

similar with respect to the preference rates for life-sustaining treatments compared with palliative care (46.9% vs 34.4% in the 60% survival group and 50.0% vs 40.6% in the 30% survival group; odds ratio [OR], 0.90; 95% CI, 0.31-2.63). A few patients were not able to formulate a preference (6 patients (18.8%) in the 60% survival group and 3 patients (9.4%) in the 30% survival group; OR, 0.423; 95% CI, 0.08-2.10). An analysis of the patients who formulated a preference showed that an attitude that mere survival is at least as important as quality of life was associated with a preference for life-sustaining treatments (OR, 10.28; 95% CI, 2.94-35.90). Increasing maternal age (OR, 0.77; 95% CI, 0.61-0.98) and childlessness (OR, 0.12; 95% CI 0.01-0.98) were associated with a preference for palliative care. Most patients would decide together with their partners (63 of 64 [98.4%]) and preferred to be empowered by their physicians in the decision-making process (48 of 64 [75%]).

Discussion | In this study, it appeared that treatment preferences originated from individual characteristics and values rather than from reasoning about numerical outcome estimates. However, generalizability is limited and the results should be interpreted in light of the methods used. Patients made a one-time decision without personal feedback and patients actually affected might indicate different preferences. More studies are needed to help to improve our understanding of the information that parents facing extremely preterm birth want and need.

André Kidszun, MD, MA
Daniel Matheisl, MD
Susanne Tippmann, MD
Julia Inthorn, PhD
Seyed Hamidreza Mahmoudpour, PhD
Norbert W. Paul, MD, MA
Eva Mildnerberger, MD

Author Affiliations: Center for Pediatric and Adolescent Medicine, Department of Neonatology, Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany (Kidszun, Matheisl, Tippmann, Mildnerberger); Center for Pediatrics, Department of Neonatology, Medical Center-University of Freiburg, Freiburg im Breisgau, Germany (Matheisl); Center for Health Care Ethics, Hannover, Germany (Inthorn); Institute for the History, Philosophy, and Ethics of Medicine, Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany (Inthorn, Paul); Institute of Medical Biostatistics, Epidemiology, and Informatics, University Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany (Mahmoudpour); Center for Thrombosis and Hemostasis, University Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany (Mahmoudpour).

Corresponding Author: André Kidszun, MD, MA, Center for Pediatric and Adolescent Medicine, Department of Neonatology, Medical Center of the Johannes Gutenberg University, Langenbeckstrasse 1, Mainz-55131, Germany (andre.kidszun@gmail.com).

Published Online: April 20, 2020. doi:10.1001/jamapediatrics.2020.0235

Author Contributions: Mr Kidszun had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. **Concept and design:** Kidszun, Matheisl, Tippmann, Inthorn, Paul, Mildnerberger. **Acquisition, analysis, or interpretation of data:** Kidszun, Tippmann, Inthorn, Mahmoudpour, Mildnerberger. **Drafting of the manuscript:** Kidszun, Paul. **Critical revision of the manuscript for important intellectual content:** Matheisl, Tippmann, Inthorn, Mahmoudpour, Paul, Mildnerberger. **Statistical analysis:** Inthorn, Mahmoudpour. **Obtained funding:** Paul.

Administrative, technical, or material support: Kidszun, Tippmann, Mildnerberger.

Supervision: Kidszun, Paul, Mildnerberger.

Other - analysis of ethical implications of findings: Inthorn.

Conflict of Interest Disclosures: None reported.

Funding/Support: Parts of this work were funded by the Deutsche Forschungsgemeinschaft grant GRK 2015 (Life sciences-Life writing).

Role of the Funder/Sponsor: The funding organization had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See Supplement 2.

