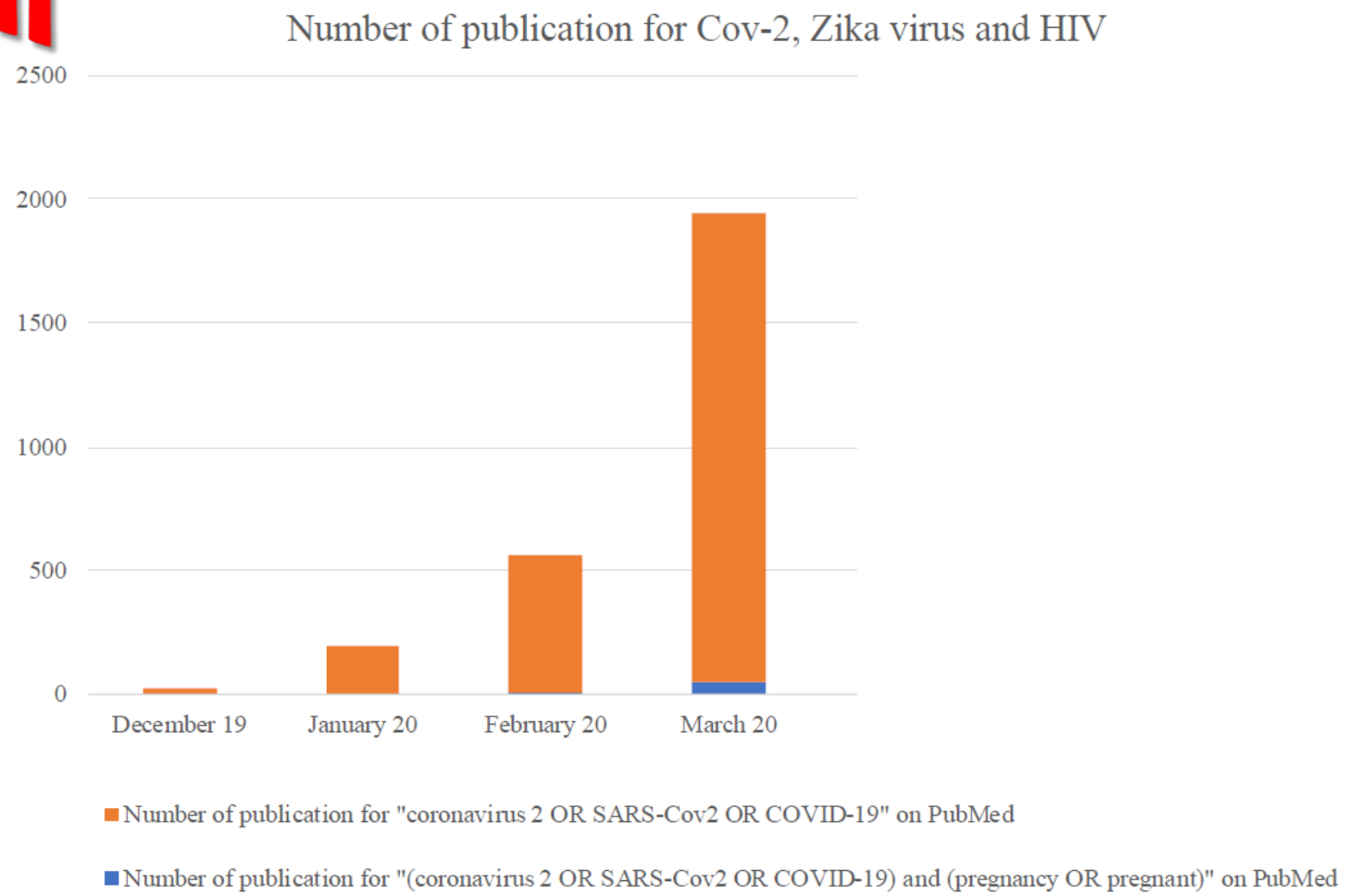
Infection & conséquences pour la grossesse

