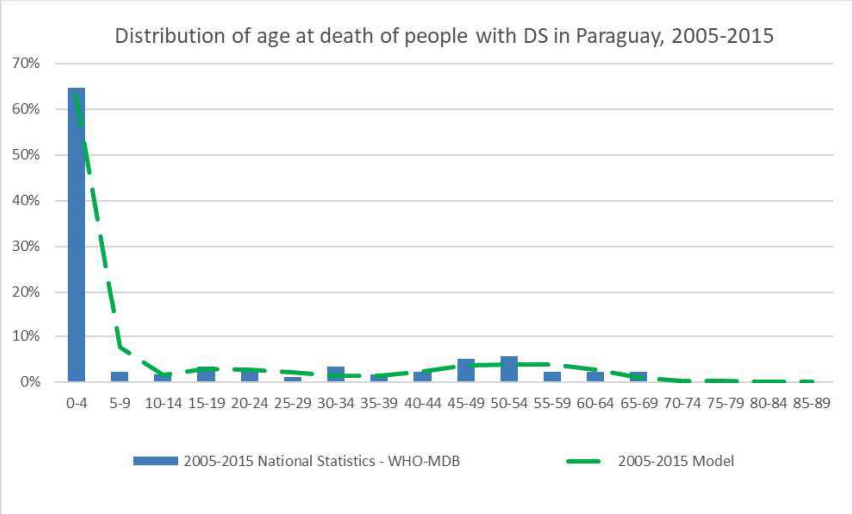
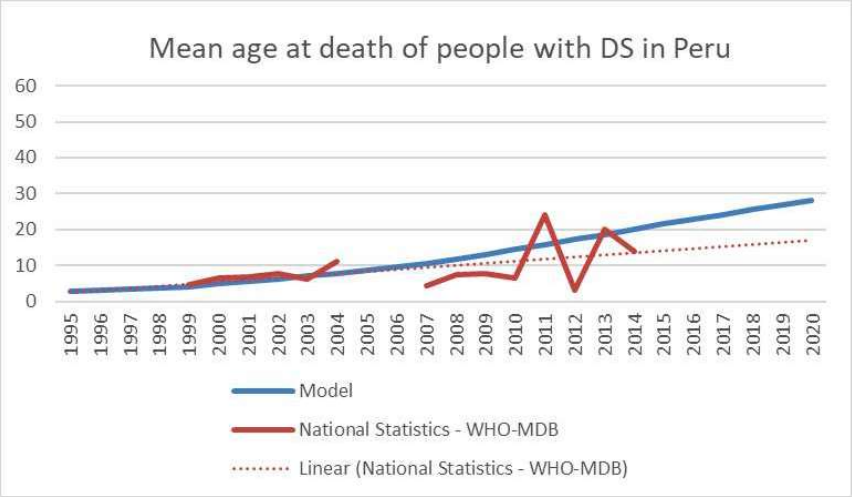
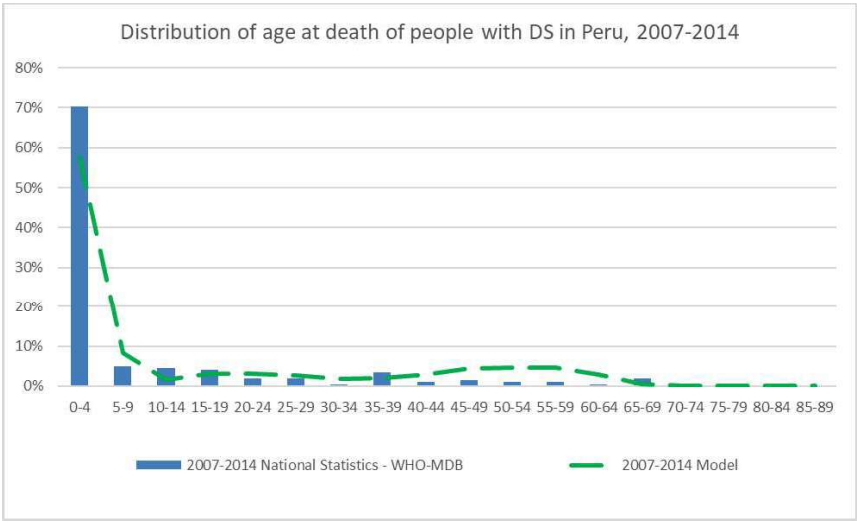


Peru

The WHO Mortality Database has data available for 1999–2004 and 2007–2014, with, on average, 31 deaths reported of people with DS as primary cause of death per year. The model predicts on average 499 annual deaths of people with DS in this period, so only 6% is covered in the registration. The mean age at death and the distribution of deaths by age group (for 2005–2015) are reasonably similar between model and data. Excluding deaths before 1 year of age does not improve the fit.



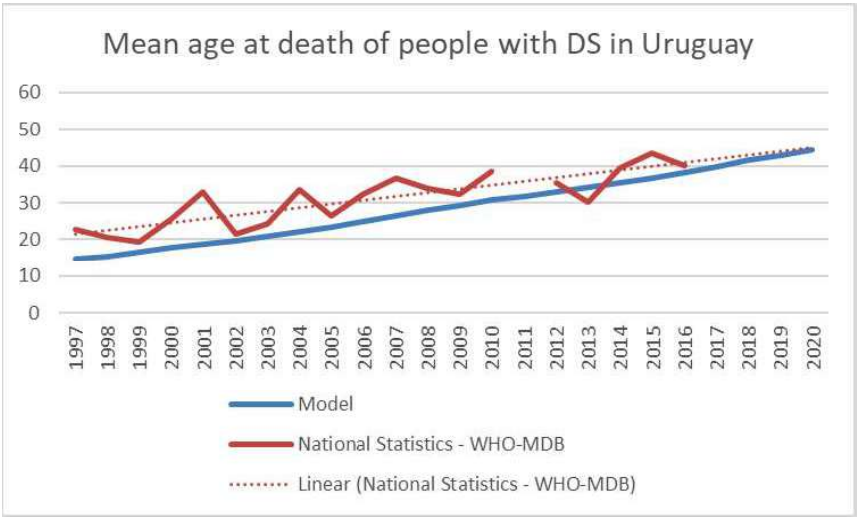


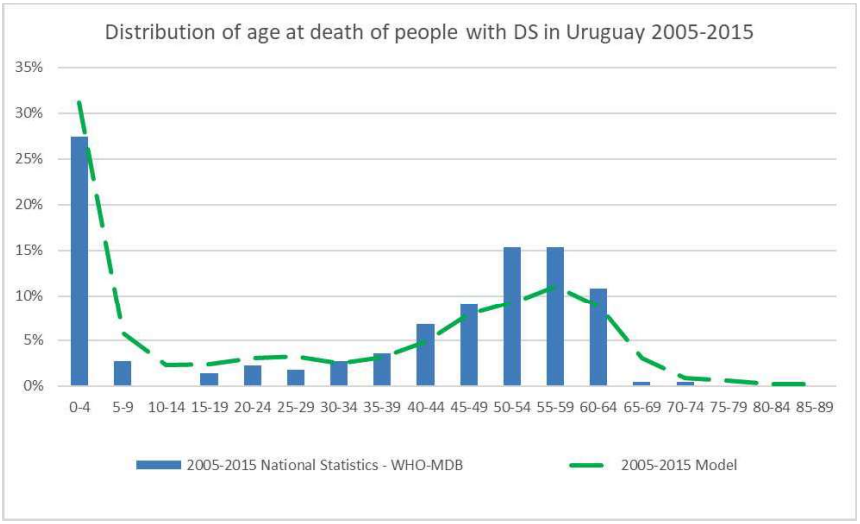
Suriname

Data for only 1996, 2000, 2003, 2007, 2010–2011, and 2013–2014. And on average 1 death (of someone with DS as primary cause of death) per year reported. Not enough data to make a comparison.

