Overzicht 24 feb 2021

Source	Findings	References	Comments
Guidelines			
NVOG (NL) https://www.nvog.nl/wp-content/uploads/ 2021/01/Standpunt-COVID-19-en-zwangerschap-en-bevalling-versie-12-januari-2021-def.pdf Last update: Jan 12, '21	Based on a recent living systematic review on COVID-19 during pregnancy **the odds of admission to the intensive care unit and the need for invasive ventilation appears to be higher among (recently) pregnant women, compared with non-pregnant women with COVID-19.** Although severe illness is uncommon in women of reproductive age, intensive care admission and invasive ventilation is more common in pregnant women with COVID-19 compared to non-pregnant women of the same age. **This is mainly applicable to the second stage of pregnancy.**	Allotey, 2020	Mail d.d. 17 feb: "De werkgroep blijft bij het standpunt dat zwangeren al vanaf 20 weken een hoger risico lopen op ernstige SARS-Cov2-infectie met IC-opname en beademing. In de review van Allotey et al staat deze termijn niet zo specifiek beschreven, **wel is er een Franse studie van Badr et al 2020 die een verschil van 11.08% versus 2.38% IC-opname laat zien bij zwangeren ten opzichte van hun niet-zwangere leeftijdsgenoten**. Deze studie wordt ook in de RCOG-guideline aangehaald."
RCOG (UK) https://www.rcog.org.uk/globalassets/documents/guidelines/2021-02-19-coronavirus-covid-19-infection-in-pregnancy-v13.pdf Last update: Feb 19, '21	The PregCOV-19 Living Systematic Review Consortium analysis concluded that **pregnant women are more likely than non-pregnant women to be admitted to intensive care (OR 1.62, 95% CI 1.33–1.96) and require invasive ventilation (OR 1.88, 95% CI 1.36–2.60).** This finding was based overwhelmingly on a single study published by CDC; **in this study two major limitations of the results were acknowledged.** The first was that admissions for indications related to pregnancy and those for COVID-19 could not be distinguished. The second was that pregnancy status was missing for three-quarters of the women of reproductive age; a pregnancy rate of 9% was identified – higher than the expected 5%. This could account for significant bias in the results. Since the last update of that systematic review, a small number of studies from the USA and Mexico have also pointed to increased illness severity from COVID-19 in pregnant women compared to non-pregnant women. Taken together, there is now growing evidence that pregnant women may be at increased risk of severe illness from COVID-19 compared with non-pregnant women, **particularly in the third trimester**. The most consistent signal of increased severity of	Allotey, 2020 Zambrano, 2020 Martinez-Portilla, 2020 DeBolt, 2020 Badr, 2020 Oakes, 2021 Lokken, 2021	Na de mail van de NVOG hierboven, is een nieuwe versie van de RCOG-guideline verschenen. Daarin zijn enkele aanpassingen doorgevoerd. Resultaten van deze geüpdatete richtlijn worden hier links beschreven.