David Baud
Lausanne, Suisse

Vrai aujourd'hui
Faux demain

PUBLICATIONS

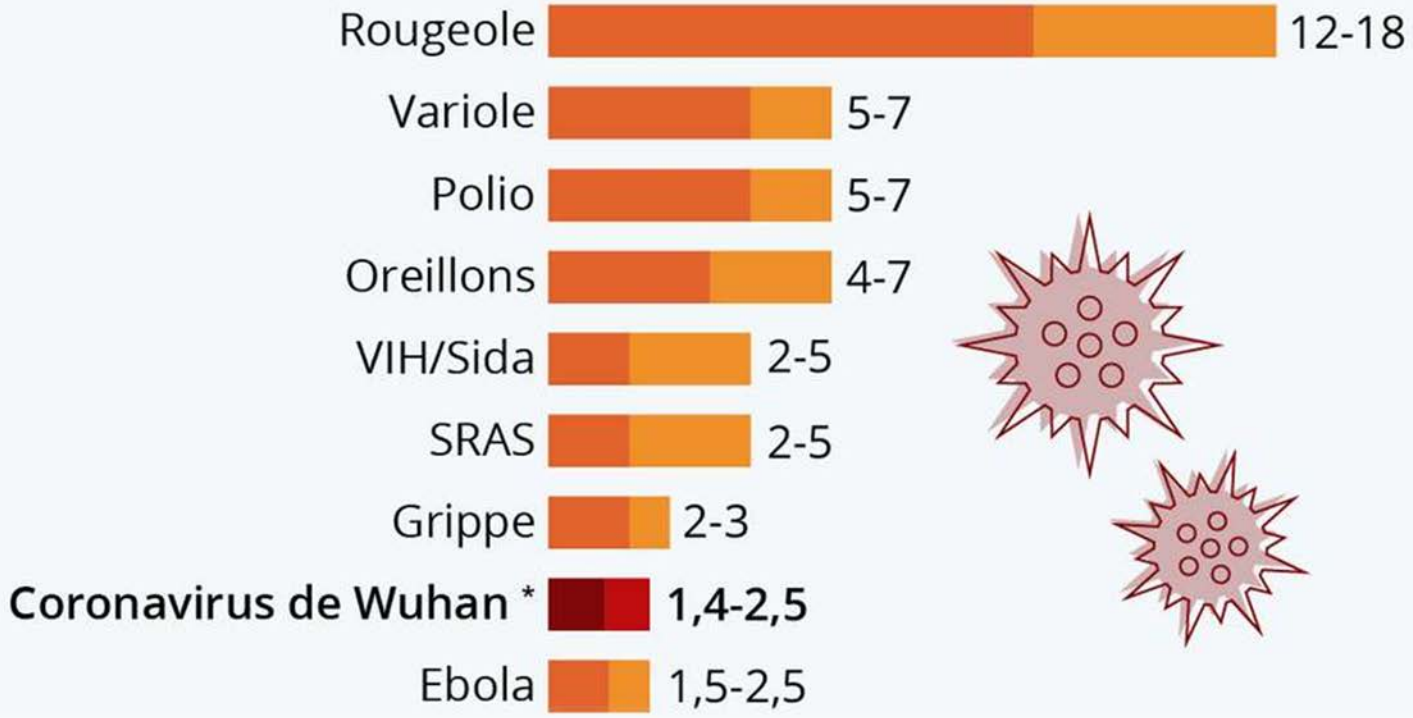


Lambelet & Baud, *in review*

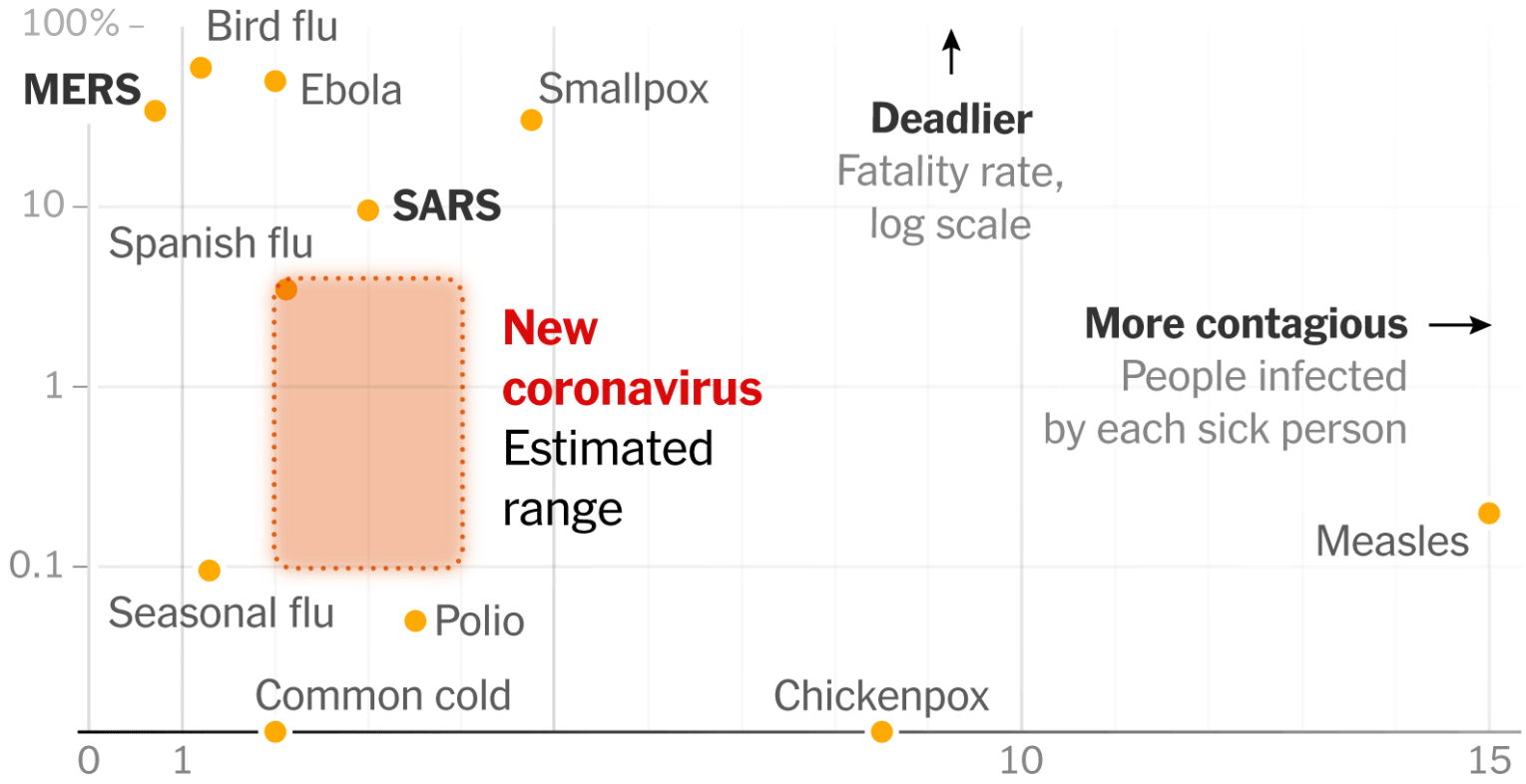
R0

Quelle est la contagiosité du coronavirus ?

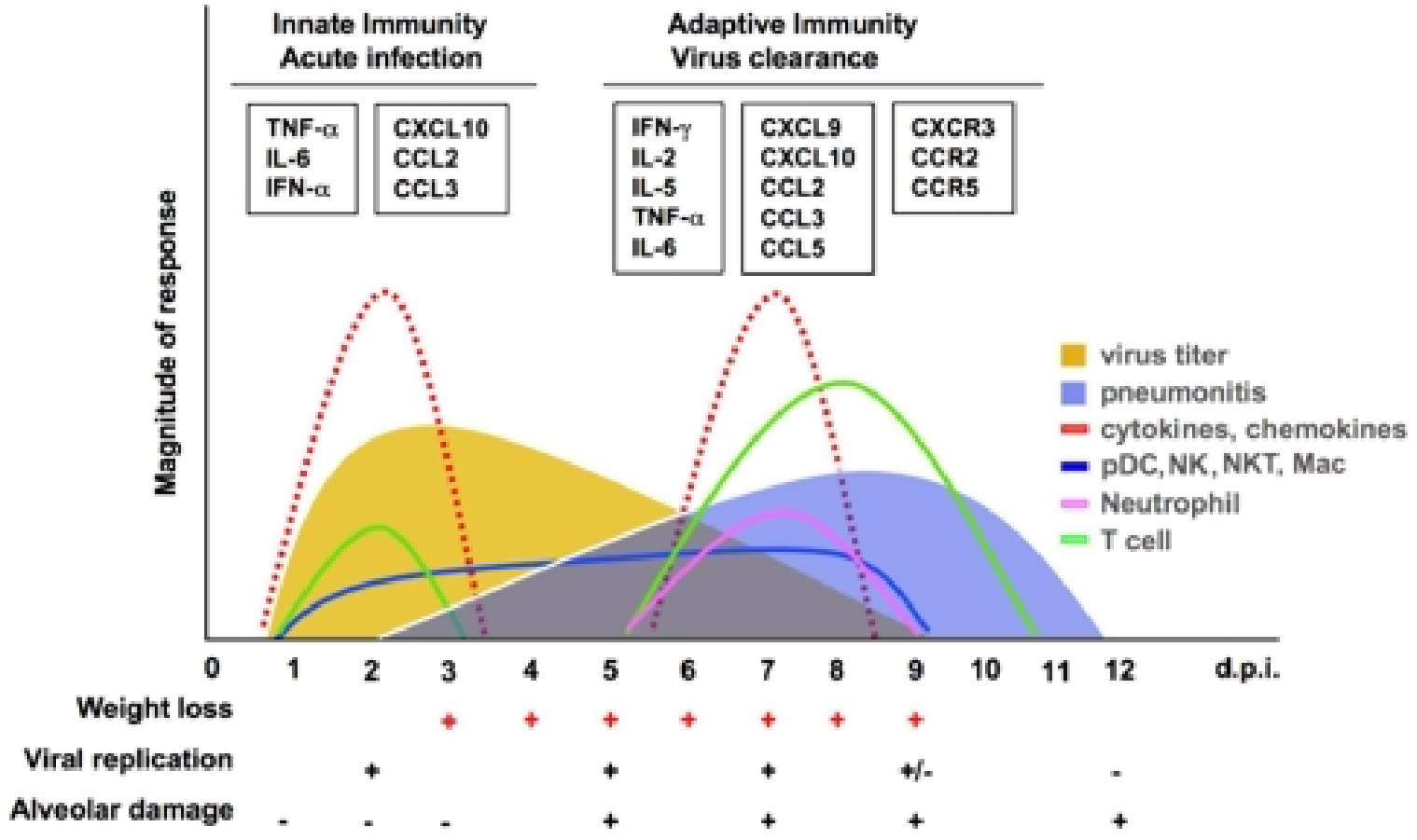
Nombre moyen de personnes auxquelles un malade risque de transmettre la maladie



