Spatiotemporal association of low birth weight with Cs-137 deposition after Fukushima at the prefecture level in Japan: an ecological study

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Abstract

Background: Perinatal mortality increased in contaminated prefectures after the Fukushima Daichi Nuclear Power Plant (FDNPP) accidents in Japan in 2011. Elevated numbers of surgeries for cryptorchidism and congenital heart malformations were observed throughout Japan from 2012 onward. The thyroid cancer detection rate (2011 to 2016) was associated with the dose-rate at the municipality level in the Fukushima prefecture. Since the birth weight is a simple and objective indicator for gestational development and pregnancy outcome, the question arises whether the annual birth weight distribution was distorted in a dose-rate-dependent manner across Japan after Fukushima.

Data and Methods: The Japanese Ministry of Health, Labour, and Welfare provides prefecture-specific annual counts for 26.158 million live births from 1995 to 2018, of which 2.366 million births (9.04%) with weights < 2500g. Prefecture-specific spatiotemporal trends of the low birth weight proportions were analyzed. Logistic regression allowing for level-shifts from 2012 onward was employed to test whether those level-shifts were proportional to the prefecture-specific dose-rates derived from Cs-137 deposition in the 47 Japanese prefectures.

Results: The overall trend of the low birth weight proportion (LBWP) in Japan discloses a jump in 2012 with a jump odds ratio (OR) 1.020, 95%-confidence interval (1.003,1.037), p-value 0.0225. A logistic regression of LBWP on the additional dose-rate after Fukushima adjusted for prefecture-specific spatiotemporal base-line trends yields an OR per µSv/h of 1.098 (1.058, 1.139), p-value < 0.0001. Further adjusting the logistic regression for the annual population size and physician density of the prefectures, as well as for the counts of the dead, the missing, and the evacuees due to earthquake and tsunami (as surrogate measures for medical infrastructure and stress) yields an OR per µSv/h of 1.109 (1.032, 1.191), p-value 0.0046.
Conclusion: This study shows increased low birth weight prevalence related to Cs-137 deposition and the corresponding additional dose-rate in Japan from 2012 onward. Previous evidence suggesting compromised gestational development and pregnancy outcome under elevated environmental ionizing radiation exposure is corroborated.

Introduction

Low birth weight (LBW) is defined as having a birth weight of < 2500 g. It is an objective and reliable indicator used as comprehensive demographic reporting measure of fetal development and pregnancy outcome [1-4]. Environmental pollutants are consistently linked to general untoward pregnancy outcome and specific reductions in birth weight [5-12]. LBW has been suggested as an indicator of genetic detriment caused by mutation in humans exposed to ionizing radiation [13]. Analyses of birth weight and duration of pregnancies in relation to maternal age, parity, and infant survival indicated that non-survivors were significantly lighter at birth than survivors [14]. LBW is closely linked to fetal and perinatal mortality and morbidity [15]. It has been reported to be associated with disorders in perinatal periods, in childhood, and in adulthood [16, 17]. Studies in Great Britain showed that people who had low birth weight were at increased risk of coronary heart disease and the disorders related to it [18]. Animal and human studies have shown that the LBW proportions (LBWp) increase with toxic exposure and with radiation exposure [19-21]. Smoking increases the LBWp in a dose-dependent manner [22], possibly due to elevated radionuclides in tabaco [23]. Females subject to pelvic radiotherapy experience an increased risk of pre-term delivery and LBW among their offspring [24]. Treatment of female childhood cancer patients may entail restricted fetal growth and pre-term births [25]. LBW was reported after dental radiography during pregnancy [26]. A cohort study in China identified multiple risk factors of LBW including radiation exposure of fathers [27]. A natural experiment in Taiwan revealed that prenatal
exposure to a continuous low-level irradiation reduced the gestational length and increased the LBW proportion [28]. In Belarus, increased LBW prevalence was reported from the highly Chernobyl-contaminated regions Gomel and Mogilev [29]. Temporarily elevated LBWp was seen in Sweden after Chernobyl [30]. Since several radiation inducible genetic and carcinogenic effects were observed in Japan after Fukushima [31–37], an increase in the LBW proportion was also conceivable. Among the investigations after the Fukushima nuclear accidents, there are reports that LBW is increasing and reports that deny the increase. In the following we shortly address two reports that are questionnaire-based surveys with a response rate in the 50% range and one survey of a small number of births in one clinic in Fukushima [38–40]. Questionnaire-based studies are prone to selection bias and studies with small populations (mostly in clinical settings) may likely entail type-2 errors [41]. A questionnaire-based pregnancy and birth survey was conducted by the Radiation Medical Science Center for the Fukushima Health Management Survey [38]. In this study, an increase of the LBW proportion is documented in the combined contaminated Iwaki and Soso regions compared to the remainder of the Fukushima prefecture: OR 1.163, p-value 0.0723. This observation is supported by a corresponding increase of the stillbirth proportion in Soso and Iwaki with OR 1.923, p-value 0.1321. Since this study [38] had a participation rate of below 60%, it is likely that significant effects would be obtained with lager populations considered during longer periods. Maternal and perinatal data (2008 to 2015) were retrospectively collected for singleton live births at a hospital located 23 km from the Fukushima nuclear power plant [39]. In 1101 births, LBWp was compared pre- and post-disaster. There was no increased LBWp in any year from 2011 onward. However, with 4 years before/after the accident, i.e., 140 births per year, which means about 10 LBW-births per year, it was unlikely to receive a meaningful result, i.e., there is a large type-2 error probability in this
study [39]. A more recent investigation considered 12,804 maternal outcomes during 2011–2014 in the Fukushima Prefecture [40]. However, this study neither analyzed perinatal outcomes with distance from the nuclear accident nor chronological factors. Therefore, it is unclear whether increases of LBW are due to a temporary cause of the earthquake/tsunami or due to radiation exposure. These surveys cover the Fukushima Prefecture only incompletely over short periods. In the Miyagi Prefecture, the overall rate of LBW infants was reported to be 8.7%, which tended to be lower than LBWp in 2012 of 9.3% and 9.8% in 2013 [42]. The spatiotemporal trends of the LBW rate in most of the surrounding prefectures have not yet been scrutinized, although data is publicly available. In this study, we analyzed data of the Japanese governments ‘Demographical Survey’, which accounts for almost all live births and LBW children registered in Japan excluding births to parents living abroad. Therefore, not only Fukushima Prefecture but also the whole country with differently contaminated prefectures was targeted, and statistical accuracy is guaranteed by using official nearly complete long-term data from 1995 to 2018, i.e., 16 years (1995 to 2010) before and 7 years (2012 to 2018) after the nuclear power plant accidents in Fukushima in March 2011.

