

# Physician Perspectives on Including Pregnant Women in Covid-19 Clinical Trials: Time for a Paradigm Change

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**Table 1.**  
**Participant Demographics**

*Participants (n = 168)*

<b>Age (n, %)</b>	
< 30 years	6/165 (3.6%)
30-40 years	57/165 (34.5%)
40-50 years	52/165 (31.5%)
50-60 years	26/165 (15.8%)
60-70 years	19/165 (11.5%)
> 70 years	5/165 (3.0%)
<b>Gender (n, %)</b>	
Female	123/164 (75.0%)
Male	39/164 (23.7%)
Nonbinary	*/164
Prefer not to answer	*/164
<b>Specialty (n, %)</b>	
Obstetrics and gynecology, maternal-fetal medicine	96/165 (58.2%)
Family medicine	28/165 (17.0%)
Infectious diseases, microbiology	28/165 (17.0%)
Critical care, respirology, anesthesiology	15/165 (9.1%)
Obstetric medicine	9/165 (5.5%)
General internal medicine	6/165 (3.6%)
Other	6/165 (3.6%)
<b>Years of practice (n, %)</b>	
< 5 years	42/164 (25.6%)
5-10 years	26/164 (15.9%)
> 10 years	96/164 (58.5%)
<b>Geographic location (n, %)</b>	
Quebec	58/163 (35.6%)
Ontario	46/163 (28.2%)
Alberta	20/163 (12.3%)
Nova Scotia, New Brunswick, PEI, Newfoundland, and Labrador	14/163 (8.6%)
British Columbia	10/163 (6.1%)
Manitoba	8/163 (4.9%)
Saskatchewan	6/163 (3.6%)
Northwest Territories	*/163
<b>Setting of practice (n, %)</b>	
Academic hospital center	88/164 (53.7%)
Community hospital setting	49/164 (29.9%)
Primarily clinic/outpatient setting	27/164 (16.5%)
<b>Proportion of practice devoted to research (n, %)</b>	
> 75%	5/164 (3.0%)
50-75%	11/164 (6.7%)
25-50%	17/164 (10.4%)
< 25%	64/164 (39.0%)
None	67/164 (40.9%)
<b>Research experience with pregnant women (n, %)</b>	
Yes	82/165 (49.7%)
No	83/165 (50.3%)

\* There were fewer than 5 answers for this category.

**Table 2.**  
**Physician Perspectives on the Inclusion of Pregnant Women in Covid-19 Trials**

<i>Themes identified</i>	<i>Exemplary quotations</i>
<b>Expressions of reluctance</b>	
Potential harm to the fetus	"Do you recall thalidomide?"
Adverse effects for the mother	"Tolerance for side effect much lower in pregnant woman."
Perception of low risk of severe illness	"Very few (if any) deaths described to date in pregnancy." "Complication rate is relatively low." "Very few [pregnant patients with Covid-19] have even required hospitalization."
Lack of demonstrated efficacy of drugs	"In Covid-19, without knowledge of safety and efficacy at baseline for the average non-pregnant individual, I would consider the risk-to-benefit ratio too great."
Fear of litigation	"Obstetrics is a litigious field."
"Culture of non-prescription"	"[Obstetricians] are reluctant to take [prescribe] medications unless there is a clear indication and effectiveness and safety has been verified."
Lack of experience with medications	"I tend to try to avoid medication that is unnecessary in pregnancy." "[A]s an OB-GYN I am not using any of these drugs."
Lack of understanding of the natural history of Covid-19	"Need to better establish natural history of Covid in pregnant woman."
<b>Barriers to inclusion</b>	
Perception of unwillingness of other team members	"Other team members may be concerned about including pregnant women in clinical trials."
Perception of unwillingness of pregnant women	"Mothers may be very reluctant to participate given that they rarely take any medication during pregnancy unless they really have to." "Pregnant women can at times be hesitant with respect to participation in trials and a change in culture and more education is necessary."
Burden of regulatory approval (Health Canada, research ethics board [REB])	"REB processes are challenging when pregnant women are considered for inclusion." "Pregnant women are easily excluded from trials and when the trial is trying to get through ethics to get started quickly it is the path of least resistance."
"Culture of exclusion"	"It's routine to exclude pregnant women." "[Pregnant women] are excluded from virtually all critical care trials."
Burden of recruitment	"Lack of time to recruit, with all that it entails"
Lack of eligible pregnant patients	"The barrier is that we have very few eligible women."
Liability concerns	"There may be perceived ethical barriers and liability concerns regarding enrolling pregnant women in Covid-19 trials." "Institution's liability concerns."
Lack of infrastructure	"[T]he infrastructure and community mindset are lacking."

