

1 **The impact of COVID-19 lockdown on infants' coronavirus exposure and**
2 **routine healthcare access in Ireland: the CORAL study at 6 months.**

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19 **Introduction**

20 The public health strategy during the SARS-CoV-2 (COVID19) pandemic of 2020-2021 led to
21 profound changes in social behaviour, affecting not only familial but also wider social
22 interactions in settings such as workplaces, schools and day care facilities. These changes
23 may have altered viral and bacterial interchange.

24

25 A significantly decreased diversity of gut and skin microbiota has been demonstrated in
26 allergic individuals compared to non-allergic subjects¹. The **CORAL** study is a longitudinal
27 study of the impact of the **C**oronavirus Pandemic on **A**llergic and autoimmune dysregulation
28 of infants born from March - May 2020, during Ireland's first lockdown (Ireland formally
29 entered national lockdown on March 27th 2020, though severe restrictions had been
30 gradually escalated for the 2 weeks prior to that date. The first release of lockdown was on
31 June 8th 2020). CORAL will follow children initially until they are 2 years old, with stool
32 sampling at 6, 12 and 24 months for microbiome diversity analysis and allergy testing and
33 blood RNA and epigenomic testing at 12 and 24 months

34

35 Now, in the immunisation phase of the pandemic response, attention is shifting from
36 immediate population protection during waves of COVID-19 to the health care and social
37 consequences of both the pandemic and the societal disruption created by lockdown. There

38 are particular concerns that important medical care (such as infant immunisations) may
39 have been delayed, or even refused, due to patient or family concerns about infection risk
40 when attending health care facilities also managing COVID-19.

41

42 We report here the impact of COVID-19 lockdown on health care access, completion of
43 immunisation and COVID-19 infection rates in Irish babies to 6 months of age enrolled in
44 the CORAL STUDY.

45

46 **Methods**

47 Ethical approval was obtained from the National Research Ethics Committee (20-NREC-
48 COV-067) and the participating hospitals' ethics committees. Informed written parental
49 consent was obtained.

50

51 Invitations were sent to families of term, singleton babies born in 2 major maternity
52 hospitals in Dublin, during March to May 2020. Exclusion criteria were pre-birth PCR-proven
53 SARS-CoV-2 infection in a parent or co-dwelling person, intravenous antibiotics in the
54 neonatal period, multiple birth or major congenital anomaly.

55

56 At 6 months (September - November 2020), families were sent a questionnaire and a stool
57 sample collected for microbiome analysis (results will be reported elsewhere). Families
58 were also offered point-of-care SARS-CoV-2 antibody testing (VivaDiagTMSARS-CoV-2
59 IgM/IgG Rapid Test) for the infants, however escalation of national travel restrictions in
60 response to the second surge of COVID-19 in September and October 2020 restricted access
61 to this testing for some infants.

62

63 **Results**

64 365 infants were enrolled. 195 babies (53.4%) were male, 94.5% were of "White Irish" or
65 "Any Other White" background and 94% of mothers were educated to third level or higher.
66 The average birth weight was 3.5kg. Most babies were either first-born (45%) or second-
67 born (37%). In infants with siblings (n=201), atopic dermatitis was most common allergic
68 condition reported (15.4%), followed by asthma (12.4%) and food allergy (11.4%). Allergic

69 rhinitis was the most commonly reported atopic condition in both mothers (36%) and
70 fathers (30%).

71

72 360 six-month questionnaires were completed. Exclusive breastfeeding rate at 6 months
73 was 38%, a further 15% were receiving breastmilk and infant formula. 92% were having
74 regular solids with a median weaning age of 5 months (range 3-6 months). The rates of
75 introduction of allergenic foods such as egg and peanut are outlined in Table 1.

76

77 99% of infants had been fully vaccinated according to the Irish Primary Childhood
78 Immunisation Schedule and 7.5% of babies had been admitted to hospital in the first 6
79 months. Antibiotics had been prescribed for 25 infants (7%) and 5 of those infants had
80 received more than one course. Possible allergic reactions to a food or environmental
81 substance were reported by 47 children (13%), but on elaboration most described a flare of
82 eczema without identifying a particular allergen.

83

84 By the age of 6 months, 30 (8.3%) had had community testing for SARS-CoV-2 PCR due to
85 symptoms or known close contact, and 2 (0.5%) were PCR positive. 268 (73%) of babies had
86 point-of-care lateral flow immunoassay testing at 6 months as part of the study, of whom
87 3(1.1%) returned positive results for IgM and IgG SARS-CoV-2 antibodies. One infant (as
88 above) had known prior PCR-proven SARS-CoV-2 infection but there two further cases with
89 no known COVID-19 exposure. Of these 1 was PCR positive (indicating very recent or current
90 infection) and the other was PCR negative. Overall 4 babies (1%) were shown to have
91 immunological evidence of exposure to SARS-CoV-2 infection before the age of 6 months.

92

93 **Discussion**

94 It is reassuring that this population of infants born during lockdown had been presented as
95 advised for routine healthcare such as immunisations, actually at even higher rates than
96 national norms. Weaning rates were in line with national trends in Ireland, and despite the
97 low rates of egg and peanut introduction, these are in line with national data, so weaning to
98 allergenic foods did not seem to have been impacted by heightened fear of adverse
99 outcomes or risk of needing to emergency care during the pandemic. In contrast the overall
100 rate of attendance at hospital for any reason (7.5%) or any use of antibiotics were lower

101 than expected, supporting our previous data about significant changes in circulation of virus
102 related illnesses in the early stages of the 2020 lockdown².

103

104 This self-selected cohort of infants is largely representative of the overall Irish population.^{3,4}
105 The proportion of first-borns (45%) is higher than the national average (38.8%) but these
106 larger maternity hospitals (more than 8000 deliveries each per annum) have high rates of
107 primigravida patients.⁴ A notable difference is the level of maternal education. In the 2016
108 Irish census 43.2% of women were educated to third level compared with 94% of mothers in
109 this study.⁵ This, along with mothers working from home during lockdown, is likely
110 contributing to the atypically high percentage of Irish infants still breastfed at 6 months; in
111 Ireland this figure is approximately 15%⁶. The rate of reported food allergy in siblings of this
112 cohort (sourced from unconfirmed parental reports rather than from health care record
113 searches) is higher than the general population, which may have contributed to parental
114 desire to enrol in this study.⁷

115

116 The rare (1%) positive SARS-CoV-2 antibody tests at 6 months suggesting recent or current
117 infection imply that in Ireland, at least, newborn babies, traditionally considered to be
118 particularly vulnerable to viral infection, appear to have been largely protected from SARS-
119 CoV-2 exposure during the first COVID-19 lockdown in 2020.

120

121 The next stage of the CORAL study commenced in February 2021. It involves a review of the
122 participants at 12 months with skin prick testing for common food and aeroallergens, a
123 further questionnaire, stool sample and SARS-CoV-2 antibody test and peripheral blood
124 sample for RNA sequencing to determine host immune responses to the COVID-19
125 lockdown.

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158 Conflict of interest

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163 Table. Introduction of allergenic foods at 6 months

Allergenic Foods at 6 months	Introduced Food (%) Total N=360
Egg	95 (26%)
Peanut	49 (13.6%)
Treenut	12 (3.3%)
Wheat	151 (42%)
Fish	59 (16.4%)
Dairy	166 (46%)
Dairy Alternatives	17 (4.7%)

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