Data And Statistical Methods

Vital statistics and auxiliary information

The Japanese Statistics Bureau publishes demographical information compiled by the Ministry of Health, Labor, and Welfare. Statistics include the annual numbers of live births and the annual counts of children with a low birth weight of < 2500 g (LBW), see Table 1 or Vital Statistics of Japan: https://www.mhlw.go.jp/english/database/db-hw/vs01.html. We investigated the spatiotemporal distribution across 47 Japanese prefectures from 1995 to 2018 of 26.158 million live births, of which 2.366 million births (9.04%) with weights <
2500 g. Since medical supply may impact the prevalence of LBW, physician density by
prefecture in Japan ([https://stats-japan.com/t/kiji/10343](https://stats-japan.com/t/kiji/10343)) was deployed as an appropriate
surrogate confounder variable in the spatiotemporal logistic regression models. The
counts of earthquake related deaths, the counts of the dead and missing after earthquake
and tsunami, as well as the number of evacuees to and within any prefecture were
obtained from official sources [43] and served as additional explicit potential ecological
confounding variables, see Table 2.

| Prefecture | ISO code | mean annual population (1000) 1995–2018 | mean physician density per 1000 population | mean annual deaths and missing after earthquake and tsunami | mean earthquake related deaths | mean evacuated persons within or to prefecture | mean annual live births 1995–2018 | mean annual LBW 1995–2018 | mean annual LBWp 1995–2018 | Jump OR in LBWp from 2012 onward | 95%-CI for jump OR in LBWp |
|------------|----------|----------------------------------------|-------------------------------------------|------------------------------------------------------------|--------------------------------|---------------------------------------------|--------------------------------|----------------------------|-----------------|--------------------------------|--------------------------|
| Hokkaido   | 1        | 5557.8                                 | 2.5                                       | 0                                                         | 3003                           | 42115.3                                    | 3880.6                         | 0.092                      | 1.046 | (1.015, 1.079)                  |
| Aomori     | 2        | 1403.0                                 | 2.1                                       | 0                                                         | 1410                           | 10842.5                                    | 924.6                          | 0.085                      | 0.953 | (0.897, 1.014)                  |
| Iwate      | 3        | 1355.5                                 | 2.1                                       | 5788                                                      | 467                            | 10560.7                                    | 915.3                          | 0.087                      | 1.047 | (0.985, 1.113)                  |
| Miyagi     | 4        | 2345.8                                 | 2.4                                       | 10761                                                     | 928                            | 127825                                     | 1724.0                         | 0.087                      | 1.059 | (1.013, 1.106)                  |
| Akita      | 5        | 1118.3                                 | 2.4                                       | 0                                                         | 1473                           | 7571.4                                     | 672.0                          | 0.089                      | 1.014 | (0.944, 1.088)                  |
| Yamagata   | 6        | 1193.1                                 | 2.3                                       | 2                                                         | 2                              | 13538                                      | 9398.9                         | 758.0                      | 0.081 | 1.094 | (1.024, 1.170)                  |
| Fukushima  | 7        | 2041.9                                 | 2.1                                       | 1810                                                      | 2250                           | 98595                                      | 17277.0                        | 1507.3                      | 0.087 | 1.078 | (1.027, 1.131)                  |
| Ibaraki    | 8        | 2958.6                                 | 1.9                                       | 25                                                        | 42                             | 6077                                       | 24918.3                        | 2234.0                      | 0.090 | 1.049 | (1.009, 1.092)                  |
| Tochigi    | 9        | 1996.8                                 | 2.3                                       | 4                                                         | 0                              | 3157                                       | 17052.7                        | 1659.5                      | 0.097 | 1.083 | (1.035, 1.133)                  |
| Gunma      | 10       | 2005.1                                 | 2.4                                       | 1                                                         | 0                              | 1974                                       | 16868.0                        | 1511.8                      | 0.090 | 1.003 | (0.956, 1.051)                  |
| Saitama    | 11       | 7080.9                                 | 1.7                                       | 0                                                         | 1                              | 4778                                       | 60963.0                        | 5470.0                      | 0.090 | 1.024 | (0.998, 1.050)                  |
| Chiba      | 12       | 6073.4                                 | 2.0                                       | 23                                                        | 4                              | 3608                                       | 51154.6                        | 4418.6                      | 0.086 | 1.025 | (0.996, 1.054)                  |
| Tokyo      | 13       | 12716.8                                | 3.2                                       | 7                                                         | 1                              | 9505                                       | 103513.0                       | 9304.9                      | 0.090 | 1.011 | (0.991, 1.031)                  |
| Kanagawa   | 14       | 8799.5                                 | 2.1                                       | 4                                                         | 3                              | 2888                                       | 77614.8                        | 7073.0                      | 0.091 | 1.017 | (0.994, 1.040)                  |
| Niigata    | 15       | 2402.7                                 | 2.1                                       | 0                                                         | 0                              | 6990                                       | 19002.3                        | 1610.8                      | 0.085 | 1.072 | (1.024, 1.122)                  |
| Toyama     | 16       | 1099.7                                 | 2.6                                       | 0                                                         | 0                              | 377                                        | 8806.5                         | 744.5                       | 0.085 | 0.976 | (0.912, 1.044)                  |
| Ishikawa   | 17       | 1170.4                                 | 3.0                                       | 0                                                         | 0                              | 499                                        | 10197.8                        | 860.6                       | 0.084 | 1.122 | (1.054, 1.195)                  |
| 県名   | 1871年 | 1872年 | 1873年 | 1874年 | 1875年 | 1876年 | 1877年 | 1878年 | 1879年 | 1880年 | 1881年 | 1882年 | 1883年 | 1884年 | 1885年 | 1886年 | 1887年 | 1888年 | 1889年 | 1890年 | 1891年 | 1892年 | 1893年 | 1894年 | 1895年 | 1896年 | 1897年 | 1898年 | 1899年 |
|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
Table 2
Mean annual population (1000) for the Japanese prefectures 1995 to 2018, dead and missing after earthquake and tsunami 2011, earth-quake related deaths, evacuated persons within or to the prefectures
(sources: National Police Agency March 8, 2019; Reconstruction Agency September 30, 2018), mean annual live births, mean annual LBW and LBWp, jump OR in LBWp from 2012 onward, and 95%-CI for jump OR in LBWp from 2012 to 2018.