R0 / MORTALITÉ



AU 7E JOUR…


Innate Immunity
Acute infection
Adaptive Immunity
Virus clearance
TNF-α
IL-6
IFN-α
CXCL10
CCL2
CCL3
IFN-γ
IL-2
IL-5
TNF-α
IL-6
CXCL9
CXCL10
CCL2
CCL3
CCL5
CXCR3
CCR2
CCR5
Magnitude of response
virus titer
pneumonitis
cytokines, chemokines
pDC, NK, NKT, Mac
Neutrophil
T cell
0 1 2 3 4 5 6 7 8 9 10 11 12 d.p.i.
Weight loss + + + + + + +
Viral replication + + + +/- -
Alveolar damage - - - + + + +

SYMPTOMES

Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China

Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention

Spectrum of disease (N = 44 415)

- Mild: 81% (36 160 cases)
- Severe: 14% (6168 cases)
- Critical: 5% (2087 cases)

Case-fatality rate

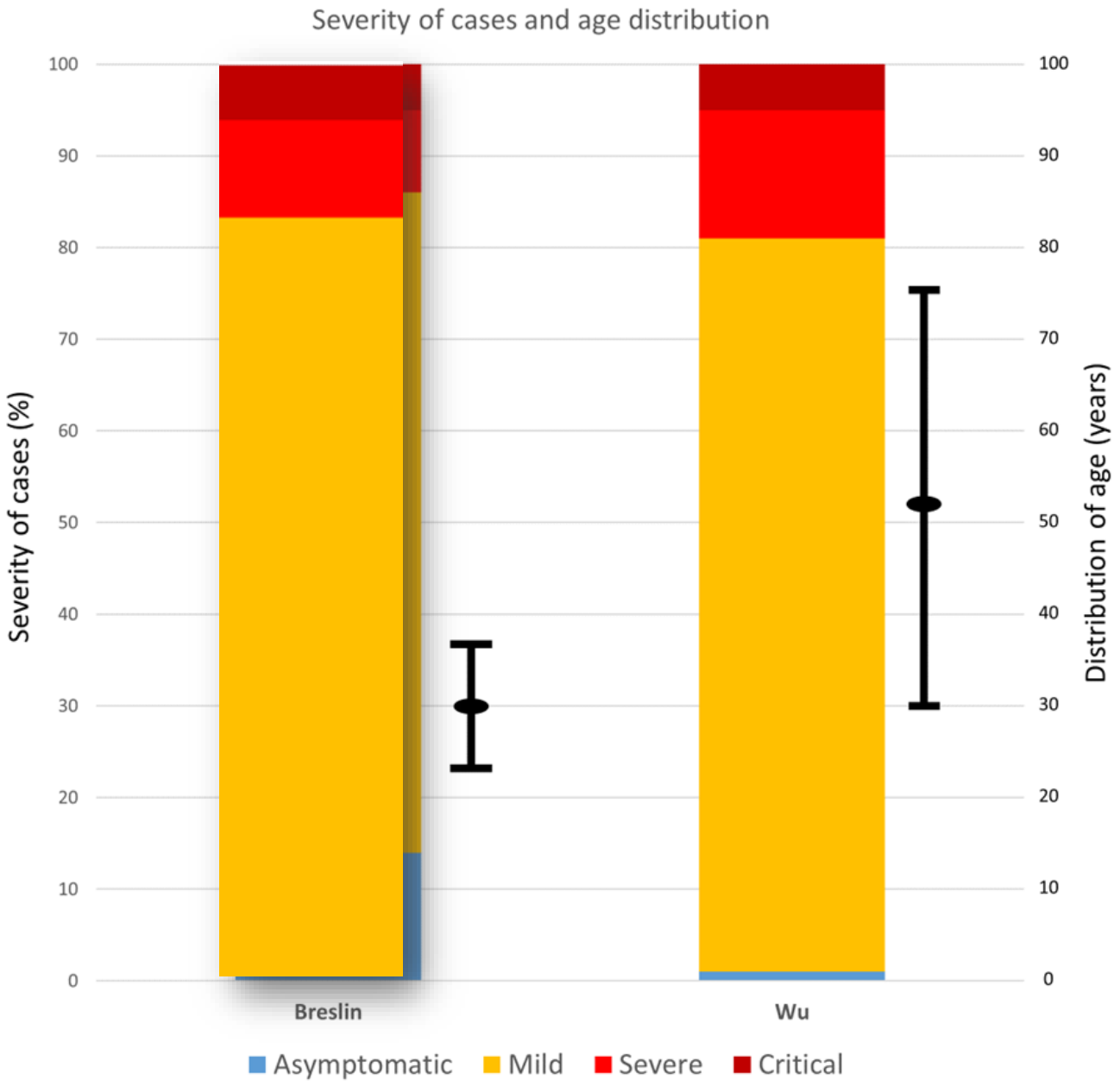
- 2.3% (1023 of 44 672 confirmed cases)

Health care personnel infected

- 3.8% (1716 of 44 672)
- 63% in Wuhan (1080 of 1716)
- 14.8% cases classified as severe or critical (247 of 1668)
- 5 deaths