	COVID-19 in pregnancy is an increase in ICU admissions for pregnant women. **However, ICU admission rates must be interpreted with caution, as the threshold for ICU admission for a pregnant woman may be lower than for a non-pregnant woman.**		
RANZCOG (Australia/New Zealand) https://ranzcog.edu.au/statements-guidelines/covid-19-statement/covid-19-vaccination-information Last update: Jan 26, '21	**It is expected that the large majority of pregnant women infected with COVID-19 will experience only mild or moderate cold/flu like symptoms. However, pregnant women are potentially at increased risk of complications from any respiratory disease due to the physiological changes that occur in pregnancy.** These include reduced lung function, increased oxygen consumption and changed immunity. In particular, pregnant women with co-morbidities are at higher risk of hospital admission, ventilation and severe illness. Currently there is no evidence of an increased risk of miscarriage or teratogenicity. There is a possibility of vertical transmission of the COVID-19 virus and an increased incidence of third trimester premature birth, probably as a result of medical intervention for maternal illness.	None reported	
SOGC (Canada) https://sogc.org/en/content/featured-news/SOGC_Statement_on_COVID-19_Vaccination_in_Pregnancy.aspx Last update: Feb 1, '21	Most pregnant women who become infected with SARS-CoV-2 will have mild-to-moderate symptoms and many can be asymptomatic. However, both Canadian and international data from large studies spanning multiple jurisdictions demonstrate that approximately 8-11% of pregnant women will require hospitalization for COVID related morbidity and between 2-4% of pregnant women will require admission to an intensive care unit (ICU). **Compared to non-pregnant individuals with COVID-19, pregnant individuals are at increased risk of invasive ventilation with an equivalent mortality to age-matched peers.** The risk of severe morbidity from COVID-19 in pregnant women appears to be associated with risk factors including age ≥35 years old, asthma, obesity, preexisting diabetes, preexisting hypertension and heart disease.	Maru, 2020 Money, 2020 Allotey, 2020 Zambrano, 2020	
ACOG (USA) https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-pregnant-and-	Available data suggest that symptomatic pregnant patients with COVID-19 are at increased risk of more severe illness compared with nonpregnant peers. **Although the absolute risk for severe COVID-19 is low, these data indicate an increased risk of ICU admission, need for mechanical ventilation and ventilatory support (ECMO), and death reported in pregnant women with symptomatic COVID-19 infection, when compared with symptomatic non-pregnant women.** Pregnant patients with comorbidities such as obesity and diabetes may be at an even higher risk of severe illness consistent with the general population with similar comorbidities. Given the growing evidence, CDC has	Ellington, 2020 Collin, 2020 Delahoy, 2020 Panagiotako-poulos, 2020 Zambrano, 2020 Knight, 2020	

lactating-patients-against-covid-19 Last update: Feb 4, '21	included pregnancy as a factor that leads to increased risk for severe COVID-19 illness (CDC).		
Systematic reviews			
Allotey et al., 2020 http://dx.doi.org/10.1136/bmj.m3320 Aug, '20 Search tot juni '20 https://www.birmingham.ac.uk/research/who-collaborating-centre/pregcov/index.aspx	• 4% (2% to 7%; 17 studies, 10.901 women) of the pregnant women with covid-19 were admitted to an intensive care unit, 3% (1% to 5%; 13 studies, 10 713 women) required invasive ventilation • **Compared with non-pregnant women of reproductive age with covid-19, the odds of admission to the intensive care unit (1.62, 95% confidence interval 1.33 to 1.96) and need for invasive ventilation (1.88, 1.36 to 2.60) were higher in pregnant and recently pregnant women** (four studies, 91 606 women) • Voor bijhouden voortgang van deze living systematic review zie onderste link kolom links. Update wordt binnenkort verwacht, nu gereviewed door BMJ	Liu, 2020 Cheng, 2020 Wei, 2020 Ellington, 2020	De (significante) gepoolde OR is overwegend gebaseerd op de studie van Ellington et al, 2020. Een kanttekening bij deze studie is o.a. dat bij driekwart van de vrouwen in de vruchtbare leeftijd informatie over hun zwangerschapsstatus ontbrak. Dit kan hebben geleid tot vertekening van de resultaten. Informatie over trimester van de zwangerschap was niet beschikbaar. In de andere studies die zijn gebruikt bij het berekenen van deze gepoolde OR was er sprake van onnauwkeurigheid (kleine steekproeven en weinig 'events', leidend tot brede betrouwbaarheidsintervallen en dus meer onzekerheid).
Papers published after last update living systematic review Allotey			
Badr et al., 2020 (France) https://doi.org/10.1016/j.ajog.2020.07.045	• The objective of the study was to compare the clinical outcomes and laboratory findings of **pregnant women at ≥20 weeks' gestation infected with SARS-CoV-2 with a cohort of nonpregnant women with a confirmed diagnosis of COVID-19** after closely matching the 2 groups using a propensity score • **Pregnant women were at higher risk for ICU admission than nonpregnant women (11.08% vs 2.38%; p=.024).** In addition, they were also at higher risk for hospital admission because of COVID-19 respiratory decompensation such as dyspnea and hypoxemia (58.21% vs 17.4%; p<.001), for the need for OT (36.04% vs 17.24%; p=.006), and for ETI (10.16% vs 1.67%; p=.022).	-	• Retrospective design • The threshold for diagnostic evaluation, hospitalization, and certain treatments may in fact be lower for pregnant women than for others
Zambrano et al., 2020 (US)	• This report provides updated information about symptomatic women of reproductive age (15–44 years) with laboratory-confirmed infection with SARS-CoV-	-	• Pregnancy status was missing for over