| Prefecture | ISO code | distance from FDNPP [km] | Cs-137 [Bq/m²] Yasunari et al. | Cs-137 [Bq/m²] rescaled | µSv/h |
|------------|----------|--------------------------|---------------------------------|--------------------------|-------|
| Fukushima  | 7        | 72.4                     | 24718.4                         | *106867.0                | 0.8696|
| Miyagi     | 4        | 113.8                    | 44696.6                         | 83416.9                  | 0.6903|
| Ibaraki    | 8        | 139.7                    | 26368.9                         | 65259.1                  | 0.5513|
| Tochigi    | 9        | 134.9                    | 17380.7                         | 40982.0                  | 0.3651|
| Iwate      | 3        | 242.6                    | 6022.7                          | 31908.4                  | 0.2954|
| Yamagata   | 6        | 140.5                    | 12755.5                         | 31826.5                  | 0.2948|
| Saitama    | 11       | 217.9                    | 5256.1                          | 24011.4                  | 0.2347|
| Tokyo      | 13       | 237.1                    | 4063.0                          | 20854.3                  | 0.2105|
| Kanagawa   | 14       | 270.1                    | 2435.5                          | 14962.8                  | 0.1652|
| Chiba      | 12       | 226.0                    | 2878.0                          | 13826.5                  | 0.1564|
| Gunma      | 10       | 208.6                    | 2317.9                          | 9971.1                   | 0.1268|
| Kochi      | 39       | 824.6                    | 137.0                           | 3921.2                   | 0.0802|
| Aomori     | 2        | 373.7                    | 401.7                           | 3860.4                   | 0.0797|
| Shizuoka   | 22       | 139.7                    | 26368.9                         | 65259.1                  | 0.5513|
| Hiroshima  | 34       | 263.9                    | 366.6                           | 2180.4                   | 0.0668|
| Akita      | 5        | 217.9                    | 5256.1                          | 24011.4                  | 0.2347|
| Tottori    | 31       | 681.3                    | 93.1                            | 2047.9                   | 0.0668|
| Tokushima  | 36       | 727.7                    | 51.0                            | 1128.6                   | 0.0595|
| Ehime      | 38       | 852.5                    | 38.4                            | 1150.7                   | 0.0589|
| Fukuai     | 18       | 464.1                    | 88.3                            | 1144.0                   | 0.0588|
| Oita       | 44       | 990.4                    | 27.7                            | 1020.7                   | 0.0579|
| Yamanashi  | 19       | 295.1                    | 146.8                           | 1018.7                   | 0.0578|
| Shimane    | 32       | 810.6                    | 35.7                            | 998.0                    | 0.0577|
| Kyoto      | 26       | 556.7                    | 48.4                            | 805.9                    | 0.0562|
| Hyogo      | 28       | 614.8                    | 41.6                            | 794.2                    | 0.0561|
| Mie        | 24       | 529.8                    | 51.0                            | 793.0                    | 0.0561|
| Gifu       | 21       | 399.2                    | 73.8                            | 776.9                    | 0.0560|
| Wakayama   | 30       | 633.8                    | 36.1                            | 718.8                    | 0.0555|
| Aichi      | 23       | 433.3                    | 48.1                            | 566.9                    | 0.0544|
| Shiga      | 25       | 503.0                    | 37.1                            | 537.1                    | 0.0541|
| Nara       | 29       | 579.5                    | 29.2                            | 513.9                    | 0.0540|
| Ishikawa   | 17       | 386.6                    | 48.1                            | 484.5                    | 0.0537|
| Miyazaki   | 45       | 1061.8                   | 11.7                            | 474.5                    | 0.0537|