- Cummings J; Committee on Fetus and Newborn. Antenatal counseling regarding resuscitation and intensive care before 25 weeks of gestation. *Pediatrics*. 2015;136(3):588-595. doi:10.1542/peds.2015-2336
- Lantos JD. Ethical problems in decision making in the neonatal ICU. *N Engl J Med*. 2018;379(19):1851-1860. doi:10.1056/NEJMra1801063
- Gaucher N, Nadeau S, Barbier A, Janvier A, Payot A. Personalized antenatal consultations for preterm labor: responding to mothers' expectations. *J Pediatr*. 2016;178(September):130-134.e7. doi:10.1016/j.jpeds.2016.08.006
- Antommaria AHM, Collura CA, Antiel RM, Lantos JD. Two infants, same prognosis, different parental preferences. *Pediatrics*. 2015;135(5):918-923. doi:10.1542/peds.2013-4044
- Guillén Ú, Mackley A, Laventhal N, et al. Evaluating the use of a decision aid for parents facing extremely premature delivery: a randomized trial. *J Pediatr*. 2019;209:52-60.e1. doi:10.1016/j.jpeds.2019.02.023
- Janvier A, Lorenz JM, Lantos JD. Antenatal counselling for parents facing an extremely preterm birth: limitations of the medical evidence. *Acta Paediatr*. 2012;101(8):800-804. doi:10.1111/j.1651-2227.2012.02695.x

Neonatal Early-Onset Infection With SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China

The coronavirus disease 2019 (COVID-19) has spread rapidly across the world. With the sharp increase in the number of infections, the number of pregnant women and children with COVID-19 is also on the rise. However, only 19 neonates born to affected mothers have been investigated, and to our knowledge, no information on early-onset infection in newborns has been published in previous studies.^{1,2}

Methods | In this cohort study, all neonates born to mothers with COVID-19 were recruited from Wuhan Children's Hospital, in Wuhan, Hubei Province, China. This study was approved by the local medical ethics committee. Written informed consent was obtained from the neonates' parents. The diagnosis and management of newborns with or at risk of COVID-19 were in accordance with guidelines provided by the National Health Commission and the Chinese Perinatal-Neonatal SARS-CoV-2 Committee.^{3,4}

Data regarding demographic, epidemiologic, and clinical features were obtained from the medical records system. In addition, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) real-time reverse transcriptase-polymerase chain reaction tests (Novel Coronavirus PCR Fluorescence Diagnostic Kit [BGI]) were conducted using nasopharyngeal and anal swab samples. Data were collected from January 2020 to February 2020. All statistical analyses were performed in Stata version 15.0 (StataCorp).

Results | Thirty-three neonates born to mothers with COVID-19, including 3 neonates with COVID-19, were identified (Table). The most common symptom was shortness of breath (4 of 33

Table. General Information and Clinical Features of 33 Newborns With Mothers With COVID-19 Pneumonia

Variable	Neonates with SARS-CoV-2, No. (%)		Patients with SARS-CoV-2		
	No (n = 30)	Yes (n = 3)	Patient 1	Patient 2	Patient 3
Male	16 (53)	3 (100)	Yes	Yes	Yes
Preterm	3 (10)	1 (33)	GA: 40 wk	GA: 40 wk + 4 d	GA: 31 wk + 2 d
Small for gestational age	2 (7)	1 (33)	No; 3250 g	No; 3360 g	No; 1580 g
Asphyxia	1 (3)	1 (33)	No	No	Yes
Symptoms and complications					
Fever	0	2 (67)	Yes	Yes	No
Pneumonia	0	3 (100)	Yes	Yes	Yes
Respiratory distress syndrome	3 (10)	1 (33)	No	No	Yes
Shortness of breath	3 (10)	1 (33)	No	No	Yes
Cyanosis	2 (7)	1 (33)	No	No	Yes
Feeding intolerance	2 (7)	1 (33)	No	No	Yes
Laboratory test, median (range)					
White blood cell count, cells/ μ L	9800 (6100-22 700)	19 200 (8600-20 400)	8600	19 200	20 400
Lymphocyte count, cells/ μ L	4300 (1500-10 700)	2600 (800-3100)	3100	2600	800
Platelets, $\times 10^3$ / μ L	184 (116-303)	245 (230-265)	245	265	230
Creatine kinase isoenzymes, U/L	13 (22.5-43)	31 (18-39)	18	31	39
Aspartate aminotransferase	27.5 (12-45)	24 (8-63)	8	24	63
Alanine aminotransferase	21 (9-95)	17 (11-88)	11	17	88
Treatment					
Mechanical ventilation	0	1 (33)	No	No	Yes
Antibiotic	6 (20)	1 (33)	No	No	Yes
Duration of neonatal intensive care unit, median (range), d	0 (0-6)	4 (2-11)	2	4	11
Death	0	0	No	No	No
Maternal features					
Fever on admission	7 (23)	1 (33)	Yes	No	No
Postpartum fever	4 (13)	1 (33)	Yes	No	No
Cough	9 (30)	1 (33)	No	Yes	No
Intensive care unit admission	0	0	No	No	No
Pneumonia per computed tomography diagnosis	30 (100)	3 (100)	Yes	Yes	Yes
Nasopharyngeal swab	30 (100)	3 (100)	Yes	Yes	Yes
Delivered by cesarean delivery	23 (77)	3 (100)	Yes	Yes	Yes
Premature rupture of membranes	2 (7)	1 (33)	Yes	No	No