CDC, (update of Ellington, 2020) https://doi.org/10.15585/mmwr.mm6944e3	2. During January 22– October 3, CDC received reports through national COVID-19 case surveillance or through the National Notifiable Diseases Surveillance System (NNDSS) of 1,300,938 women aged 15–44 years with laboratory results indicative of acute infection with SARS-CoV-2. Data on pregnancy status were available for 461,825 (35.5%) women with laboratory-confirmed infection, 409,462 (88.7%) of whom were symptomatic. Among symptomatic women, 23,434 (5.7%) were reported to be pregnant • After adjusting for age, race/ethnicity, and underlying medical conditions, **pregnant women were significantly more likely than were nonpregnant women to be admitted to an intensive care unit (ICU)** (10.5 versus 3.9 per 1,000 cases; adjusted risk ratio [aRR] = 3.0; 95% confidence interval [CI] = 2.6–3.4), **receive invasive ventilation** (2.9 versus 1.1 per 1,000 cases; aRR = 2.9; 95% CI = 2.2–3.8) • Although the absolute risks for severe COVID-19–associated outcomes among women were low, pregnant women were at significantly higher risk for severe outcomes compared with nonpregnant women. This finding might be related to physiologic changes in pregnancy, including increased heart rate and oxygen consumption, decreased lung capacity, a shift away from cell-mediated immunity, and increased risk for thromboembolic disease		one half (64.5%) of reported cases • When estimating the proportion of cases with severe outcomes, the observational data collected through passive surveillance might be subject to reporting bias, wherein preferential ascertainment of severe cases is likely • The study focused on symptomatic women and is therefore less biased (i.e., than previous study Ellington) by women being admitted principally for obstetric reasons
Martinez-Portilla et al., 2020 (Mexico) https://doi.org/10.1002/uog.23575	• The cohort comprised 5183 pregnant and 175 905 non-pregnant women with COVID-19. The crude (unmatched) rates of death, pneumonia, intubation and ICU admission in pregnant compared with nonpregnant women were 1.5% vs 1.5%, 9.9% vs 6.5%, 8.1% vs 9.9% and 13.0% vs 6.9%, respectively. • After propensity score matching (5183 pregnant and 5183 non-pregnant matched women), **pregnant women had a higher odds of death (odds ratio (OR), 1.84; 95%CI, 1.26–2.69), pneumonia (OR, 1.86; 95%CI, 1.60–2.16) and ICU admission (OR, 1.86; 95%CI, 1.41–2.45) than non-pregnant women**, but similar odds of intubation (OR, 0.93; 95%CI, 0.70–1.25)	-	• Data were available for the secondary outcomes of ICU admission and intubation in only a proportion of women (n=14 910).
DeBolt et al., 2020 (US)	• 38 pregnant women admitted to hospital with severe or critical COVID-19 were compared to 94 non-pregnant women with severe or critical COVID-19. Pregnant women were more likely to be admitted to ICU (39.5% versus 17.0%, P < 0.01;	-	• Small sample size (study performed in New York area)