Uruguay

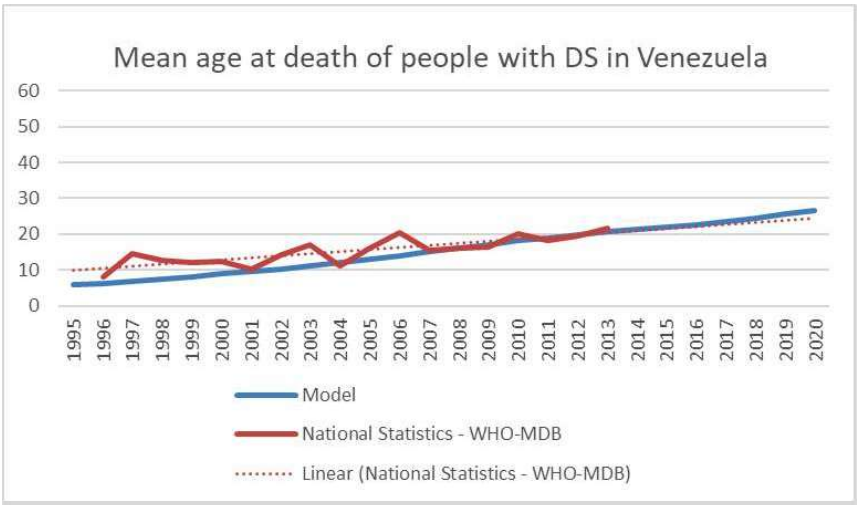
The WHO Mortality Database has data available for 1997–2010 and 2012–2016, with on average 24 deaths reported of people with DS as primary cause of death per year. The model predicts on average 31 annual deaths of people with DS in this period, so 77% is covered in the registration. The mean age at death and the distribution of deaths by age group (for 2005–2015) are reasonably similar between model and data. However, the data show higher percentages in the deaths of people with DS in the age range 50–65 years of age in 2005–2015 (years of birth: 1940–1965). It might be that historical survival of this cohort was more favorable than modeled. Out of the people with DS in 2020, according to our model, only 5% were born before 1965. Therefore, adapting these numbers would have a very limited effect on the estimates of total population prevalence of DS in Uruguay.

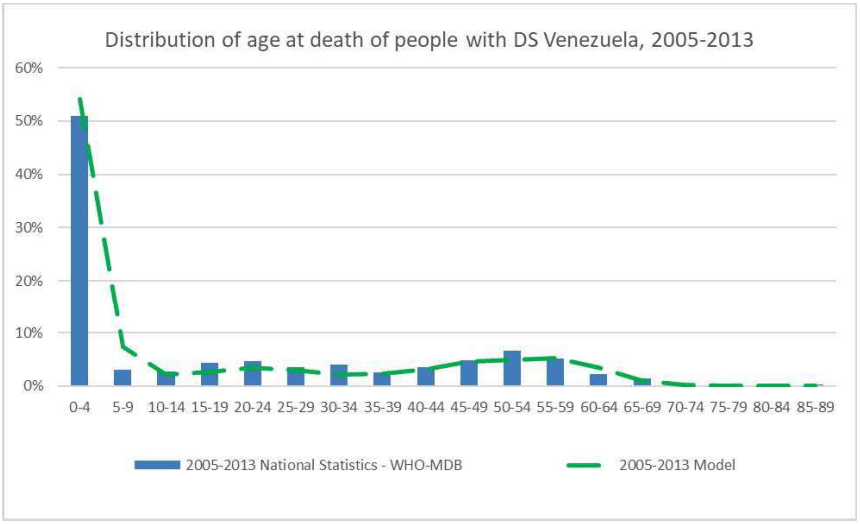




Venezuela

The WHO Mortality Database has data available for 1996–2013, with on average 112 deaths reported of people with DS as primary cause of death per year. The model predicts on average 314 annual deaths of people with DS in this period, so 36% is covered in the registration. The mean age at death and the distribution of deaths by age group (for 2005–2015) are similar between model and data.



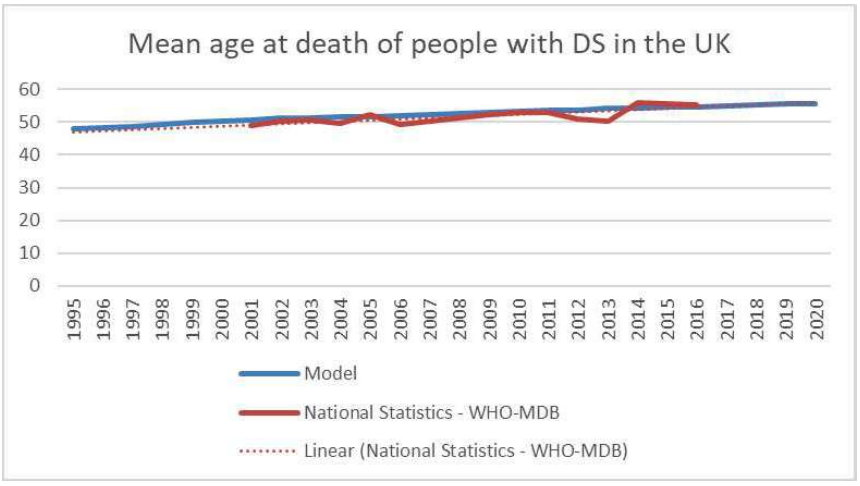


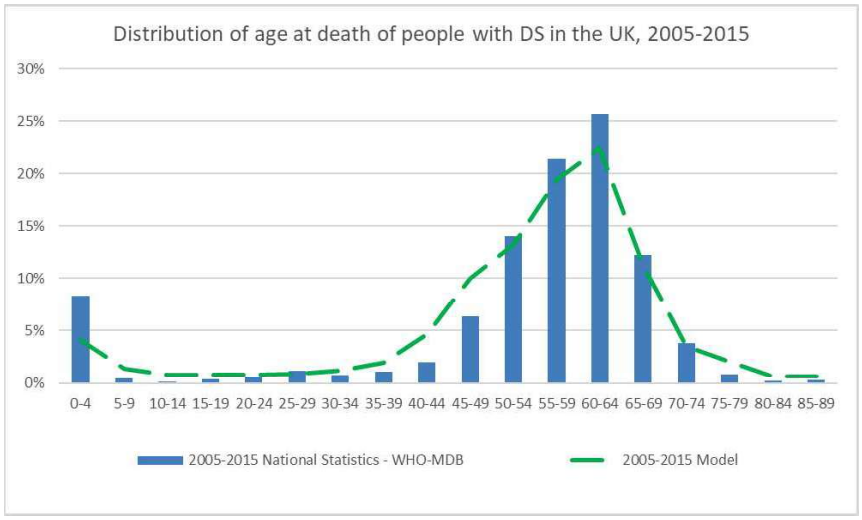
The 4 comparison countries

We have added the 4 comparison countries (which are not in the Caribbean of Latin America) that we had used earlier in comparing the model with counts of people with DS alive. We wanted to double check if the model works out for these countries.

United Kingdom

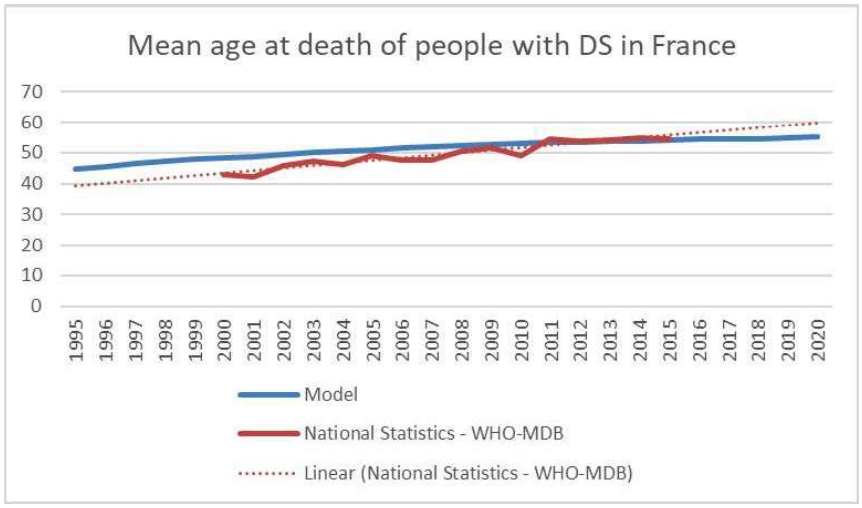
The WHO Mortality Database has data available for 2002–2015, with on average 368 deaths reported of people with DS as primary cause of death per year. The model predicts on average 737 annual deaths of people with DS in this period, so 50% is covered in the registration. The mean age at death and the distribution of deaths by age group (for 2005–2015) are similar between model and data.