JAMA The Journal of the American Medical Association

GROSSESSE



Favre & Baud, *in review*

ISSUES

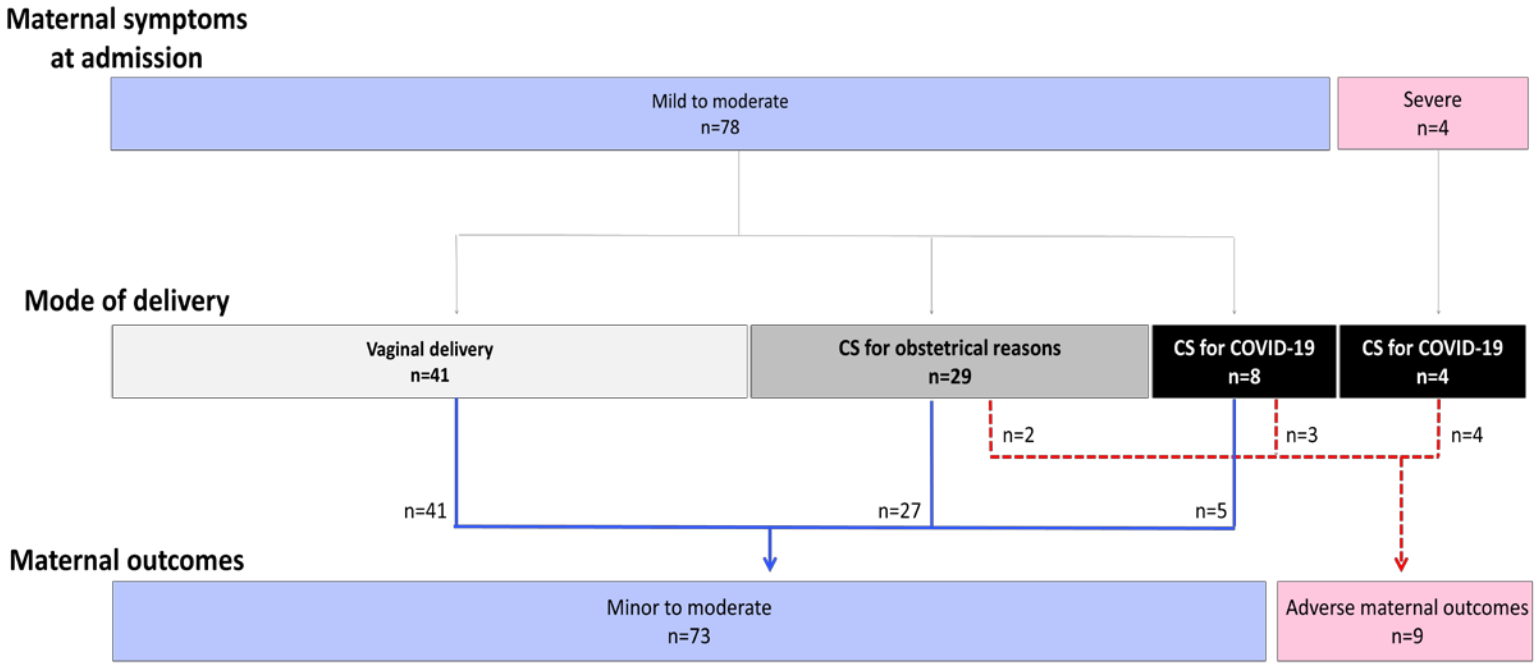
Outcome	Pooled proportions (95% CI)
PTB <37 weeks	24.30 (12.5-38.6)
PTB <34 weeks	21.79 (12.5-32.9)
PE	16.21 (4.2-34.1)
PPROM	20.72 (9.5-34.9)
FGR	11.66 (3.2-24.4)
Miscarriage	39.08 (20.2-59.8)
Cesarean delivery	83.91 (73.8-91.9)

Outcome	Pooled proportions (95% CI)
Fetal distress	34.15 (20.3-49.5)
Apgar score < 7	6.08 (1.3-13.9)
Neonatal asphyxia	0 (0-15.7)
Admission to NICU	57.16 (3.6-99.8)
Perinatal death	11.11 (84.8-19.6)
Vertical transmission	0 (0-10.7)