https://doi.org/10.1016/j.ajog.2020.11.022	adjusted OR 5.2, 95% CI 1.5–17.5)		
Oakes et al., 2021	• This study compared 22 pregnant women with symptomatic COVID-19 to 240 non-pregnant controls • After adjusting for covariates potentially associated with the primary outcome, symptomatic pregnant women were at a significantly increased risk of severe coronavirus disease 2019 compared with nonpregnant women using both the World Health Organization Ordinal Scale for Clinical Improvement (adjusted relative risk, 3.59; 95% CI, 1.49–7.01) and Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (adjusted relative risk, 5.65; 95% CI, 1.36–17.31) criteria		• The study used clinical criteria, not admission data, to determine severe COVID-19
Lokken et al., 2021 (US) https://doi.org/10.1016/j.ajog.2020.12.1221	• The study analyzed data on 240 women who tested positive for COVID-19 in pregnancy. Of these, 24 women (10%) were admitted to hospital specifically for COVID-19-related respiratory concerns; this is approximately three times the hospitalization rate with COVID-19 compared to all adults aged 20–39 years in Washington state (RR 3.5, 95% CI 2.3–5.3) • Of the 24 women who were admitted unwell with COVID-19, **the median gestation was 32+4 weeks** (interquartile range [IQR] 26–36+1 weeks of gestation).	-	• No comparison group of non-pregnant reproductive-aged women with SARS-CoV-2 infections
Nederlandse data (Nethoss, not yet published)			

<table>
<tr>
<td>Overtoom et al., 2021

Accepted for publication - vertrouwelijk</td>
<td>

Of 376 registered pregnant women with confirmed SARS-CoV-2 infection, 74/376 (20%) were admitted to hospital, of whom 6/74 (8%) to intensive care and 9/74 (12%) to obstetric high care units.
Hospital and intensive care admission were higher compared to the fertile age COVID cohort (OR 6.75, 95%CI 5.18-8.81 and OR 2.52, 95%CI 1.11-5.77 respectively).

<table>
<tr><th>Zwangerschapsduur (in weken)</th><th>Opname IC/OCCU

N (%)</th><th>O2-therapie

N (%)</th><th>O2-mask

N (%)</th><th>O2-intubatie

N (%)</th></tr>
<tr><td><22</td><td>7 (13.0)</td><td>10 (11.6)</td><td>3 (8.1)</td><td>2 (14.3)</td></tr>
<tr><td>22-27</td><td>11 (20.4)</td><td>26 30.2)</td><td>13 (35.1)</td><td>2 (14.3)</td></tr>
<tr><td>28-31</td><td>11 (20.4)</td><td>17 (18.8)</td><td>4 (10.8)</td><td>2 (14.3)</td></tr>
<tr><td>32-36</td><td>13 (24.1)</td><td>18 (20.9)</td><td>8 (21.6)</td><td>3 (21.4)</td></tr>
<tr><td>>37</td><td>9 (16.7)</td><td>12 (14.0)</td><td>7 (18.9)</td><td>4 (28.6)</td></tr>
<tr><td>Postpartum</td><td>3 (5.6)</td><td>3 (3.5)</td><td>2 (5.4)</td><td>1 (7.1)</td></tr>
<tr><td>Totaal</td><td>54</td><td>86</td><td>37</td><td>14</td></tr>
</table>
</td>
<td>Van de 376 zwangere vrouwen bevonden zich er 49 (13%) in het 1e trimester, 101 (27%) in het 2e, en 200 in het 3e trimester (54%).

De verdeling van zwangerschapsduur bij IC opname etc. (tabel in kolom hiernaast) hebben we ontvangen via de mail d.d. 19 feb

Als gevolg van het testbeleid werden aanvankelijk alleen vrouwen met aanzienlijke symptomen getest waarbij ziekenhuisopname vereist was. Vrouwen met milde of geen symptomen zijn hierdoor wrs. ondervertegenwoordigd</td>
</tr>
</table>