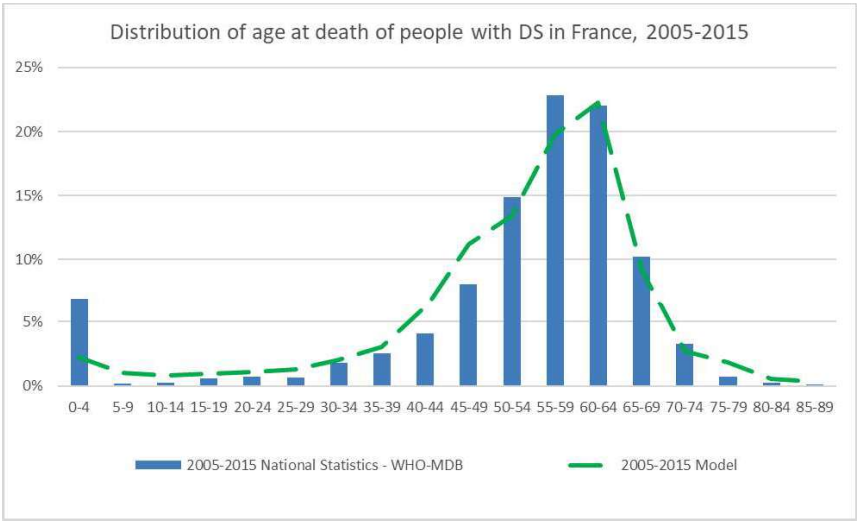




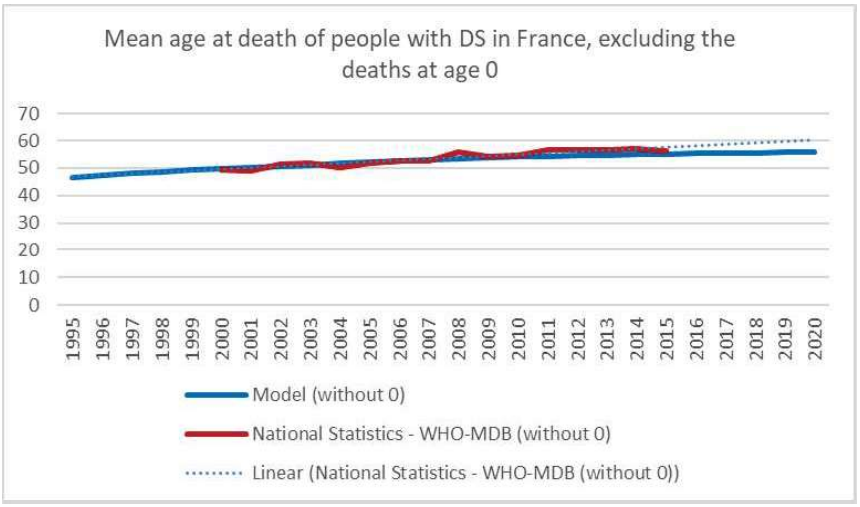
France

The WHO Mortality Database has data available for 2000–2015, with on average 223 deaths reported of people with DS as primary cause of death per year. The model predicts on average 532 annual deaths of people with DS in this period, so 42% is covered in the registration. The mean age at death and the distribution of deaths by age group (for 2005–2015) are reasonably similar between model and data. It is possible that the mortality in very young children with DS is higher than modeled.



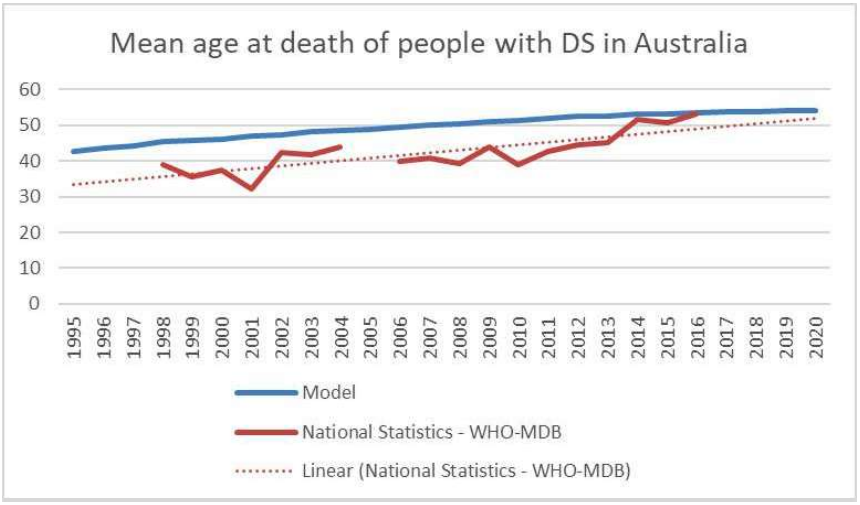


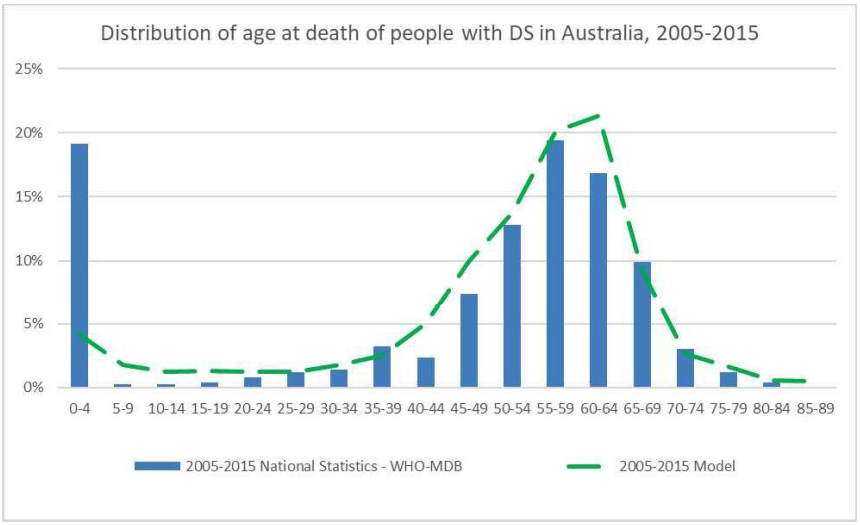
However, perhaps doctors are relatively more often inclined to report DS as the primary cause of death in very young children. For the figure below, we have excluded from both the data and the model the children who died before 1 year of age. It results in a better fit, so this might be the explanation for the small difference between model and data, which appeared in the figures above.



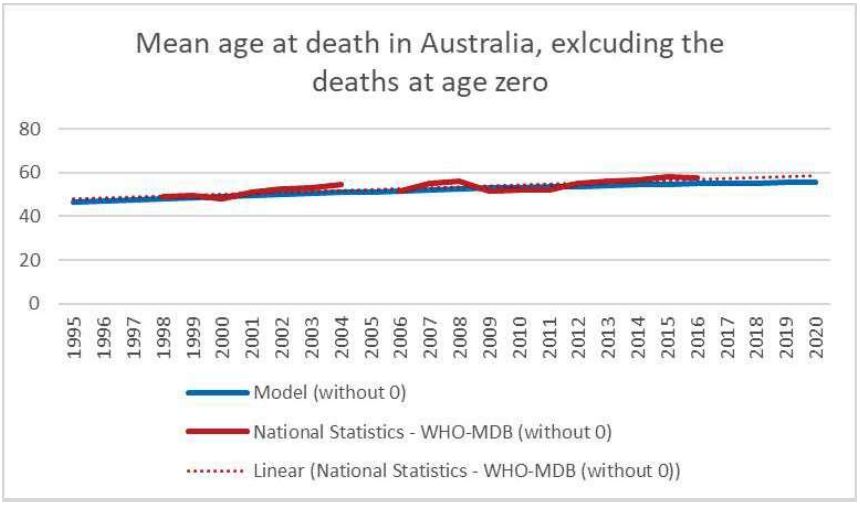
Australia

The WHO Mortality Database has data available for 1998–2004 and 2006–2016, with on average 59 deaths reported of people with DS as primary cause of death per year. The model predicts on average 179 annual deaths of people with DS in this period, so 33% is covered in the registration. The mean age at death and the distribution of deaths by age group (for 2005–2015) differ between model and data—i.e., there is a higher percentage of very young children with DS in the WHO Mortality Database than the model predicts. Perhaps, the mortality in very young children with DS is estimated too low in the model.