| Kagawa     | 37       | 730.6                    | 18.9                            | 457.8                    | 0.0535|
| Kagoshima  | 46       | 1150.0                   | 9.5                             | 430.1                    | 0.0533|
| Osaka      | 27       | 586.9                    | 24.0                            | 429.8                    | 0.0533|
| Okayama    | 33       | 706.9                    | 17.5                            | 405.0                    | 0.0531|
| Yamaguchi  | 35       | 928.0                    | 11.8                            | 397.5                    | 0.0531|
| Hokkaido   | 1        | 674.5                    | 16.0                            | 347.1                    | 0.0527|
| Saga       | 41       | 1092.6                   | 7.9                             | 333.3                    | 0.0526|
| Fukuoka    | 40       | 1034.8                   | 8.5                             | 332.7                    | 0.0526|
| Nagasaki   | 42       | 1126.0                   | 6.8                             | 299.1                    | 0.0523|
| Niigata    | 15       | 184.2                    | 77.2                            | 279.7                    | 0.0522|
| Nagano     | 20       | 302.8                    | 36.7                            | 263.9                    | 0.0520|
| Kumamoto   | 43       | 1070.2                   | 5.1                             | 209.1                    | 0.0516|
| Toyama     | 16       | 346.3                    | 13.4                            | 116.0                    | 0.0509|
| Okinawa    | 47       | 1727.5                   | 0.8                             | 63.5                     | 0.0505|

* According to n = 2160 locations with Cs-137 Bq < 2.0E + 6 in the file of [45]; https://www.unscear.org/docs/publications/2013/UNSCEAR_2013_Annex-A_Attach_C-2.xls.
Cs-137 deposition

Yasunari et al. published average prefecture-specific Cs-137 deposition after the Fukushima nuclear power plant accidents for the 47 prefectures of Japan [44]; see Table 3 or http://www.pnas.org/content/108/49/19530.full. The Yasunari et al. data understate the true Cs-137 deposition, which underestimation may be supported by the following facts:

Yasunari et al.'s data based on measurements restricted to March 20th to April 19th, 2011. Yasunari et al. report a value of 24.7 kBq/m$^2$ Cs-137 for Fukushima prefecture (see Table 3), whereas the UNSCEAR data set 2013/2014 documents a mean value of 153.957 kBq/m$^2$ Cs-137, which amounts to a factor 6 underestimation of the deposition in Fukushima by Yasunari et al. [44], see the data file https://www.unscear.org/docs/publications/2013/UNSCEAR_2013_Annex-A_Attach_C-2.xls [45]. Fukushima is implausibly lesser contaminated than Miyagi, and Ibaraki, see Table 3. The Yasunari et al. data decay with $r^{-3.27}$ at distance $r$ from the FDNPP, see Figure 1, whereas a theoretical decay law of $r^{-1.42}$ is expected according to UNSCEAR [46], and has empirically confirmed for the Fukushima prefecture [31].

Since strong underestimation of radiation exposure would exaggerate any dose-specific radiation risk estimates, we suggest and propagate a correction and a rescaling of the Yasunari et al. deposition data despite the disadvantages listed above. The rationale behind this is that the Yasunari et al. data, while restricted to a narrow time frame, nevertheless reflect a valid relative mutual exposure status amongst the prefectures. To this end, we firstly increased the original deposition value 24,718.4 Bq/m$^2$ of the Fukushima prefecture by a factor of 4.3 to 106,867.0 Bq/m$^2$ based on the MEXT/USCEAR data [45] excluding 20 locations in the immediate vicinity of FDNPP with more than 2.0E + 6 Bq/m$^2$, with less likely importance for public exposure. Secondly, we rescaled the deposition data with the original decay-rate $r^{-3.27}$ to a decay of $r^{2.00}$, which is a compromise between the theoretical decay $r^{-1.42}$ by UNSCEAR [46] and the Yasunari decay $r^{-3.27}$. The rescaling details and results are depicted in Fig. 1 and listed in Table 3. Figure 2 shows a geographic region value plot for the rescaled Cs-137 deposition in the
Japanese prefectures.