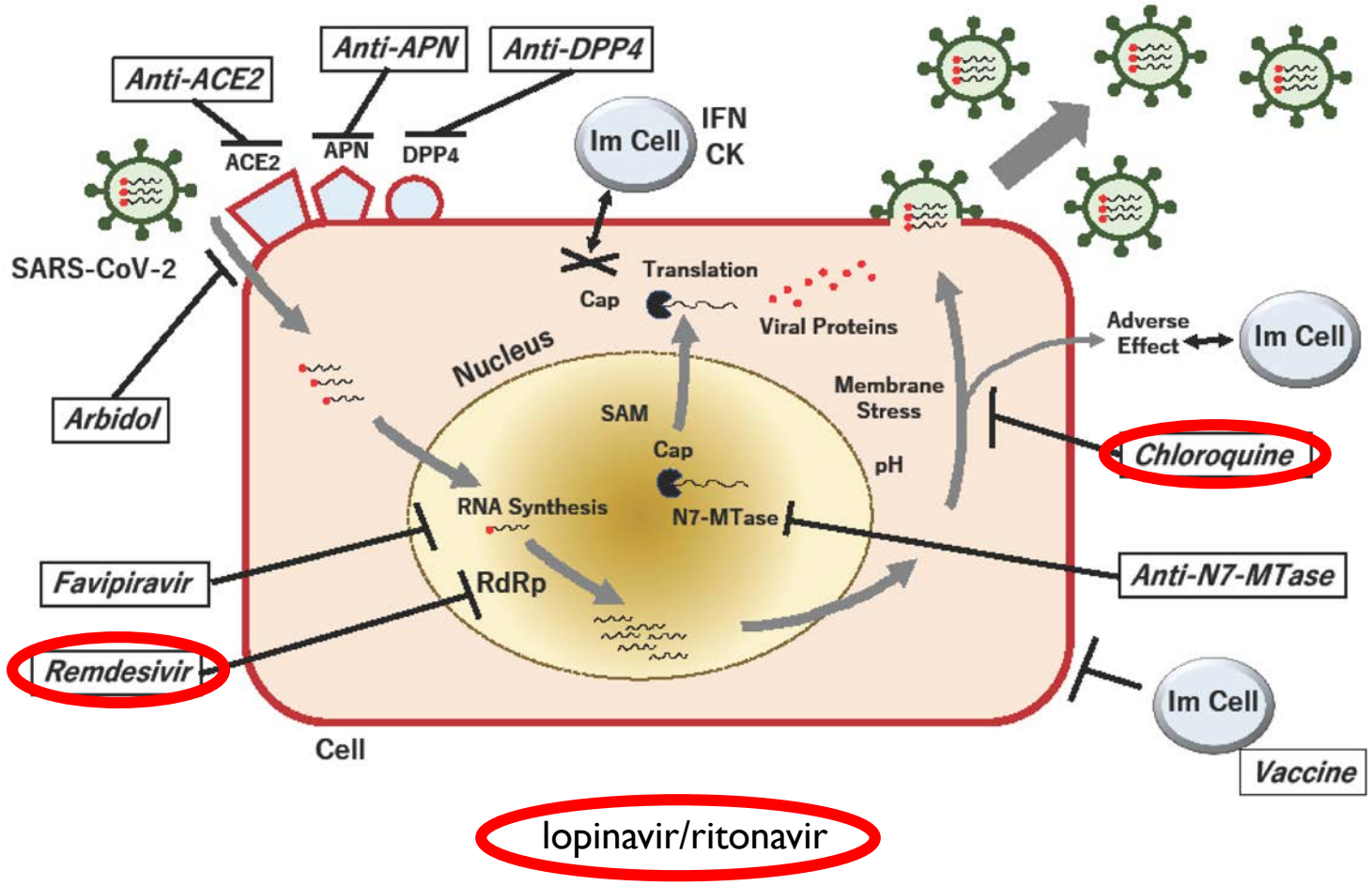
Di Mascio & D'Antonio, AJOG-MFM

COVI-PREG

International COVID-19 and Pregnancy Registry

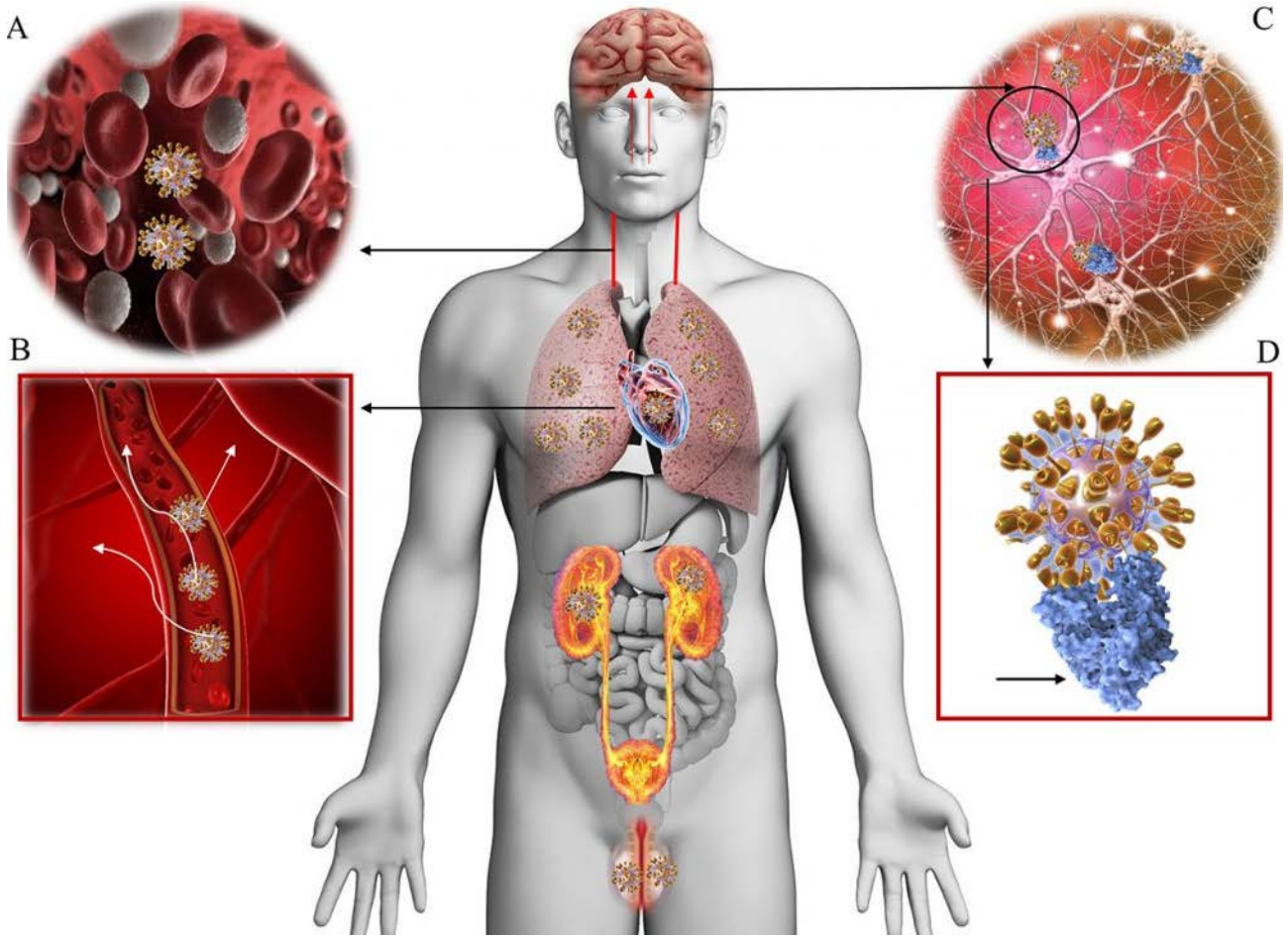


CYCLE & TRAITEMENTS



lopinavir/ritonavir

RECEPTEUR ACE2



PLOS ONE

RESEARCH ARTICLE

The SARS-CoV-2 receptor ACE2 expression of maternal-fetal interface and fetal organs by single-cell transcriptome study

Mengmeng Li[1☯], Liang Chen[2☯], Jingxiao Zhang[3], Chenglong Xiong[2,4*], Xiangjie Li[3*]

EDITORIAL

JAMA The Journal of the American Medical Association

Can SARS-CoV-2 Infection Be Acquired In Utero?
More Definitive Evidence Is Needed

David W. Kimberlin, MD; Sergio Stagno, MD

RESEARCH LETTER

Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn

Time	Laboratory test	Value	Reference range
Feb 22	White blood cell count, $\times 10^9$/L	18.08	3.5-9.5
	SARS-CoV-2 IgG, AU/mL	140.32	<10
	SARS-CoV-2 IgM, AU/mL	45.83	<10
Feb 24	PCR of nasopharyngeal swab	–	–
Feb 27	PCR of nasopharyngeal swab	–	–
Mar 1	PCR of nasopharyngeal swab	–	–
Mar 6	PCR of nasopharyngeal swab	–	–
Mar 7	SARS-CoV-2 IgG, AU/mL	69.94	<10
	SARS-CoV-2 IgM, AU/mL	11.75	<10
Mar 9	PCR of nasopharyngeal swab	–	–

RESEARCH LETTER

Antibodies in Infants Born to Mothers With COVID-19 Pneumonia

Clinical value	Reference range	1	2	3	4	5	6
IgM, AU/mL	<10	39.6	16.25	3.79	1.9	0.96	0.16
IgG, AU/mL	<10	125.5	113.91	75.49	73.19	51.38	7.25

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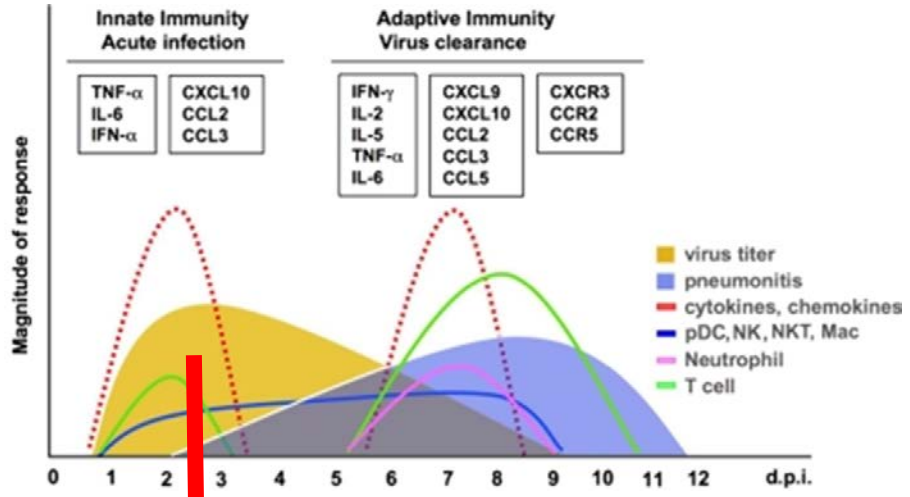
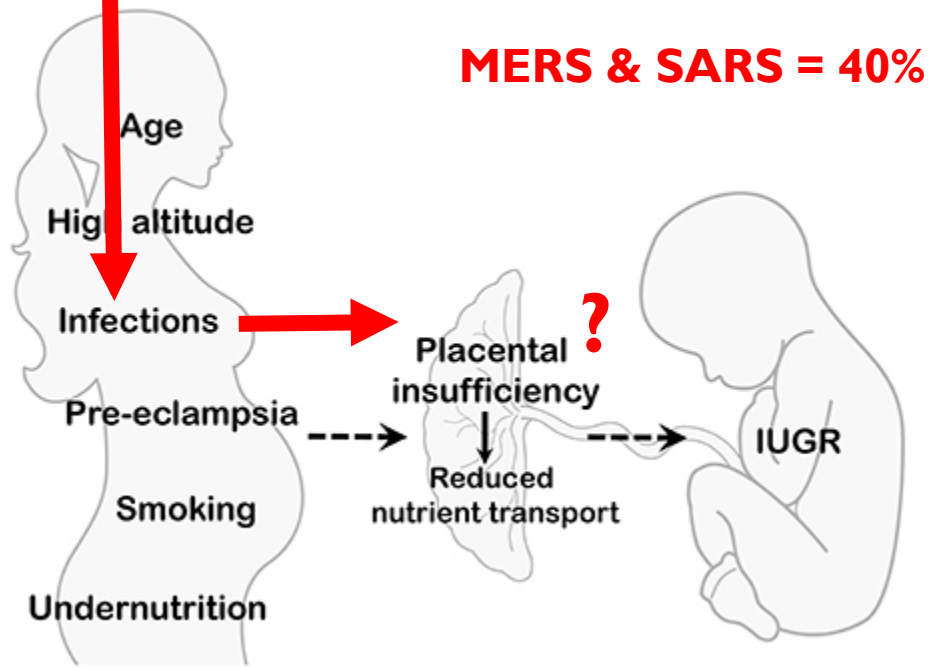