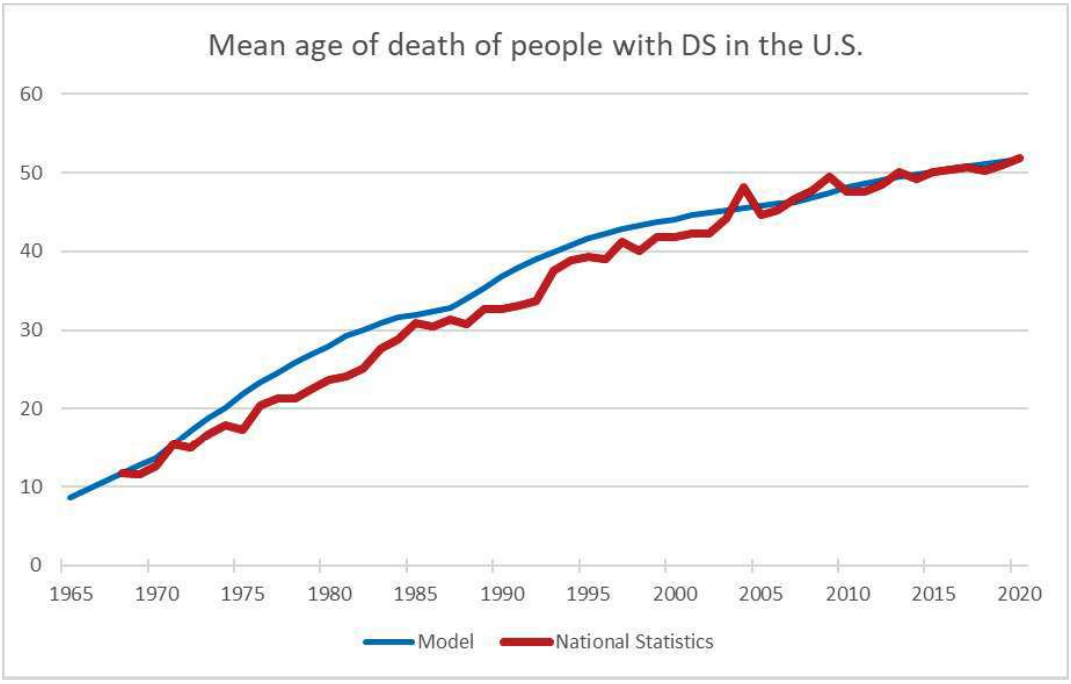


However, we think that another explanation is more plausible. The chance to be reported with DS as primary cause of death is probably higher in infancy than later in life because a doctor would be more inclined to allocate DS as primary cause of death in infants. For the figure below, we have excluded from both the data and the model the children who died before 1 year of age. This results in a good fit.

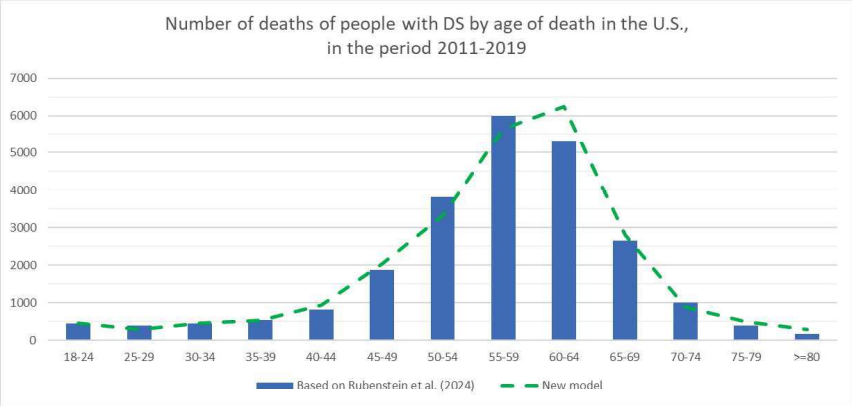


United States (U.S)

Earlier, de Graaf et al. published data on age of death of people with DS up to 2010.[10] We updated these on the basis of death certificate data of the CDC, with DS as primary or additional cause of death.[40] De Graaf et al. smoothed the ages at death by working with 5-year running averages. We have not done that for this study, but we instead used the data by single year. The CDC has counted 80,814 deaths (on average 1,525 per year) with DS from 1968 to 2020; the model predicts 134,162 deaths (on average 2,531 per year).[41] The death certificates cover 60%. In the Figure below, the results regarding the mean age of death are compared with the predictions of our model. Especially in recent decades, the match is good.

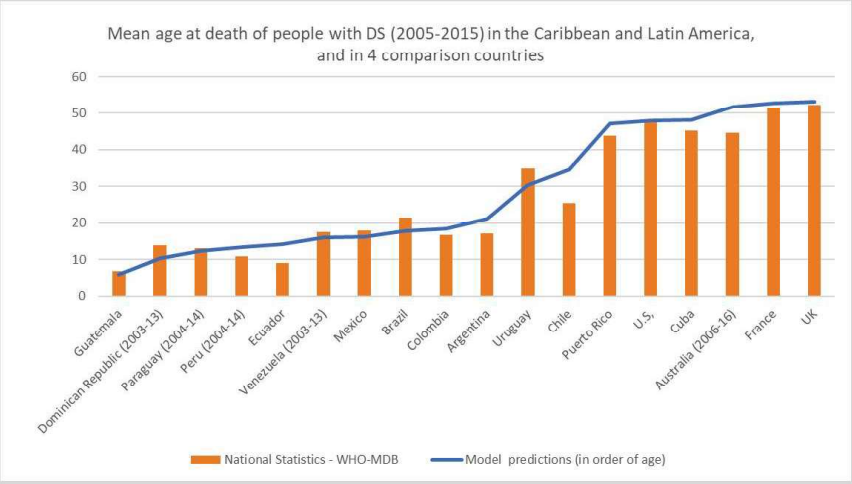


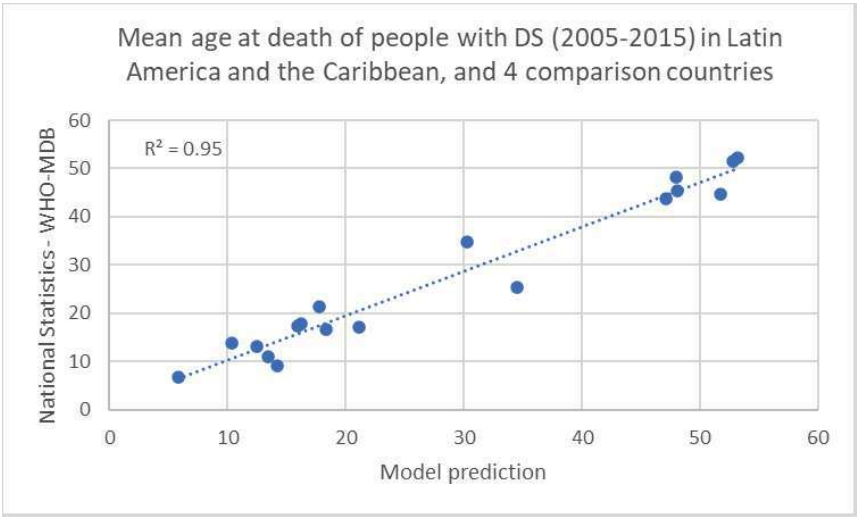
Secondly, we made a comparison with data of deaths of people with DS from the study of Rubenstein et al. (2024).[39] These authors provided us with the data by age of diseased people with DS enrolled in Medicaid and/or Medicare in the period 2011-2019. Our model predicts very similar numbers for the same period.