References

1. Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, et al. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22-October 3, 2020. CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team. MMWR Morb Mortal Wkly Rep 2020;69:1641-7. Available at: https://www.cdc.gov/mmwr/volumes/69/wr/mm6944e3.htm
2. Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD, et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22-June 7, 2020. MMWR Morb Mortal Wkly Rep 2020;69:769-75. Available at: https://www.cdc.gov/mmwr/volumes/69/wr/mm6925a1.htm
3. Knight M, Bunch K, Vousden N, Morris E, Simpson N, Gale C, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. UK Obstetric Surveillance System SARS-CoV-2 Infection in Pregnancy Collaborative Group. BMJ 2020;369:m2107. Available at: https://www.bmj.com/content/369/bmj.m2107
4. Panagiotakopoulos L, Myers TR, Gee J, Lipkind HS, Kharbanda EO, Ryan DS, et al. SARS-CoV-2 infection among hospitalized pregnant women: reasons for admission and pregnancy characteristics - eight U.S. health care centers, March 1-May 30, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1355-9. Available at: https://www.cdc.gov/mmwr/volumes/69/wr/mm6938e2.htm
5. Delahoy MJ, Whitaker M, O'Halloran A, Chai SJ, Kirley PD, Alden N, et al. Characteristics and maternal and birth outcomes of hospitalized pregnant women with laboratory-confirmed COVID-19 - COVID-NET, 13 states, March 1-August 22, 2020. COVID-NET Surveillance Team. MMWR Morb Mortal Wkly Rep 2020;69:1347-54. Available at: https://www.cdc.gov/mmwr/volumes/69/wr/mm6938e1.htm

6. Collin J, Byström E, Carnahan A, Ahrne M. Public Health Agency of Sweden's Brief Report: pregnant and postpartum women with severe acute respiratory syndrome coronavirus 2 infection in intensive care in Sweden. Acta Obstet Gynecol Scand 2020;99:819-22. Available at: https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/aogs.13901
7. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ 2020;370:m3320
8. Badr DA, Mattern J, Carlin A, et al. Are clinical outcomes worse for pregnant women at >/=20 weeks' gestation infected with coronavirus disease 2019? A multicenter case-control study with propensity score matching. Am J Obstet Gynecol 2020 Jul 27
9. Maru S, Patil U, Carroll-Bennett R, et al. Universal screening for sars-cov-2 infection among pregnant women at elmhurst hospital center, queens, new york. PLoS One. 2020;15:e0238409. Available at https://www.ncbi.nlm.nih.gov/pubmed/33301498.
10. Money D. Canadian surveillance of covid-19 in pregnancy: Epidemiology, maternal and infant outcomes. Report #1: Released december 2nd, 2020early release: Maternal and infant outcomes (march 1, 2020 to september 30, 2020) from three canadian provinces 2020. Available at https://med-fomridresearch.sites.olt.ubc.ca/files/2020/12/CANCOVID-Preg-report-1-BC-AB-ON-data_02DEC2020-V2.pdf
11. Martinez-Portilla RJ, Sotiriadis A, Chatzakis C, et al. Pregnant women with SARS-CoV-2 infection are at higher risk of death and severe pneumonia: propensity score-matched analysis of a nationwide prospective cohort study (COV19Mx). Ultrasound Obstet Gynecol 2020;10.1002/uog.23575.
12. DeBolt CA, Bianco A, Limaye MA, et al. Pregnant women with severe or critical coronavirus disease 2019 have increased composite morbidity compared with nonpregnant matched controls. Am J Obstet Gynecol 2020;S0002-9378(20)31312-0.
13. Oakes MC, Kernberg AS, Carter EB, et al. Pregnancy as a risk factor for severe coronavirus 2019 (COVID-19) disease using standardized clinical criteria. Am J Obstet Gynecol MFM 2021;100319.
14. Lokken EM, Huebner EM, Taylor GG, et al.; Washington State COVID-19 in Pregnancy Collaborative. Disease Severity, Pregnancy Outcomes and Maternal Deaths among Pregnant Patients with SARS-CoV-2 Infection in Washington State. Am J Obstet Gynecol 2021;S0002- 9378(21)00033-8.

Published after Allotey et al.