MERS & SARS = 40% RCIU



TAKE HOME MESSAGE

Comme la population générale… de 50-60 ans

Plus de CS (détresse fœtale), prémat, RCIU

Pas de transmission verticale

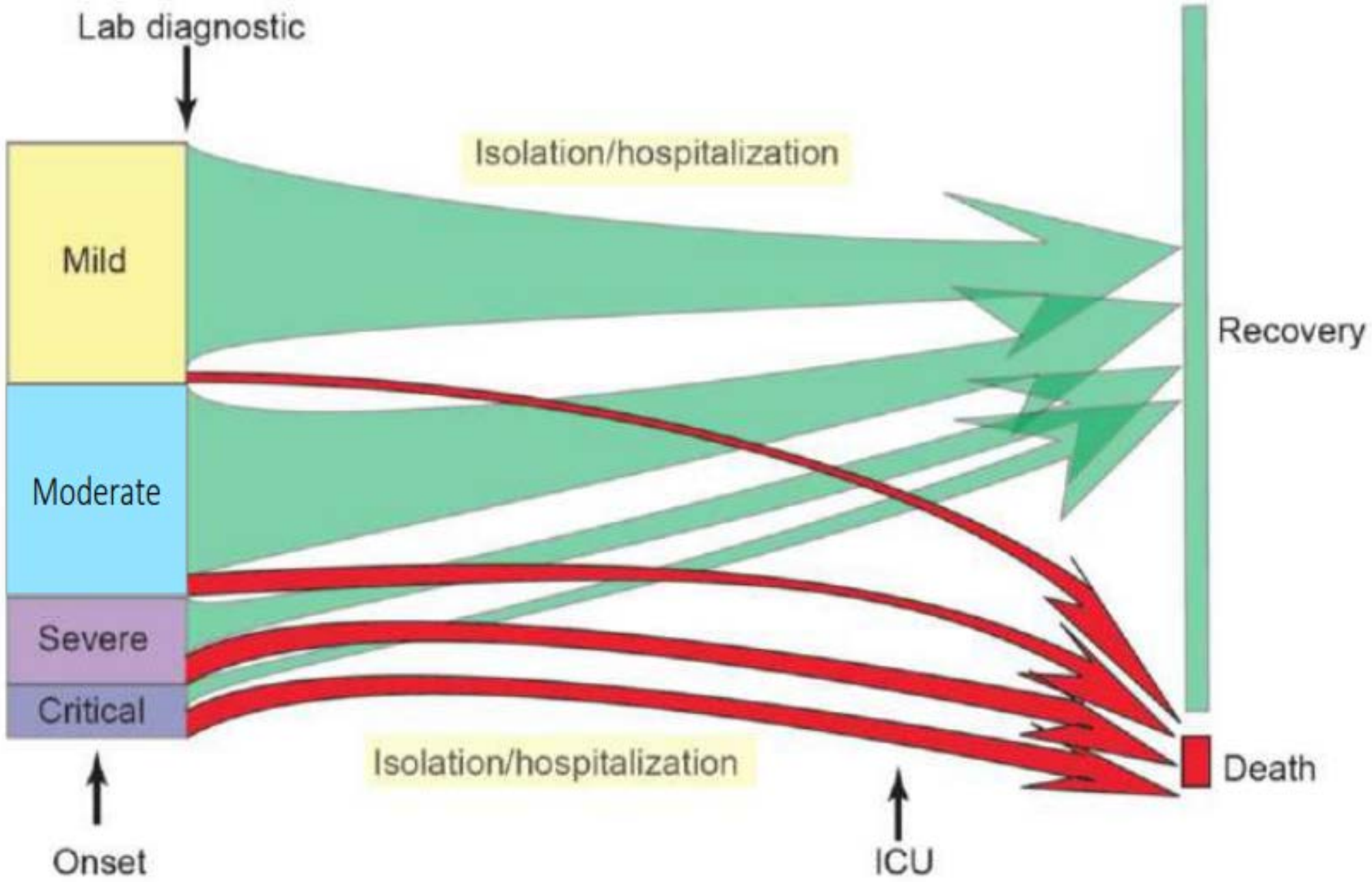
Mais…

APRÈS

Author	Year	Country	Title	Key Finding
Chen et al. (12)	2020	China	Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records	◦ COVID-19 in pregnant woman can cause fetal distress but does not infect newborns.
Chua et al. (18)	2020	China	From the frontlines of COVID-19–How prepared are we as obstetricians: a commentary	◦ No evidence of intrauterine infection of COVID-19 caused by vertical transmission for fetus. ◦ Infected or suspect mothers should refrain from breastfeeding. ◦ All mothers infected with COVID-19 should be monitored carefully during pregnancy and after delivery.
Liu et al. (17)	2020	China	Pregnancy and Perinatal Outcomes of Women with COVID-19 Pneumonia: A Preliminary Analysis	◦ Pregnancy and childbirth did not aggravate the course of symptoms or CT features of COVID-19 Pneumonia.
Liu et al. (16)	2020	China	Coronavirus Disease 2019 (COVID-19) During Pregnancy: A Case Series	◦ No evidence to suggest the potential risk of intrauterine vertical transmission.
Lu et al. (19)	2020	China	Coronavirus disease (COVID-19) and neonate: What neonatologist need to know	◦ There is currently no evidence of transplacental transmission of SARSCoV-2 from the mother to the newborn.
Mardani et al. (3)	2020	Iran	A Controversial Debate: Vertical Transmission of COVID-19 in Pregnancy	◦ Neonates born to women with suspected or confirmed COVID-19 infection should be isolated for at least two weeks after birth and not be breastfed. ◦If 2019-nCoV infection is confirmed during pregnancy, both the mother and fetus should be followed up extensively.
Qiao et al. (2)	2020	China	What are the risks of COVID-19 infection in pregnant women?	◦There is not sufficient evidence about intrauterine vertical transmission.
Rasmussen et al. (4)	2020	USA	Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know	◦Fetal distress and preterm delivery were seen in some newborns. ◦The babies of all pregnant women with COVID-19 were tested for SARS-CoV-2 after delivery and had negative results.
Wang et al. (15)	2020	China	A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery	◦ There is no evidence of fetus distress or neonatal infection with COVID-19. ◦ COVID-19 in pregnancy can be mild to severe and result in preterm delivery.
Zhu et al. (20)	2020	China	Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia	◦ Perinatal 2019-nCoV infection may have adverse effects on newborns, causing problems such as fetal distress, premature labor, respiratory distress, thrombocytopenia accompanied by abnormal liver function, and even death.
Liang et al. (20)	2020	China	Novel corona virus disease (COVID-19) in pregnancy: What clinical recommendations to follow?	◦ There is no evidence for vertical transmission of COVID-19 in pregnant woman. ◦All mothers with COVID-19 should be monitored carefully.
Faver et al. (21)	2020	China	2019-nCoV epidemic: what about pregnancies?	◦Infection with COVID-19 in pregnant women can have adverse effects including miscarriage, fetal growth restriction, and preterm birth or death of the mother.
Schwartz et al. (22)	2020	China	Potential Maternal and Infant Outcomes from Coronavirus 2019-nCoV (SARS-CoV-2) Infecting Pregnant Women: Lessons from SARS, MERS, and Other Human Coronavirus Infections	◦ There is limited knowledge regarding coronavirus infections that occur during pregnancy. ◦ Previous experiences with coronavirus infections in pregnancy indicate that these agents are capable of causing adverse clinical outcomes.