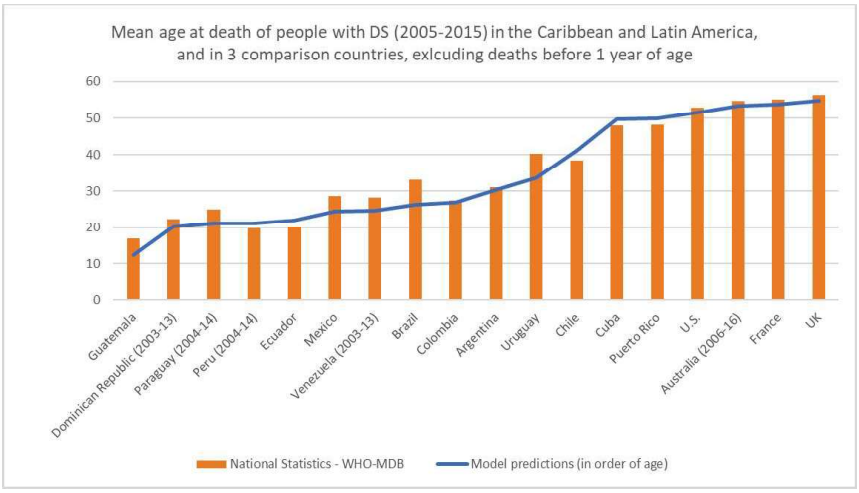


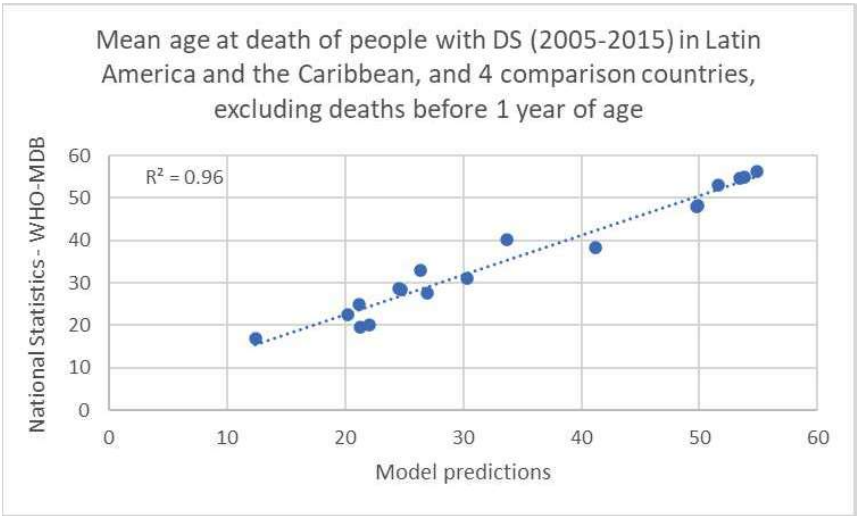
Overview of all countries/territories

In the Figures below, we show for all the countries/territories under consideration how the model and the data fit, comparing the mean age at death in the period 2005–2015 (or a series of years available for the specific country/territory that is as close as possible to 2005–2015). In the first two figures, deaths at any age are included; in the last two figures deaths before 1 year of age are excluded. The last two figures have a better fit, as the fit of countries/territories which had seemingly a too high mortality in the youngest age group improves. The discrepancy between the model and the data for these countries/territories in the first two figures are probably an artifact of doctors being more inclined to allocate DS as the primary cause of death in infants.









We conclude that the new model has a satisfactory fit with the empirical data on age at death of people with DS.

Supplementary Findings 1: Results by country/territory

Countries/territories in the Caribbean

Anguilla

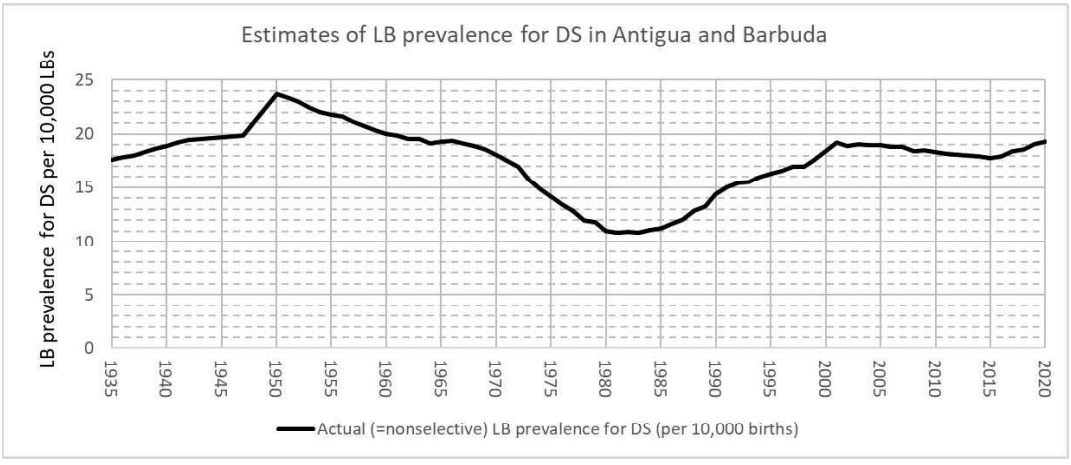
On the basis of maternal ages, LB prevalence of DS would be around 14.6 per 10,000 LBs as of 2020. However, the number of LBs in the general population (between 2016–2020) is on average 153 per year, which implies that only once in every 3 years a child with DS will be born in Anguilla. Based on our model, we expect there to be around 12 individuals (95% CI: 5-19) with DS living in Anguilla, as of 2020 (7.8 per 10,000 inhabitants). We consider more details not useful given the very small numbers and therefore very large uncertainty.

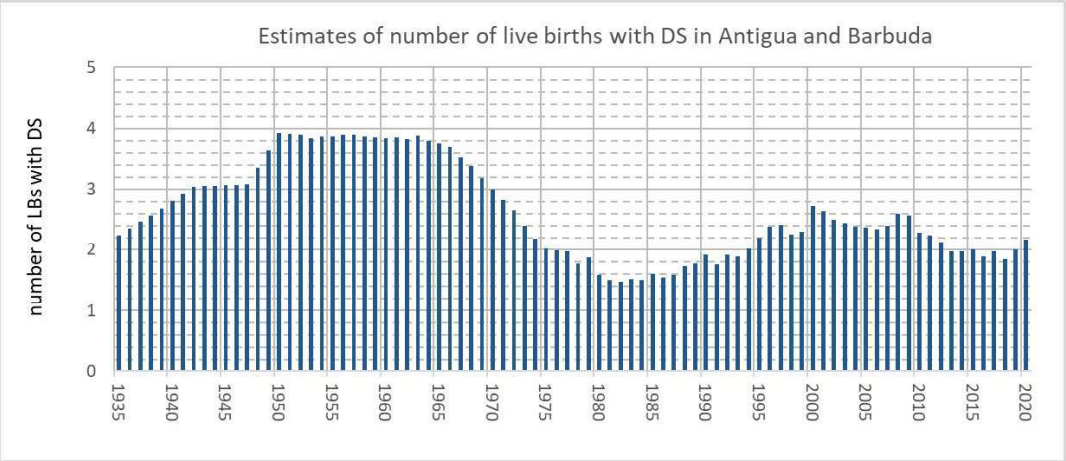
Antigua and Barbuda

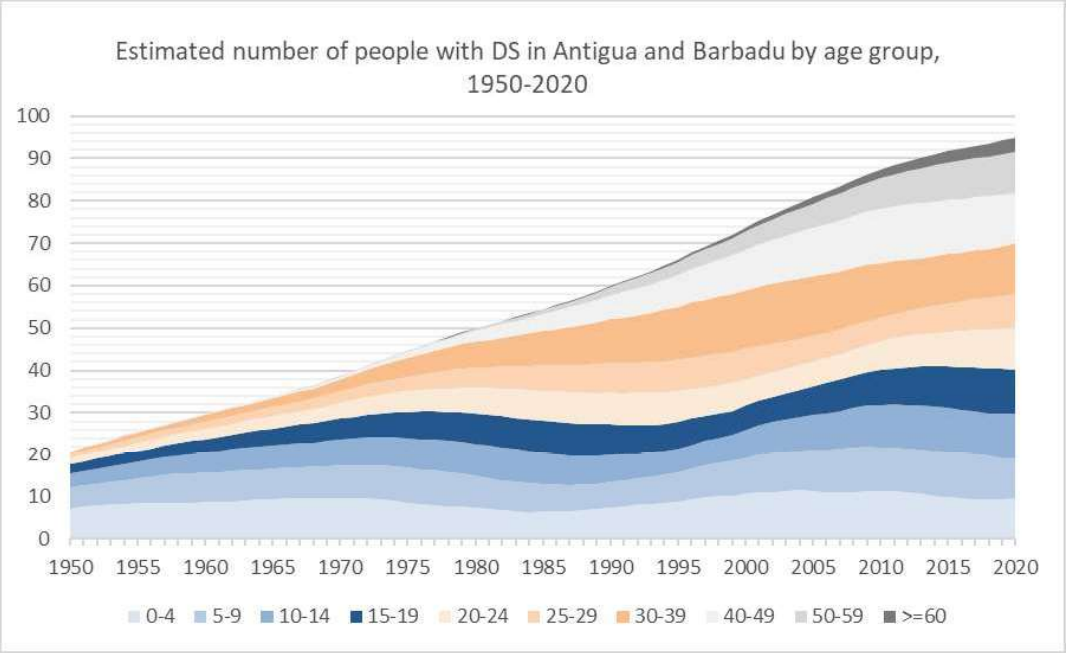
Based on our model, we expect there to be around 95 individuals (95% CI: 76-114) with DS living in Antigua and Barbuda, as of 2020 (10.2 per 10,000 inhabitants). The figures below provide more details and historical information on LBs and population. However, the reader should be aware that the uncertainty is large given the small numbers.

