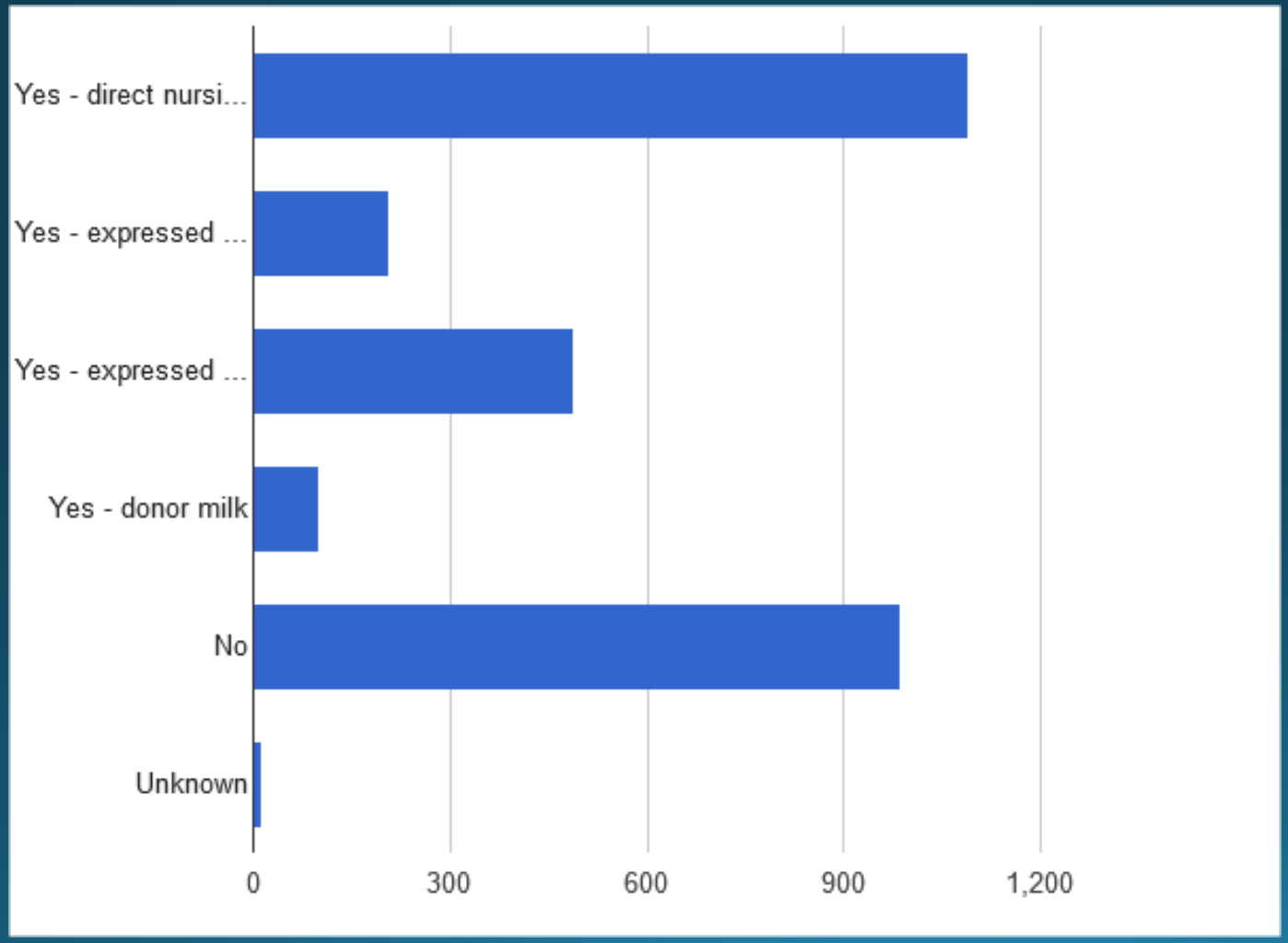
PCR + vs. PCR – Infants: Infants

Infant Characteristic	Infants with + PCR in hospital (n=43)	Infants with – PCR in hospital (n=2068)
Mean birth weight (g)	2771	3109
Mean gestational age (wk)	36.5	38.1
Sex (% male)	51	52
Apgar at 5 minutes	8.4	8.8
LOS (days)	10.6	5.0
Signs of COVID-19 (%)	30.2	16.3