Abbreviations: COVID-19, coronavirus disease 2019; GA, gestational age; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

SI conversion factors: To convert the white blood cells and lymphocytes to cells $\times 10^9$ /L, multiply by 0.001; to convert platelets to cells $\times 10^9$ /L, multiply by 1.0; to convert creatinine, aspartate aminotransferase, and alanine aminotransferase to μ kat/L, multiply by 0.0167.

neonates). Radiographic findings were nonspecific. No deaths were reported.

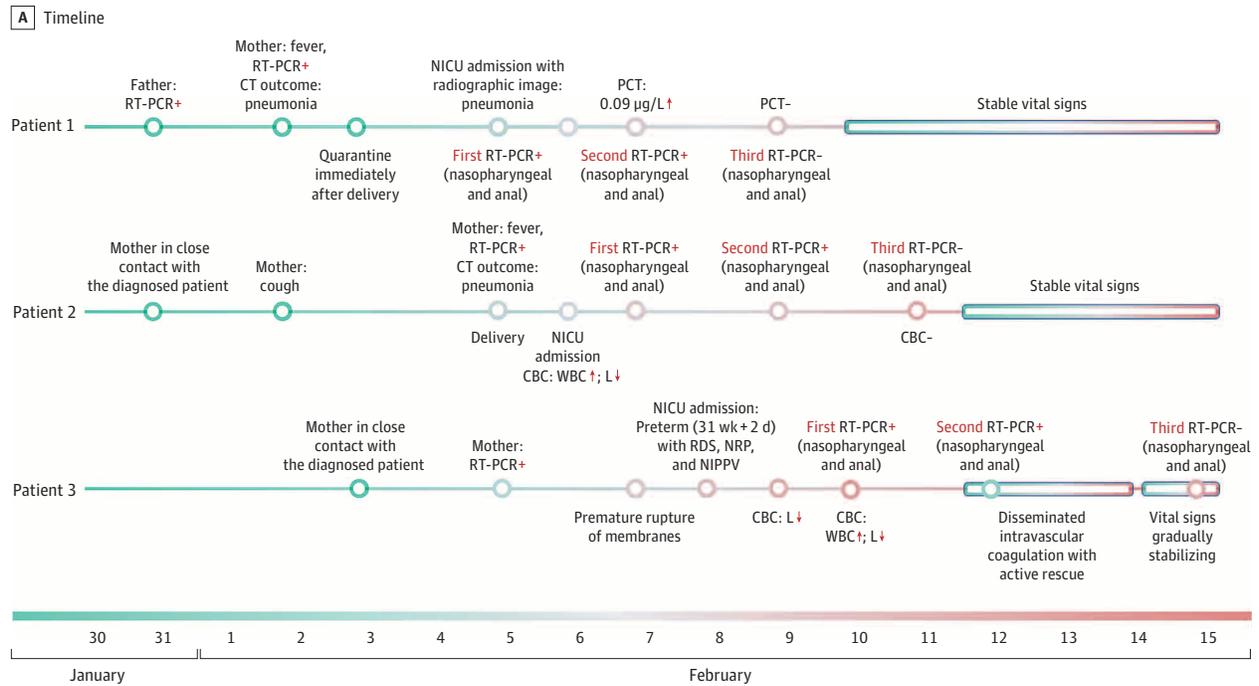
We provide details of the 3 infected neonates (Figure). Patient 1 was born at 40 weeks' gestation. The delivery was by cesarean delivery because of meconium-stained amniotic fluid and confirmed maternal COVID-19 pneumonia. On day 2 of life, the infant experienced lethargy and fever, with unremarkable physical examination results, and was moved to the neonatal intensive care unit. A chest radiographic image showed pneumonia, but other laboratory tests (except procalcitonin) were normal. Nasopharyngeal and anal swabs were positive for SARS-CoV-2 on days 2 and 4 of life and negative on day 6.