| Prefecture | ISO code | distance from FDNPP [km] | Cs-137 [Bq/m²] Yasunari et al. | Cs-137 [Bq/m²] rescaled | µSv/h |
|------------|----------|--------------------------|-------------------------------|--------------------------|-------|
| Fukushima  | 7        | 72.4                     | 24718.4                       | 10686.7                  | 0.8696 |
| Miyagi     | 4        | 113.8                    | 44696.6                       | 83416.9                  | 0.6903 |
| Ibaraki    | 8        | 139.7                    | 26368.9                       | 65259.1                  | 0.5513 |
| Tochigi    | 9        | 134.9                    | 17380.7                       | 40982.0                  | 0.3651 |
| Iwate      | 3        | 242.6                    | 6022.7                        | 31908.4                  | 0.2954 |
| Yamagata   | 6        | 140.5                    | 12755.5                       | 31826.5                  | 0.2948 |
| Saitama    | 11       | 217.9                    | 5256.1                        | 24011.4                  | 0.2347 |
| Tokyo      | 13       | 237.1                    | 4063.0                        | 20854.3                  | 0.2105 |
| Kanagawa   | 14       | 270.1                    | 2435.5                        | 14962.8                  | 0.1652 |
| Chiba      | 12       | 226.0                    | 12755.5                       | 31826.5                  | 0.2948 |
| Gunma      | 10       | 208.6                    | 12755.5                       | 31826.5                  | 0.2948 |
| Kochi      | 39       | 824.6                    | 31908.4                       | 0.2954                   | 0.0797 |
| Aomori     | 2        | 373.7                    | 401.7                         | 3860.4                   | 0.0797 |
| Shizuoka   | 22       | 360.0                    | 284.7                         | 13826.4                  | 0.0686 |
| Hiroshima  | 34       | 805.1                    | 87.0                          | 2409.4                   | 0.0586 |
| Akita      | 5        | 263.9                    | 366.6                         | 2180.4                   | 0.0668 |
| Tottori    | 31       | 681.3                    | 93.1                          | 2047.9                   | 0.0595 |
| Tokushima  | 36       | 727.7                    | 51.0                          | 1228.6                   | 0.0595 |
| Ehime      | 38       | 852.5                    | 38.4                          | 1150.7                   | 0.0589 |
| Fukui      | 18       | 464.1                    | 88.3                          | 1144.0                   | 0.0588 |
| Oita       | 44       | 990.4                    | 27.7                          | 1020.7                   | 0.0579 |
| Yamanashi  | 19       | 295.1                    | 146.8                         | 1018.7                   | 0.0578 |
| Shimane    | 32       | 810.6                    | 35.7                          | 998.0                    | 0.0577 |
| Kyoto      | 26       | 556.7                    | 48.4                          | 805.9                    | 0.0562 |
| Hyogo      | 28       | 614.8                    | 41.6                          | 794.2                    | 0.0561 |
| Mie        | 24       | 529.8                    | 51.0                          | 793.0                    | 0.0561 |
| Gifu       | 21       | 399.2                    | 73.8                          | 776.9                    | 0.0560 |
| Wakayama   | 30       | 633.8                    | 36.1                          | 718.8                    | 0.0555 |
| Aichi      | 23       | 433.3                    | 48.1                          | 566.9                    | 0.0544 |
| Shiga      | 25       | 503.0                    | 37.1                          | 537.1                    | 0.0541 |
| Nara       | 29       | 579.5                    | 29.2                          | 513.9                    | 0.0540 |
| Ishikawa   | 17       | 386.6                    | 48.1                          | 484.5                    | 0.0537 |
| Miyazaki   | 45       | 1061.8                   | 0.017                         | 474.5                    | 0.0537 |
| Kagawa     | 37       | 730.6                    | 18.9                          | 457.8                    | 0.0535 |
| Kagoshima  | 46       | 1150.0                   | 9.5                           | 430.1                    | 0.0533 |
| Osaka      | 27       | 586.9                    | 24.0                          | 429.8                    | 0.0533 |
| Okayama    | 33       | 706.9                    | 17.5                          | 405.0                    | 0.0531 |
| Yamaguchi  | 35       | 928.0                    | 11.8                          | 397.5                    | 0.0531 |
| Hokkaido   | 1        | 674.5                    | 16.0                          | 347.1                    | 0.0527 |
| Saga       | 41       | 1092.6                   | 7.9                           | 333.3                    | 0.0526 |
| Fukuoka    | 40       | 1034.8                   | 8.5                           | 322.7                    | 0.0526 |
| Nagasaki   | 42       | 1126.0                   | 6.8                           | 299.1                    | 0.0523 |
| Niigata    | 15       | 184.2                    | 77.2                          | 279.7                    | 0.0522 |
| Nagano     | 20       | 302.8                    | 36.7                          | 263.9                    | 0.0520 |
| Kumamoto   | 43       | 1070.2                   | 3.1                           | 209.1                    | 0.0516 |
| Toyama     | 16       | 346.3                    | 13.4                          | 116.0                    | 0.0509 |
| Okinawa    | 47       | 1727.5                   | 0.8                           | 63.5                     | 0.0505 |

* According to n=2160 locations with Cs-137 Bq < 2.0E+6 in the file of [45];

https://www.unscear.org/docs/publications/2013/UNSCEAR_2013_Annex-A_Attach_C-2.xls.