## Appendix A:

# Survey on Physician Willingness to Include Pregnant Women in COVID-19 Clinical Trials

This survey is intended for Canadian physicians only.

*Despite efforts to include pregnant women in clinical trials, their systematic exclusion from this area of clinical research remains common practice. Indeed, pregnant women have mostly been excluded from Coronavirus Disease 2019 (COVID-19) clinical trials. This survey will help evaluate physician perspectives on the inclusion of pregnant women in COVID-19 clinical trials. Thank you for your participation.*

There are 24 questions in this survey

## Demographics

### [] Please indicate your age:

Choose one of the following answers

Please choose **only one** of the following:

- <30 years
- 30-40 years
- 40-50 years
- 50-60 years
- 60-70 years
- >70 years

[]

### Please indicate your gender:

Choose one of the following answers

Please choose **only one** of the following:

- Female
- Male
- Non-binary
- Prefer not to answer

[]

### Please indicate your specialty:

Check all that apply

Please choose **all** that apply:

- General Internal Medicine
- Obstetric Medicine
- Respiriology
- Critical Care
- Anesthesiology

- Infectious Diseases
- Microbiology
- Obstetrics & Gynecology
- Maternal Fetal Medicine
- Family Medicine
- Other

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## How long have you been in practice (time since graduation)?

Choose one of the following answers

Please choose **only one** of the following:

- <5 years
- 5-10 years
- >10 years

[]

## What proportion of your practice is devoted to clinical research?

Choose one of the following answers

Please choose **only one** of the following:

- >75%
- 50-75%
- 25-50%
- <25%
- None

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## Have you ever been a researcher in a study involving pregnant women?

Choose one of the following answers

Please choose **only one** of the following:

- Yes
- No

[]

## What is the primary setting of your practice?

Choose one of the following answers

Please choose **only one** of the following:

- Academic hospital centre
- Community hospital setting

Primarily clinic/outpatient setting

[]  
**Please indicate the location where you practice primarily:**

Choose one of the following answers

Please choose **only one** of the following:

- Alberta
- British Columbia
- Manitoba
- Saskatchewan
- Ontario
- Quebec
- Prince Edward Island
- New Brunswick
- Newfoundland and Labrador
- Nova Scotia
- Yukon
- Northwest Territories
- Nunavut

## COVID-19 Experience

**[ ] How many patients with COVID-19 have you cared for to date?**

Choose one of the following answers

Please choose **only one** of the following:

- >100
- 51-100
- 26-50
- 1-25
- None

**[ ] How many pregnant patients with COVID-19 have you cared for to date?**

Choose one of the following answers

Please choose **only one** of the following:

- >20
- 11-20
- 6-10
- 1-5
- None

**[ ] Is your hospital recruiting patients for enrollment in COVID-19 clinical trials (i.e. is your hospital a participating centre of CATCO, REMAP-CAP or other trial)?**

Choose one of the following answers

Please choose **only one** of the following:

- Yes
- No
- Unsure

**[ ] If yes, are pregnant women eligible for enrollment in COVID-19 clinical trials at your hospital?**

**Only answer this question if the following conditions are met:**

Answer was 'Yes' at question '11 [trialparticipation]' (Is your hospital recruiting patients for enrollment in COVID-19 clinical trials (i.e. is your hospital a participating centre of CATCO, REMAP-CAP or other trial)? )

Choose one of the following answers

Please choose **only one** of the following:

- Yes, for all
- Yes, for some but not all
- No
- Unsure

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**At the hospital where you work, have any pregnant women with COVID-19 received treatment with experimental drugs (e.g. hydroxychloroquine, chloroquine, lopinavir/ritonavir, remdesivir, tocilizumab, or others) outside of a clinical trial setting?**

Choose one of the following answers

Please choose **only one** of the following:

- Yes
- No
- Unsure

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**If yes, select all that apply:**

**Only answer this question if the following conditions are met:**

Answer was 'Yes' at question '13 [trialdrugspregpts]' (At the hospital where you work, have any pregnant women with COVID-19 received treatment with experimental drugs (e.g. hydroxychloroquine, chloroquine, lopinavir/ritonavir, remdesivir, tocilizumab, or others) outside of a clinical trial setting? )

Check all that apply

Please choose **all** that apply:

- Hydroxychloroquine
- Chloroquine
- Lopinavir/ritonavir
- Remdesivir
- Tocilizumab
- Other

## Perspectives and Opinion

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**Do you believe that it would be appropriate for pregnant women to be included in some COVID-19 clinical trials?**

Choose one of the following answers

Please choose **only one** of the following:

- Very appropriate
- Highly appropriate
- Somewhat appropriate
- Not appropriate

[]

**Do you believe it would be appropriate to include pregnant women in COVID-19 clinical trials involving repurposed drugs with a safety track record in pregnancy (e.g. hydroxychloroquine or lopinavir/ritonavir)?**

Choose one of the following answers

Please choose **only one** of the following:

- Very appropriate
- Highly appropriate
- Somewhat appropriate
- Not appropriate

[]

**If not appropriate, please elaborate why:**

**Only answer this question if the following conditions are met:**

Answer was 'Not appropriate' at question '16 [appropriaterepurpose]' (Do you believe it would be appropriate to include pregnant women in COVID-19 clinical trials involving repurposed drugs with a safety track record in pregnancy (e.g. hydroxychloroquine or lopinavir/ritonavir)? )

Please write your answer here:



[]

## **If yes, how urgent is the need to include pregnant women in COVID-19 clinical trials?**

**Only answer this question if the following conditions are met:**

Answer was 'Very appropriate' or 'Highly appropriate' or 'Somewhat appropriate' at question '16 [appropriaterepurpose]' (Do you believe it would be appropriate to include pregnant women in COVID-19 clinical trials involving repurposed drugs with a safety track record in pregnancy (e.g. hydroxychloroquine or lopinavir/ritonavir)? )

Choose one of the following answers

Please choose **only one** of the following:

- Critically urgent (severe)
- Highly urgent (high)
- Somewhat urgent (medium)
- Not urgent (low)

[]

## **If not urgent, please elaborate why:**

**Only answer this question if the following conditions are met:**

Answer was 'Not urgent (low)' at question '18 [urgency]' (If yes, how urgent is the need to include pregnant women in COVID-19 clinical trials? )

Please write your answer here:

[]

## **How comfortable would you be enrolling pregnant women in COVID-19 clinical trials involving experimental drugs otherwise thought to be safe during pregnancy (e.g. hydroxychloroquine or lopinavir/ritonavir)?**

Choose one of the following answers

Please choose **only one** of the following:

- Very comfortable
- Somewhat comfortable
- Slightly uncomfortable
- Very uncomfortable

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## **If uncomfortable, please elaborate why:**

**Only answer this question if the following conditions are met:**

Answer was 'Slightly uncomfortable' or 'Very uncomfortable' at question '20 [comfort]' (How comfortable would you be enrolling pregnant women in COVID-19 clinical trials involving experimental drugs otherwise thought to be safe during pregnancy (e.g. hydroxychloroquine or lopinavir/ritonavir)? )

Please write your answer here:

## Final Questions

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**Have you identified any barriers for the inclusion of pregnant women in COVID-19 clinical trials?**

Choose one of the following answers

Please choose **only one** of the following:

Yes

No

[]

**If yes, please elaborate:**

**Only answer this question if the following conditions are met:**

Answer was 'Yes' at question '22 [barriers]' (Have you identified any barriers for the inclusion of pregnant women in COVID-19 clinical trials? )

Please write your answer here:

[]

**Please provide any additional comments regarding the inclusion of pregnant women in COVID-19 clinical trials or feedback for this study:**

Please write your answer here:

Thank you!

10-31-2020 – 00:00

Submit your survey.

Thank you for completing this survey.

## Appendix B. Subanalyses by Respondent Characteristics

### Responses according to medical specialty

	Obstetrics/ maternal-fetal medicine (n = 91)	Other (n = 74)	P-value
<b>Appropriateness of inclusion</b>			
“Very appropriate” or “highly appropriate”	66 (73%)	53 (72%)	0.90
<b>Comfort with enrollment</b>			
“Very comfortable” or “somewhat comfortable”	77 (85%)	66 (89%)	0.39

### Responses according to research experience with pregnant women

	Research experience with pregnant women (n = 82)	No research experience with pregnant women (n = 83)	P-value
<b>Appropriateness of inclusion</b>			
“Very appropriate” or “highly appropriate”	60 (73%)	59 (71%)	0.77
<b>Comfort with enrollment</b>			
“Very comfortable” or “somewhat comfortable”	73 (89%)	69 (83%)	0.27

### Responses according to experience caring for patients with Covid-19

	Experience caring for patients with Covid-19 (n = 97)	No experience caring for patients with Covid-19 (n = 68)	P-value
<b>Appropriateness of inclusion</b>			
“Very appropriate” or “highly appropriate”	68 (70%)	51 (75%)	0.49
<b>Comfort with enrollment</b>			
“Very comfortable” or “somewhat comfortable”	81 (84%)	61 (90%)	0.26