Supplementary Table 6. Details on perinatal deaths

Author	Year	Type of CoV	Details on perinatal deaths
Zhu	2020	Sars-CoV-2	*1 Neonatal death*: The baby was delivered at a gestational age of 34+5 weeks and admitted 30 minutes after delivery due to shortness of breath and moaning. Eight days later, he developed refractory shock, multiple organ failure, and disseminated intravascular coagulation, which were treated by the transfusion of platelets, suspended red blood cells, and plasma; he died on the 9th day.
Liu	2020	Sars-CoV-2	*1 stillbirth*, no other available details
Assiri	2016	Mers-CoV	*1 stillbirth*: At 34 weeks, the mother complained shortness of breath since 3 days and was admitted for elevated blood pressure and 3+ proteinuria consistent with preeclampsia, and pneumonia was diagnosed by means of chest radiography. Fetal heart tones were absent, and intrauterine fetal demise was suspected. A stillborn infant was delivered the same day. *1 neonatal death*: At 24 weeks gestation, the mother presented to the hospital on 23 October with cough and myalgia, and chest radiography at admission showed a right lower lobe opacity. Her respiratory status deteriorated during hospitalization, and she was admitted to the ICU on 28 October for ARDS requiring intubation and mechanical ventilation. On 31 October, the patient delivered a 240-gram infant by cesarean delivery. The infant died 4 hours after birth.
Payne	2015	Mers-CoV	*1 stillbirth:* During the outbreak period, the mother's acute respiratory symptoms (fever, rhinorrhea, fatigue, headache, and cough) occurred concurrently with vaginal bleeding and abdominal pain on the seventh day of illness, and she spontaneously delivered a stillborn infant.


Lab diagnostic
Isolation/hospitalization
Mild
Moderate
Severe
Critical
Recovery
Death
Isolation/hospitalization
Onset
ICU

Congenital infection with intrauterine fetal death /stillbirth		
Fetal tissues or autopsy material	Confirmed	Detection of the virus by PCR from fetal or placental tissue or electron microscopic detection of viral particle in tissue or viral growth in culture from fetal or placental tissue
	Possible	Detection of the virus by PCR in surface swab from fetus or placental swab on fetal side
	Unlikely	Detection of the virus by PCR in surface swab from maternal side of placenta only and no testing done or no detection of the virus by PCR from fetal or placental tissue
	Not infected	No detection of the virus by PCR or by electron microscopy in fetal tissue(s) on autopsy
Congenital infection in live born neonate		
Clinical features of infection in newborn and mother with	Confirmed	Detection of the virus by PCR in umbilical cord blood[b] or neonatal blood collected within first 12 hours of birth or amniotic fluid collected prior to rupture of membrane[c]
	Probable	Detection of the virus by PCR in nasopharyngeal swab at birth