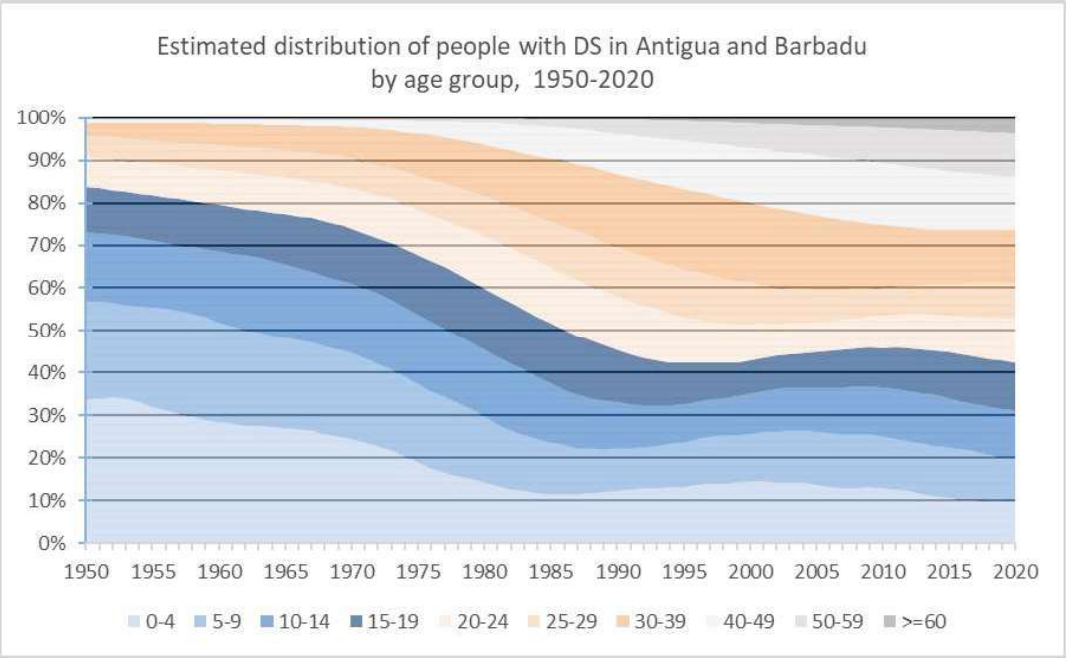
If desired, the 95% CI can be approximated (as the proportion of people with DS in the population is very small) for any given number of people with DS:

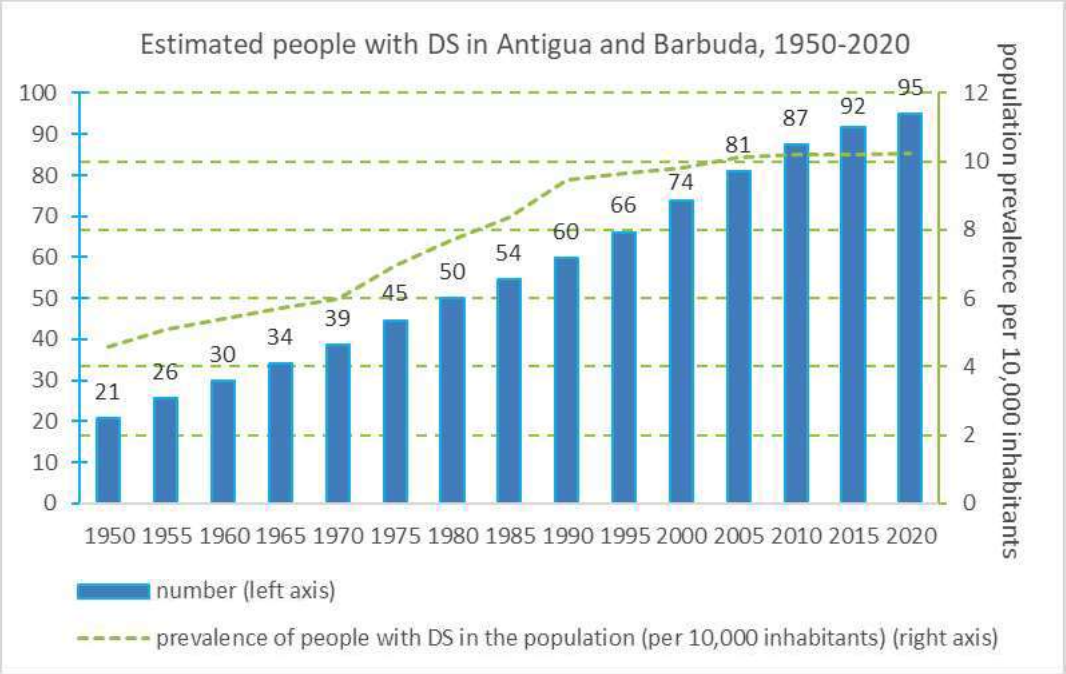
$number\ of\ people\ with\ DS\ \pm\ 1.96\sqrt{number\ of\ people\ with\ DS}$**. For instance, as of 2020, there are 9 people with DS estimated in the age group 0–4 years. The 95% CI is approximated by** $9\ \pm\ 1.96\sqrt{9}$ **= 3–15.**

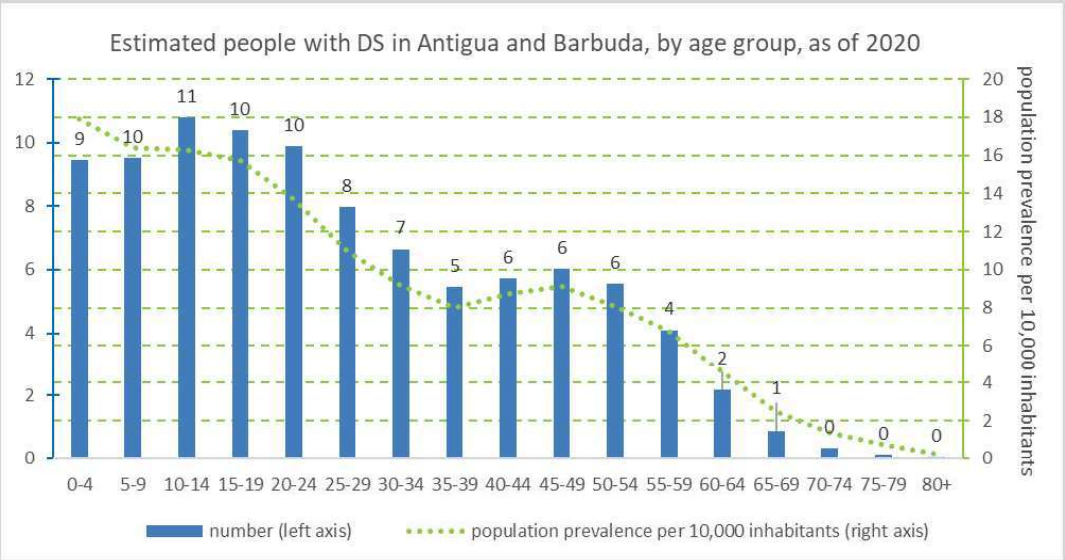



Estimates of number of live births with DS in Antigua and Barbuda
number of LBs with DS
0
1
2
3
4
5
1935
1940
1945
1950
1955
1960
1965
1970
1975
1980
1985
1990
1995
2000
2005
2010
2015
2020


Estimated number of people with DS in Antigua and Barbadu by age group, 1950-2020
100
90
80
70
60
50
40
30
20
10
0
1950
1955
1960
1965
1970
1975
1980
1985
1990
1995
2000
2005
2010
2015
2020
0-4
5-9
10-14
15-19
20-24
25-29
30-39
40-49
50-59
>=60