Patient 2 was born at 40 weeks' and 4 days' gestation by cesarean delivery because of confirmed maternal COVID-19 pneumonia. He presented with lethargy, vomiting, and fever. A physical examination was unremarkable. Laboratory tests showed leukocytosis, lymphocytopenia, and an

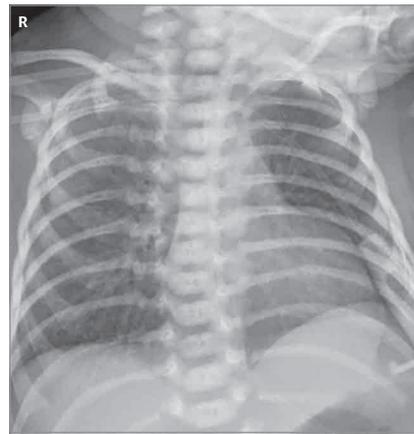
elevated creatine kinase-MB fraction. A chest radiographic image showed pneumonia. Nasopharyngeal and anal swabs were positive for SARS-CoV-2 on days 2 and 4 of life and negative on day 6.

Patient 3 was born at 31 weeks' and 2 days' gestation by cesarean delivery because of fetal distress and confirmed maternal COVID-19 pneumonia. Resuscitation was required. The infant's Apgar scores were 3, 4, and 5 at 1, 5, and 10 minutes after birth. Neonatal respiratory distress syndrome and pneumonia confirmed by chest radiographic image on admission resolved on day 14 of life after treatment with noninvasive ventilation, caffeine, and antibiotics. He also had suspected sepsis, with an *Enterobacter* agglomerates-positive blood culture, leukocytosis, thrombocytopenia (11 cells $\times 10^3$ / μ L; to convert to cells $\times 10^9$ /L, multiply by 1.0), and coagulopathy (prothrombin time, 21 seconds; activated partial thromboplastin time, 81.9 seconds), which improved with antibiotic treatment. Nasopharyngeal and anal swabs

Figure. Timeline and Imaging Findings of 3 Neonates Infected With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)



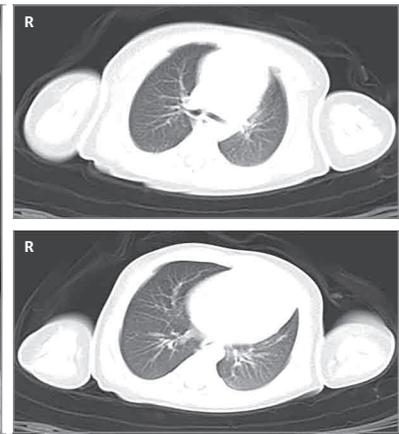
B Chest radiographic image of patient 1



C Chest radiographic image of patient 2



D Computed tomography of patient 3



Normal ranges: lymphocytes (L), 3000 to 8000 cells/ μ L (to convert to cells $\times 10^9$ /L, multiply by 0.001); procalcitonin (PCT), $<0.05 \mu$ g/L; white blood cell count (WBC), 8000-15000 cells/ μ L (to convert to cells $\times 10^9$ /L, multiply by 0.001). CBC indicates complete blood cell count; CT, computed tomography;