Separation vs. Rooming-in

Descriptor	Separation (n=1123)	Rooming-in (n=974)
Positive infant PCR	22/1123 (2.0 %)	21/974 (2.2 %)
Mother was sick at home or required hospitalization for COVID-19	378/1123 (33.7%)	137/974 (14.0%)

Breastfeeding



Observations and questions

- Minorities are overrepresented
- No clear impact of separation vs. rooming-in on rate of positive PCR tests in infants in hospital, but:
  - Choice was influenced by maternal status
  - ? Higher infectivity among mothers with separation
- Need to provide better definition of maternal infectivity
- COVID-19 and separation reduced breast feeding

Thoughts

- New knowledge develops rapidly
- Outcomes thus far are laboratory tests and not clinical signs
- Actual infectivity of many mothers may be uncertain
- Large numbers were necessary to provide reassurance about rate of positive testing under different protective strategies
- Need early clinical outcomes after hospital discharge to understand real impact of perinatal COVID-19

Florida NPC-19 Centers

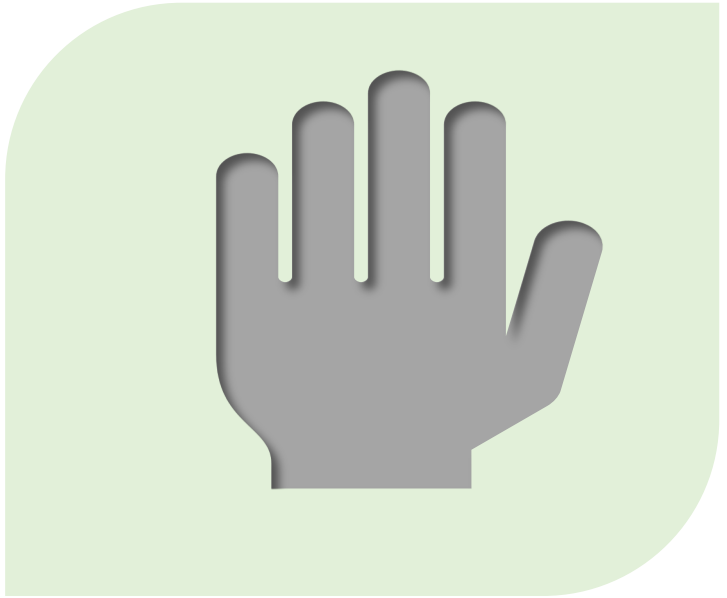
Jenelle Ferry	Morton Plant Hospital	Clearwater	FL
William Liu	Golisano Children's Hospital	Ft. Myers	FL
David Burchfield	UF Health Shands Gainesville	Gainesville	FL
Josef Cortez	UF Health Jacksonville	Jacksonville	FL
Colby Day-Richardson	Wolfson Children's Hospital	Jacksonville	FL
Shahnaz Duara	Holtz Childrens at Jackson Memorial Hospital	Miami	FL
Jenelle Ferry	St. Joseph Hospital South	Riverview	FL
Jenelle Ferry	Mease Countryside Hospital	Safety Harbor	FL
Jenelle Ferry	St. Joseph Womens Hospital	Tampa	FL
Tara Randis	Tampa General Hospital (USF Health)	Tampa	FL

Final thought:

Please consider joining!

Questions?

PLEASE ENTER YOUR AUDIO PIN ON YOUR PHONE SO WE ARE ABLE TO UN-MUTE YOU FOR DISCUSSION.



IF YOU HAVE A QUESTION, PLEASE ENTER IT IN THE QUESTION BOX OR RAISE YOUR HAND TO BE UN-MUTED.

Other Questions?

fpqc@usf.edu

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