**Table 3.** Distances of the centers of the Japanese prefectures’ area polygons from the FDNPP, Cs-137 deposition in the Japanese prefectures after the Fukushima nuclear power plant accidents as of March 2011 according to [44], rescaled Cs-137 deposition according
to [44-46], and dose-rate [µSv/h] derived from the rescaled deposition.

Dose-rate (µSv/h) derived from Cs-137 deposition

The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) published Cs-137 deposition and corresponding dose-rate readings at 2180 locations in the Fukushima prefecture or close to the borders of the Fukushima prefecture. These data were provided by the Government of Japan as described in the report titled ‘Summarized version of the results of the research on distribution of radioactive substances discharged by the accident at TEPCO's Fukushima Daiichi NPP’. The Japan Atomic Energy Authority (JAEA) conducted the survey with cooperation of universities and research institutes. The Ministry of Education, Culture, Sports, Science, and Technology in Japan (MEXT) was responsible for the measurements and their validity. UNSCEAR reviewed and published the dataset: https://www.unscear.org/docs/publications/2013/UNSCEAR_2013_Annex-A_Attach_C-2.xls [45]. The single dose-rate readings range from 0.040µSv/h to 54.800 µSv/h, with mean 1.259 µSv/h and median 0.40µSv/h. The single C-137 measurements range from 590 Bq/m² to 15,450,928 Bq/m², with mean 153,957 Bq/m² and median 2,180 Bq/m². A 2nd degree regression of the dose-rate on the Cs-137 deposition allows the translation of fallout to dose-rate. The functional details of this association are presented in Fig. 3 and the resulting dose-rates are listed in Table 3.

Statistical methods

A powerful method to assess data that contains spatial as well as temporal information is spatiotemporal (logistic) regression [47–52]. The basic idea is to adjust a regression model for region-specific trend functions and to allow for local or global level-shifts at certain points in time, or, preferably, to allow for the heights of local drops or jumps to be
proportional to the contamination level of the regional strata. The advantage of this spatiotemporal method is optimization of adjustment and minimization of confounding by considering partial trends of regional units. Values of the outcome variable (here LBWp) in those partial trends are modeled and compared within the same regional stratum, as the target variable describing the interesting characteristic (LBW) varies from year to year. Information on several regional units is combined in a global spatiotemporal model, giving rise to tests of local or global change-points in time as well as spatial trends in the outcome variable with regionally determined contamination or exposure. In the present study, we considered the 47 prefectures of Japan with their documented individual annual LBW proportions (1995 to 2018), their original [44] and rescaled Cs-137 depositions, and the associated dose-rates compiled in Table 3. We tested whether possible changes of LBWp from 2012 onward were dependent on Cs-137 fallout at the prefecture level. We further adjusted the spatiotemporal logistic regression model for the annual population size of the prefectures (1995 to 2015), the number of physicians per 1000 population, as well as for the counts of the dead, the missing, and the evacuees due to the earthquake and the tsunami as surrogate measures for the available prefecture-specific medical infrastructure and for the stress associated with this triple catastrophe and its aftermath, see Table 2. For data processing, statistical analyses, and results display, we used Microsoft Excel 2016 (Office 365), R 3.5.1 (Version 2017-10-04), Wolfram MATHEMATICA 11.3, and mostly SAS/STAT software 9.4 (SAS Institute Inc: SAS/STAT User’s Guide, Version 9.4, Cary NC: SAS Institute Inc, © 2002–2012).

Results

Figure 4A shows the annual marginal LBW distribution for all of Japan 1995 to 2018, excluding the births to Japanese parents in foreign countries (number of births abroad: 3774, LBWp = 0.052). See the columns ‘Total’ in Table 1 for the corresponding absolute
counts and the LBW proportions (LBWp). As a first step, we fit to this overall LBWp a smooth 4th degree polynomial allowing for a change-point in 2012 after the Fukushima nuclear power plant accidents. This approach discloses a significant jump in 2012 with a jump odds ratio (OR) 1.020, 95%-CI (1.003, 1.037), p-value 0.0225, see Fig. 4A.

Considering the possibility that the jump height in 2012 may be associated with the Cs-137 fallout in the prefectures, we analyze and depict in a second step the behavior of LBWp in the 3 strata of prefectures according to Table 1: in the 37 least contaminated prefectures, in the 5 moderately contaminated prefectures (Yamagata, Saitama, Tokyo, Kanagawa, Chiba), and in the 5 most contaminated prefectures (Fukushima, Miyagi, Ibaraki, Tochigi, Iwate). Figures 4B-4D display the result: the higher the fallout in the prefectures, the higher the jumps in LBWp from 2012 to 2018.