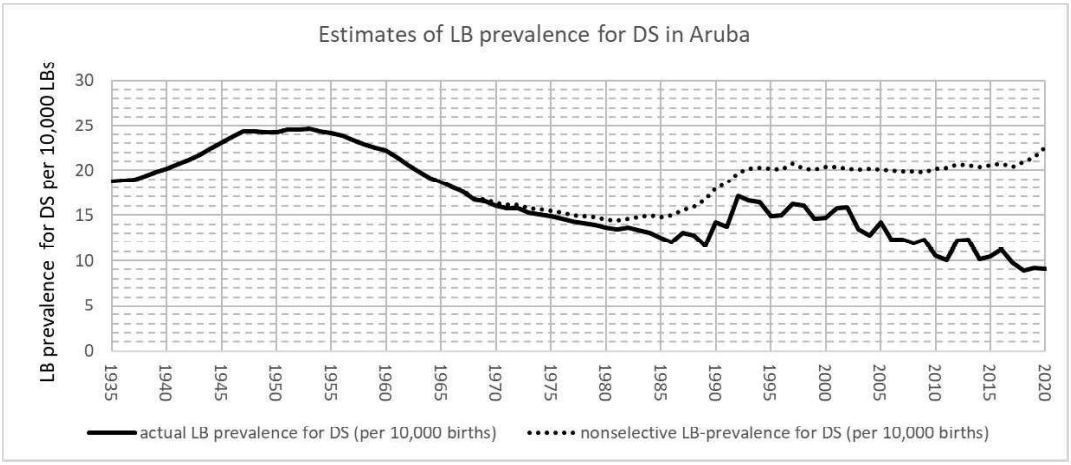

Estimated distribution of people with DS in Antigua and Barbadu
by age group, 1950-2020
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1950 1955 1960 1965 1970 1975 1980 1985 1990 1995 2000 2005 2010 2015 2020
0-4 5-9 10-14 15-19 20-24 25-29 30-39 40-49 50-59 >=60

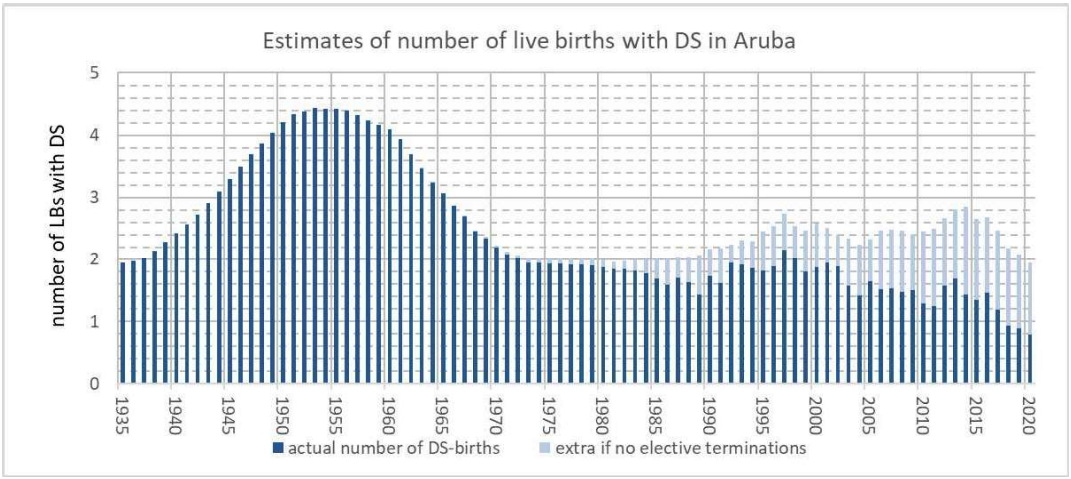

Estimated people with DS in Antigua and Barbuda, 1950-2020
population prevalence per 10,000 inhabitants
100
90
80
70
60
50
40
30
20
10
0
12
10
8
6
4
2
0
21
26
30
34
39
45
50
54
60
66
74
81
87
92
95
1950 1955 1960 1965 1970 1975 1980 1985 1990 1995 2000 2005 2010 2015 2020
number (left axis)
prevalence of people with DS in the population (per 10,000 inhabitants) (right axis)

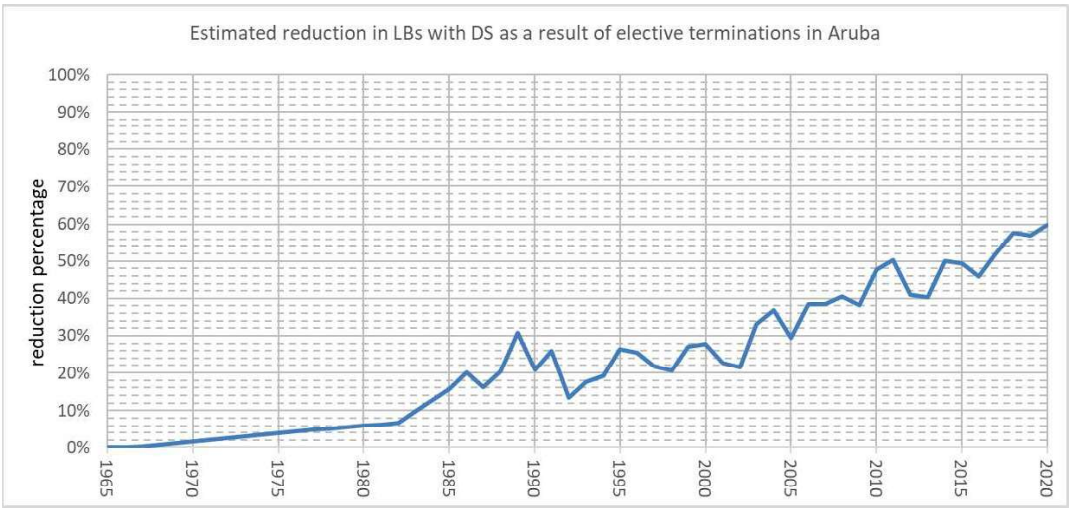

Estimated people with DS in Antigua and Barbuda, by age group, as of 2020
population prevalence per 10,000 inhabitants
0-4
5-9
10-14
15-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
75-79
80+
9
10
11
10
10
8
7
5
6
6
6
4
2
1
0
0
0
number (left axis)
population prevalence per 10,000 inhabitants (right axis)