NICU, neonatal intensive care unit; NIPPV, noninvasive positive-pressure ventilation; NRP, neonatal resuscitation program; RDS, respiratory distress syndrome; RT-PCR, reverse transcriptase-polymerase chain reaction.

were positive for SARS-CoV-2 on days 2 and 4 of life and negative on day 7.

Discussion | Consistent with previous studies, the clinical symptoms from 33 neonates with or at risk of COVID-19 were mild and outcomes were favorable.^{1,2,5} Of the 3 neonates with symptomatic COVID-19, the most seriously ill neonate may have been symptomatic from prematurity, asphyxia, and sepsis, rather than SARS-CoV-2 infection.

In this cohort, 3 of 33 infants (9%) presented with early-onset SARS-CoV-2 infection. Because strict infection control

and prevention procedures were implemented during the delivery, it is likely that the sources of SARS-CoV-2 in the neonates' upper respiratory tracts or anuses were maternal in origin. Although 2 recent studies^{1,2} have shown that there were no clinical findings or investigations suggestive of COVID-19 in neonates born to affected mothers, and all samples, including amniotic fluid, cord blood, and breast milk, were negative for SARS-CoV-2, the vertical maternal-fetal transmission cannot be ruled out in the current cohort. Therefore, it is crucial to screen pregnant women and implement strict infection control measures, quarantine of

infected mothers, and close monitoring of neonates at risk of COVID-19.

Lingkong Zeng, MD
Shiwen Xia, MD
Wenhao Yuan, MD
Kai Yan, MD
Feifan Xiao, MS
Jianbo Shao, MD
Wenhao Zhou, MD

Author Affiliations: Department of Neonatology, Institute of Maternal and Child Health, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China (Zeng, Yuan); Department of Neonatology, Maternal and Child Health Hospital of Hubei Province, Wuhan, China (Xia); National Children's Medical Center, Children's Hospital of Fudan University, Shanghai, China (Yan, Xiao, Zhou); Institute of Maternal and Child Health, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China (Shao).

Accepted for Publication: March 10, 2020.

Corresponding Author: Wenhao Zhou, MD, National Children's Medical Center, Children's Hospital of Fudan University, 399 Wanyuan Rd, Shanghai 201102, China (zhouwenhao@fudan.edu.cn).

Published Online: March 26, 2020. doi:10.1001/jamapediatrics.2020.0878

Author Contributions: Dr Zeng had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Zeng, Shao, Zhou.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: All authors.

Critical revision of the manuscript for important intellectual content: Xia, Yuan, Xiao, Shao, Zhou.

Statistical analysis: Zeng, Yuan, Yan, Xiao.

Administrative, technical, or material support: Zeng, Xia, Yan, Shao, Zhou.

Supervision: Shao, Zhou.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank Shoo K. Lee, MD, Department of Obstetrics and Gynecology and Department of Public Health, University of Toronto, for editing assistance. He was compensated for his contribution. We thank the patients' families for granting permission to publish this information.

1. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr*. 2020;9(1):51-60. doi:10.21037/tp.2020.02.06
2. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet*. 2020;395(10226):809-815. doi:10.1016/S0140-6736(20)30360-3
3. National Health Commission of China. New coronavirus pneumonia prevention and control program (4th edition). Accessed March 9, 2020. <http://www.gov.cn/zhengce/zhengceku/2020-01/28/5472673/files/0f96c10cc09d4d36a6f9a9f0b42d972b.pdf>.
4. Wang L, Shi Y, Xiao T, et al; Working Committee on Perinatal and Neonatal Management for the Prevention and Control of the 2019 Novel Coronavirus Infection. Chinese expert consensus on the perinatal and neonatal management for the prevention and control of the 2019 novel coronavirus infection (first edition). *Ann Transl Med*. 2020;8(3):47. doi:10.21037/atm.2020.02.20
5. Wei M, Yuan J, Liu Y, Fu T, Yu X, Zhang ZJ. Novel coronavirus infection in hospitalized infants under 1 year of age in China. *JAMA*. 2020. doi:10.1001/jama.2020.2131