Table 2 and Fig. 5 generalize and visualize the effect seen in Fig. 4 by listing and plotting the prefecture-specific level-shifts in 2012 in the LBWp trends against the average dose-rate in the prefectures. The combination of the 37 least contaminated prefectures in one group in Fig. 5 avoids a too scattered picture for those only fractionally impacted regions. In Fig. 5, a variance weighted straight line regression of the individual jump odds ratios against the dose-rates discloses a significant linear relationship ($R^2 = 0.82$) with slope 0.11 per µSv/h and p-value < 0.0001.

A more direct approach is logistic regression of LBWp on the additional dose-rate after Fukushima adjusted for prefecture-specific spatiotemporal base-line trends [52]. This yields an OR per µSv/h of 1.098 (1.058, 1.139), p-value < 0.0001. By additionally adjusting the logistic regression for the counts of the earthquake related deaths, the dead and the missing after earthquake and tsunami, and the counts of evacuees within and to the prefectures as surrogate measures for specific disaster-related stress from 2011 onward (see Table 2), as well as additionally taking into account the prefecture-specific population
size and physician density per 1000 population as surrogate measures of general stress and available medical infrastructure, we obtain a somewhat larger, however less precise adjusted OR per µSv/h 1.109 (1.032, 1.191), p-value = 0.0046. The decreased precision resulting from this additional adjustment may be explained by variance inflation in the spatiotemporal logistic regression model due to the correlated surrogate confounder measures. In summary, the increase of the background dose-rate by 1 µSv/h elevates the prevalence odds of low birth weight babies by approximately 10%. Note, 1 µSv/h translates to an annual dose of 8.8 mSv/a. Importantly, without the suggested rescaling of the Yasunari et al. exposure data, the dose-rate specific effect would be 50% in place of 10%, and this would likely be an overestimation of the radiation effect due to an obvious underestimation of the overall Cs-137 deposition across Japan by Yasunari et al. [44].

To more directly assess and display the relative impacts of the earthquake and the tsunami versus the effects of the Cs-137 deposition and the associated dose-rate on LBW, we compared the three contaminated prefectures Fukushima, Iwate, and Miyagi, where the dead and missing persons due to earthquake and tsunami were numerous (n = 18,359), to the somewhat weaker contaminated Ibaraki, Tochigi, and Yamagata where only relatively few immediate deaths occurred and few persons were missing (n = 31), see Table 2. Figures 6A and 6B show that for the less versus strongly earthquake and tsunami impacted groups of prefectures, the LBWp jump heights are similar with largely overlapping 95%-CIs and with similar p-values. Therefore, the long-term increasing LBWp is essentially independent of the direct or protracted impact of earthquake and tsunami.

Discussion

This study strengthens the evidence provided by previous investigations [19, 25-30] that elevated exposure to medical or environmental ionizing radiation increases the prevalence of low birth weight (LBW) children. The proportion of low birth weight babies in Japan
(LBW < 2500 g) was increasing continuously from 1995 to a peak value in 2006, see Fig. 4A. Control of maternal weight gain in reproductive-age women in the general Japanese population appeared to be a major factor involved in the increase in LBW babies before 2006 [4]. Since 2006, the conventional practice of ‘suppressing weight gain during pregnancy to within 10 kg’ has been changed to not reducing the weight gain too much. This may be the reason why most of the prefectures have stopped increasing LBW since peaking around 2006. The revision may spread rapidly in prefectures with large cities and high physician density, and, therefore, the degree of spread may vary between the prefectures. This situation suggests the adjustment of the spatiotemporal LBWp logistic regression models not only for its estimable and known spatiotemporal base-line trend parameters and possible determinants, such as Cs-137 deposition and earthquake-related stress measures, but also for the annual population size and the physician density of the prefectures. In Table 2 we compiled these potential ecological confounders. However, the adjustment for the additional confounders (population counts, physician density, and the triple-disaster-related stress indicators from 2012 onward) does not change our effect estimate of approximately 10% per 1 μSv/h. The reason for this may be that all major prefecture-specific information is already captured by the prefecture-specific spatiotemporal base-line trends accounted for in the adopted spatiotemporal regression approach [52].