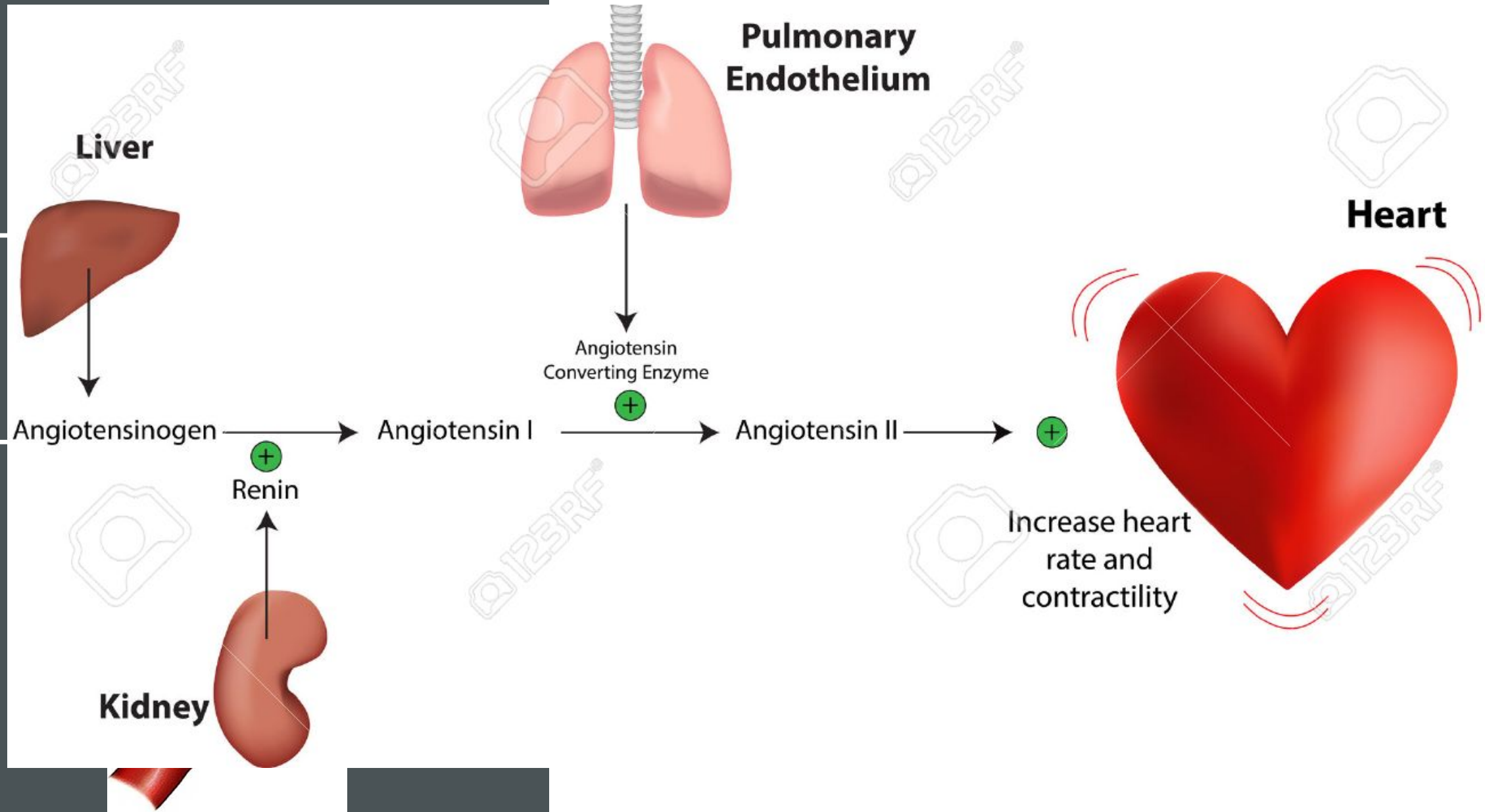
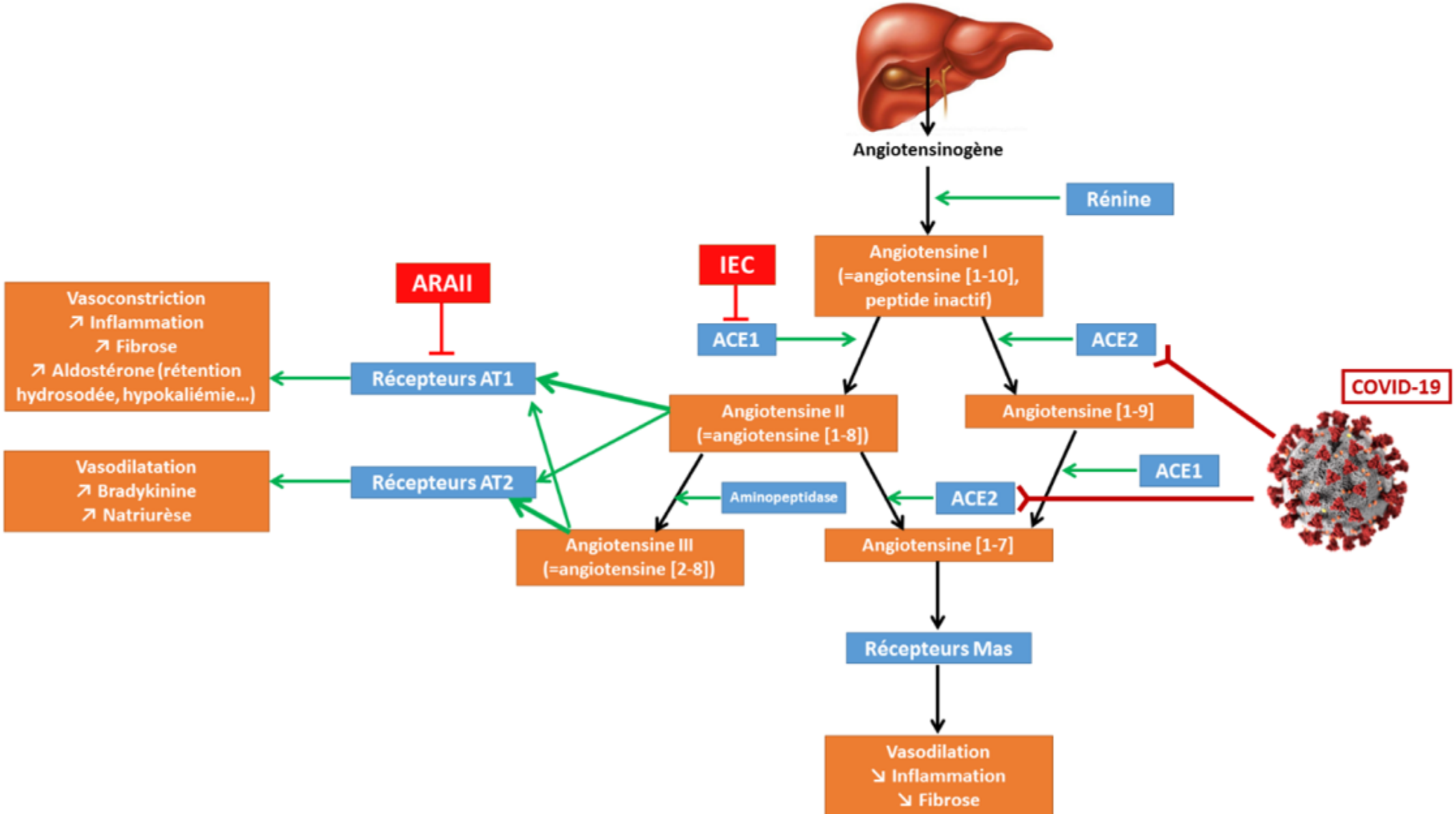

Liver
Pulmonary Endothelium
Heart
Angiotensin Converting Enzyme
Angiotensinogen
Angiotensin I
Angiotensin II
Renin
Increase heart rate and contractility
Kidney

Figure 2


Angiotensinogène
Rénine
Angiotensine I
(=angiotensine [1-10],
peptide inactif)
IEC
ACE1
ACE2
ARAII
Vasoconstriction
↗ Inflammation
↗ Fibrose
↗ Aldostérone (rétention
hydrosodée, hypokaliémie…)
Récepteurs AT1
Angiotensine II
(=angiotensine [1-8])
Angiotensine [1-9]
COVID-19
Vasodilatation
↗ Bradykinine
↗ Natriurèse
Récepteurs AT2
Aminopeptidase
ACE2
ACE1
Angiotensine III
(=angiotensine [2-8])
Angiotensine [1-7]
Récepteurs Mas
Vasodilation
↘ Inflammation
↘ Fibrose

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	Case reports	Case series				Total
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Maternal Characteristics						
Age (years) (Mean ± SD)	31 ±4	30	29±3	32±5	30±6	
Gestational age in days (Mean ± SD)	253 ± 25	N/A	271 ± 10	224 ± 8	260±14	
Delivery Characteristics						
Total number of deliveries	50	6	16	11	3	86/108 (80%)
Patients not delivered at time of reporting of studies	8	10	0	4	0	22/108 (20%)
Delivery by cesarean section	44	6	16	10	3	79/86 (92%)
Vaginal delivery	6	0	0	1	0	7/86 (8%)

			nancy: What clinical recommendations to follow?	of COVID-19 in pregnant woman. ◦All mothers with COVID-19 should be monitored carefully.
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Vaginal delivery	6	0	0	1	0	7/86 (8%)
Laboratory Characteristics						
Lymphocytopenia (<1x10^9/L)	18[a]	9	N/A	12	1	40/68 (59%)
Elevated c-reactive protein concentration (mg/L)	19[b]	13	N/A	10	3	45/64 (70%)
Confirmed SARS-CoV-2	58	16	16	15	3	108/108 (100%)
Other parameters						
Maternal mortality	0	0	0	0	0	0/108 (0%)
Maternal ICU admission	3	0	0	0	0	3/108 (3%)
Neonatal mortality	1[c]	0[d]	0	0[f]	0	1/87 (1%)
Intrauterine fetal death	1[c]	0[d]	0	0[f]	0	1/87 (1%)
Vertical transmission	1[c]	N/A	0[e]	0[f]	0	1/75 (1%)

PUBLICATIONS