Patterns of Mean Age at Drug Use Initiation Among Adolescents and Emerging Adults, 2004-2017

Use of alcohol, marijuana, and other drugs at an early age (eg, before age 18 years) increases the likelihood of drug use disorder,^{1,2} which may disrupt brain development.³ A recent

US report⁴ showed decreased incidence of some drugs, such as marijuana and tobacco, among people aged 12 to 17 years, while the contrary is true among those aged 18 to 25 years. This suggests an increase in the mean age at initiation of some drugs, although we have found no confirmation of this in recent literature. In this study, we examine recent trends in the mean age at initiation for 18 internationally regulated drugs (including alcohol and tobacco), focusing on the critical neurodevelopmental period (ages 12-21 years), using data from the National Survey on Drug Use and Health (NSDUH).

Methods | Each year from 2004 to 2017, staff from the NSDUH drew a random, nationally representative sample of the US population ages 12 years and older through multistage sampling to assess drug-use and drug-associated behaviors. The NSDUH staff used audio computer-assisted self-interviews to collect data on alcohol and drug use, including age at first use, after obtaining informed consent/assent. We analyzed publicly available, deidentified NSDUH data that included 338 268 individuals aged 12 to 21 years who completed self-interviews on their initiation of alcohol, tobacco, and other drugs. Because all data came from deidentified, publicly available files, the Washington State University institutional review board ruled that the plan to analyze these data was not human subjects research.

In this study, we identified individuals who initiated drug use within 12 months prior to assessment. We analyzed 18 drugs, including alcohol and tobacco products (Figure), to estimate the year-by-year drug-specific mean age at initiation among individuals aged 12 to 21 years. Analysis weights account for the complex survey design of the data. We conducted joinpoint regression using log-linear model to estimate the slope of analysis-weighted, drug-specific mean ages between 2004 and 2017. Finally, meta-analysis with a DerSimonian and Laird random effects estimator was used to summarize year-by-year mean age estimates for initiation of each drug.⁵ All analyses were conducted using Stata SE15 (Stata-Corp), with the statistical significance level at .05. Data analysis occurred from April 2019 to June 2019.

Results | Between 2004 and 2017, 84 317 adolescents and young adults initiated use of any drug. Estimated year-by-year mean ages, slopes, and annual percentage changes for each drug are visible in the Figure. Of the 18 drugs analyzed, we observed an increase in the mean age at initiation for 12 drugs since 2004 (including cigar use, $\beta = 0.003$; $P < .001$; cocaine, $\beta = 0.005$; $P < .001$; ecstasy, $\beta = 0.003$; $P = .03$; hallucinogens, $\beta = 0.004$; $P = .004$; heroin, $\beta = 0.005$; $P = .02$; inhalants; $\beta = 0.004$; $P = .02$; marijuana, $\beta = 0.002$; $P < .001$; smokeless tobacco, $\beta = 0.001$; $P = .002$; stimulants, $\beta = 0.005$; $P = .007$; and tobacco cigarettes, $\beta = 0.006$; $P < .001$). The mean age at initiation increased from 2004 to 2014 for alcohol ($\beta = 0.005$; $P < .001$), but there was no increase in this mean age at initiation after 2014 ($\beta = -0.004$; $P = .06$). The mean age at lysergic acid diethylamide (LSD) initiation increased from 2004 to 2009 ($\beta = 0.013$; $P = .03$) and declined significantly after 2009 ($\beta = -0.014$; $P = .04$). No statistical difference in the mean ages at initiation for crack cocaine, methamphetamines, opioids,