Our investigation disclosed a positive association between the Cs-137 deposition across Japan after Fukushima with the prevalence of low birth weight (< 2500 g). Therefore, previously reported epidemiological health detriment after Fukushima [31–37, 53] can be generalized and corroborated. Nevertheless, the question whether ionizing radiation exposure of future parents or peri-conceptional and embryonic radiation exposure impair fetal and post-natal development remains a controversial issue. There are articles in favor
of and against this hypothesis, e.g., [54, 55]. One problem with statistically negative studies in the clinical setting is sample size - typically in the range of only a few thousand [55] or below. Small sample sizes generally entail low statistical power implying large type-2 error probabilities. It may be rather improbable to detect relevant changes in low birth weight proportions, say in the order of 10%, with population sizes ranging only in the thousands. For example, a two-sided one-sample binominal test for testing a hypothetically increased LBWp of 0.11 against a typical null-LBWp of 0.10 (i.e. 10% increase) requires a sample size of 7,248 to achieve a statistical power of at least 80%. For more realistic two-sample scenarios, additional independent LBW-determinants, and higher biological variability, the required sample sizes for obtaining meaningful results would be even larger. Therefore, it is of no surprise that no unequivocal evidence has been obtained yet. Under the headline “Radiation-induced mutation rates in man”, UNSCEAR [13] emphasized already in the year 1958 “All the results obtained are subject to an inevitable sampling error which necessitates the collection of a very large amount of data. A number of quantitative characters, such as birth weight, size and various anthropometric measurements, as well as statistical data, such as neo-natal mortality, have been suggested and examined. Unfortunately, the precise genetic component in these variables is not known; on the contrary, they are known to be dependent upon factors which are economic (standard of living), demographic (age of parents, order of birth, etc.) and sociological (medical care).” The sample size issue may be resolved when instead of at most thousands of births in clinical settings many millions of births in ecological studies can be considered: After the nuclear accidents of Chernobyl and Fukushima, the populations of whole countries have been exposed to significant additional ionizing radiation [51, 56-58]. Moreover, in a large-scale ecological design, as the one presented here, the socio-demographic and environmental determinants of the low birth weight
prevalence can be considered similar in and comparable between the regional units (prefectures). The differences within and between the regional trends from 2012 onward can be assessed by spatiotemporal logistic regression adjusted for appropriately chosen base-line trend parameters and further LBW determinants and ecological confounders [52].

Conclusion

This study shows increased low birth weight prevalence across Japan related to the prefecture-specific dose-rate derived from Cs-137 deposition after Fukushima. One (1) µSv/h (equivalent to 8.8 mSv/a) increases the odds of observing low birth weight events by 10% in the order of magnitude. Therefore, previous investigations suggesting compromised gestational development and impaired pregnancy outcome under elevated ionizing radiation levels have been corroborated by the present study. These findings, in the overall view, call for intensifying bio-physical research in exposure mechanisms and exposure pathways of natural or artificial ionizing radiation. Biological, epidemiological, and medical research should aim at clarifying the genetic and carcinogenic consequences of enhanced radiation in the environment. Radiation-induced genetic effects may occur without immediately obvious link to spectacular incidents or accidents [58, 59]. Therefore, the legislator, the nuclear industry, and the nuclear and radio-pharmaceutical medicine must impose and exert even greater care when processing, employing, and disposing radioactive materials.

Abbreviations

95%-CI or ( , , ) 95%-confidence interval
µSv/h Micro-Sieverts per hour
Cs-137 Cesium-137
Declarations

Ethical Approval and Consent to participate

Not applicable. Ethics approval and consent to participate are not required and not necessary, since only publicly available data and previously published information is being used.

Consent for publication

Not applicable. Only anonymous data is being used.

Availability of supporting data

The employed data has exclusively been published previously and/or it is contained in the
Tables and in the Figures included in this paper.

**Competing interests**

The authors declare that they have no conflicts of interest.

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**Authors' contributions**

KH conceived of the study, developed the study design, organized the data, and provided an initial manuscript. HS elaborated the statistical methodology, processed and analyzed the data, designed and produced the figures, gathered additional literature. Both authors edited and created the final paper.

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Figures
Figure 1

Deposition of Cs-137 in the 47 Japanese prefectures according to Yasunari et al. [44] by the prefectures’ distances from the Fukushima Daichi Nuclear Power Plant (FDNPP); gray circles: original Yasunari et al. data; black dots: deposition for Fukushima corrected and remaining depositions rescaled to a decay of r-2 with distance r, see Table 3.
Geographic region value plot of the decadic logarithm for the rescaled Cs-137 deposition in 47 Japanese prefectures after the Fukushima nuclear power plant accidents as of March 2011 [44], see Table 3; indication of the positions of the earthquake epi-center, the FDNPP, and a 300 km geo-circle around FDNPP; for the prefecture codes see Table 2 or Table 3.
Association of the dose-rate [µSv/h] at 1 m height with the Cs-137 deposition [kBq/m²] in and near the Fukushima prefecture for 2180 positive deposition measurements and 2175 positive dose-rate readings; see https://www.unscear.org/docs/publications/2013/ UNSCEAR_2013_Annex-A_Attach_C-2.xls [45] and Figure 5A in [31].
Figure 4

Low birth weight (LBW) proportion in Japan 1995 to 2018; 4th degree polynomial logistic regression trends allowing for jumps from 2012 onward; A: Japan; B: Japan excluding 10 exposed prefectures; C: 5 moderately exposed prefectures; D: 5 highly exposed prefectures.
Odds ratios for the jumps in the LBWp trends from 2012 onward by the dose-rate derived from rescaled prefecture-specific Cs-137 deposition in the Japanese prefectures from March 20th to April 19th 2011; restricted linear regression yields trend p-value < 0.0001; the left data point summarizes and represents 37 slightly radiologically impacted prefectures, see Table 1.
Low birth weight (LBW) proportion and parsimonious constant trends allowing for jumps in 2012 in 6 Japanese Fukushima exposed prefectures (2005 to 2018) stratified by tsunami impact; A: low tsunami impact in Ibaraki, Tochigi, and Yamagata; B: high tsunami impact in Fukushima, Iwate, and Miyagi.