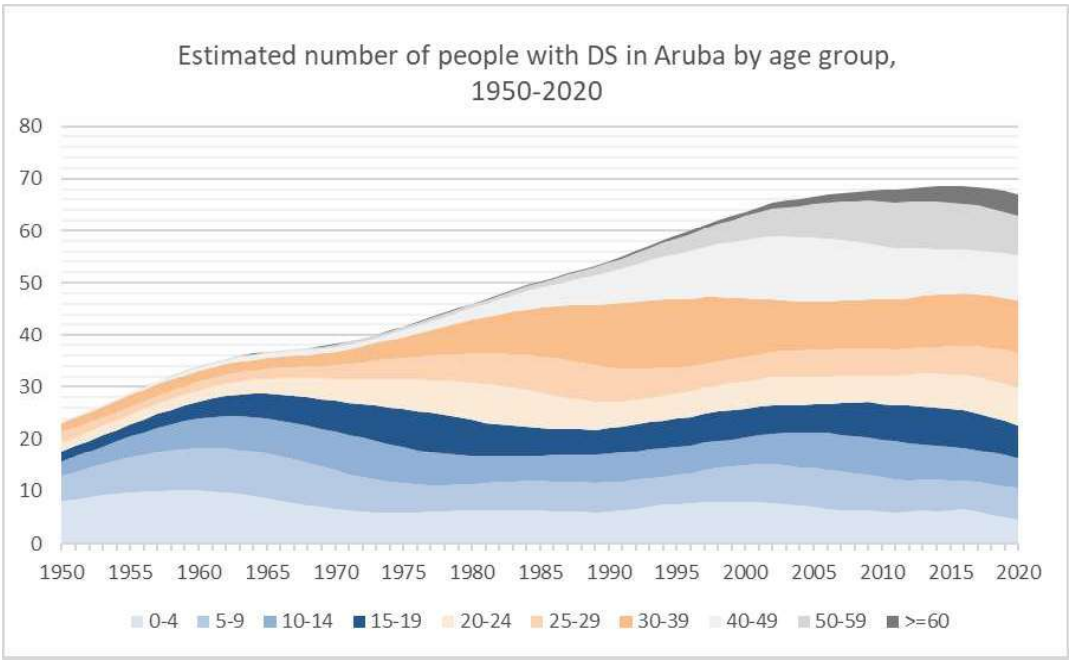
Aruba

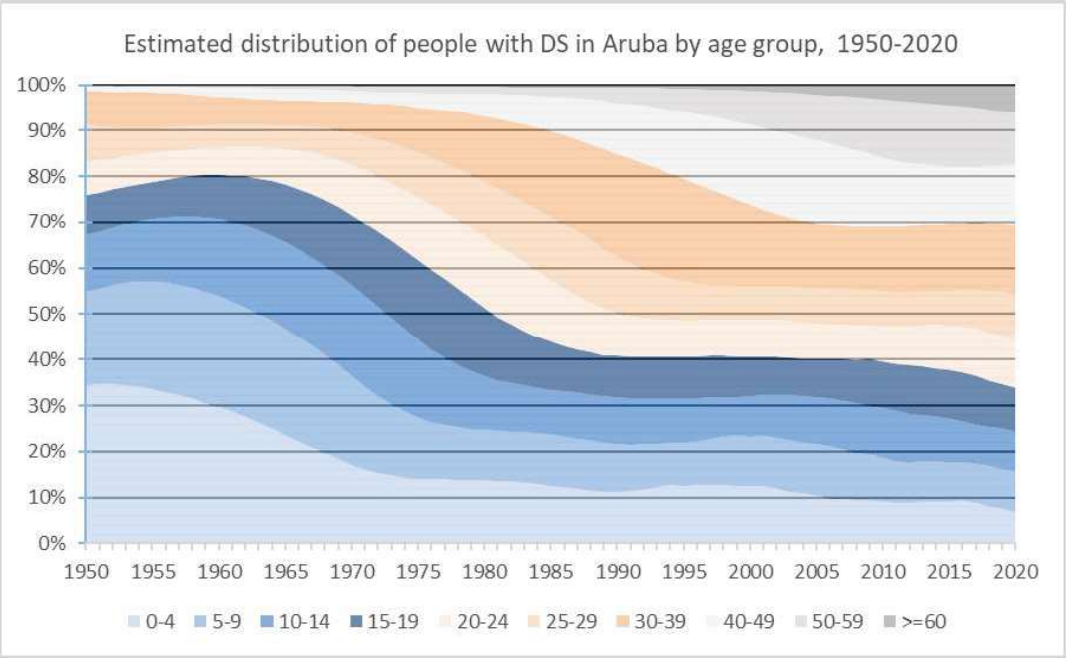
Based on our model, we expect there to be around 67 individuals (95% CI: 51–83) with DS living in Aruba, as of 2020 (6.3 per 10,000 inhabitants). In absence of elective terminations, this would have been 90 (95% CI: 72–109). The figures below provide more details and historical information on LBs and population. However, the reader should be aware that the uncertainty is large given the small numbers.

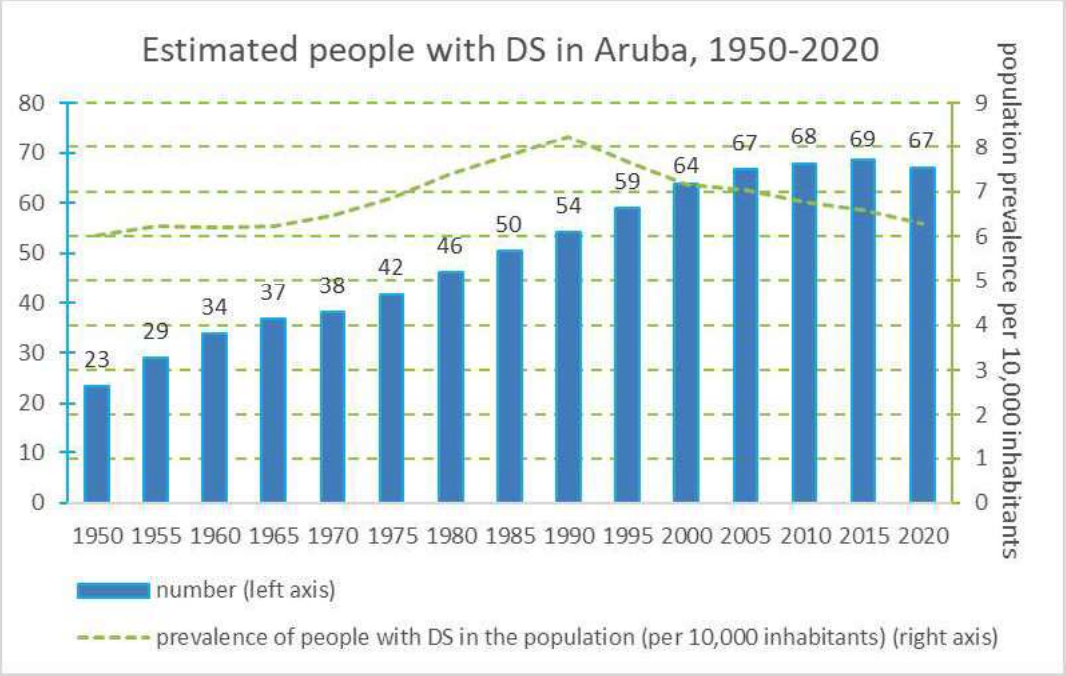


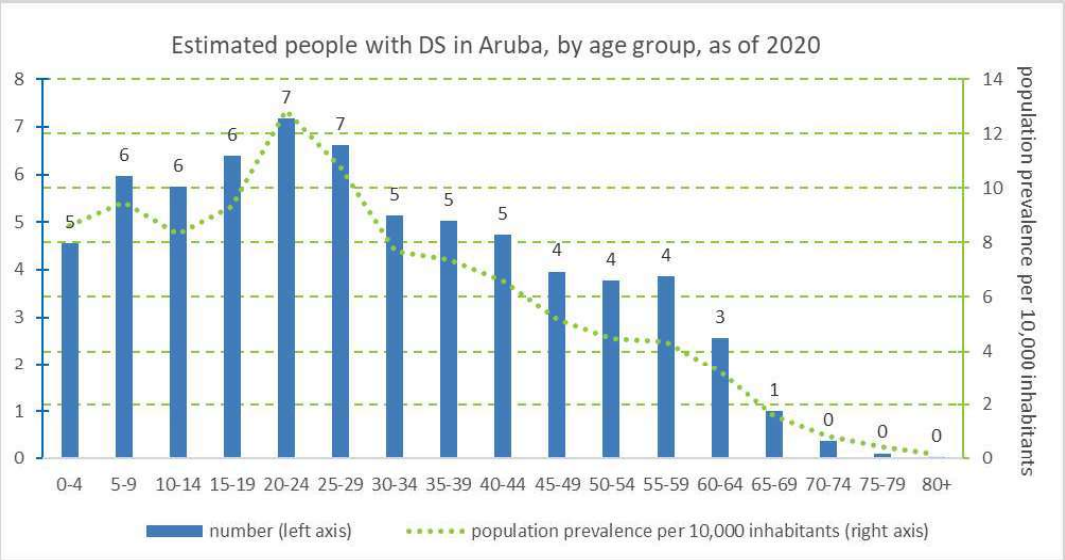



Estimated reduction in LBs with DS as a result of elective terminations in Aruba
reduction percentage
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1965
1970
1975
1980
1985
1990
1995
2000
2005
2010
2015
2020


Estimated number of people with DS in Aruba by age group, 1950-2020
80
70
60
50
40
30
20
10
0
1950
1955
1960
1965
1970
1975
1980
1985
1990
1995
2000
2005
2010
2015
2020
0-4
5-9
10-14
15-19
20-24
25-29
30-39
40-49
50-59
>=60


Estimated distribution of people with DS in Aruba by age group, 1950-2020
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1950 1955 1960 1965 1970 1975 1980 1985 1990 1995 2000 2005 2010 2015 2020
0-4 5-9 10-14 15-19 20-24 25-29 30-39 40-49 50-59 >=60


Estimated people with DS in Aruba, 1950-2020
80
70
60
50
40
30
20
10
0
9
8
7
6
5
4
3
2
1
0
population prevalence per 10,000 inhabitants
23
29
34
37
38
42
46
50
54
59
64
67
68
69
67
1950 1955 1960 1965 1970 1975 1980 1985 1990 1995 2000 2005 2010 2015 2020
number (left axis)
prevalence of people with DS in the population (per 10,000 inhabitants) (right axis)


Estimated people with DS in Aruba, by age group, as of 2020
population prevalence per 10,000 inhabitants
0-4
5-9
10-14
15-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
75-79
80+
5
6
6
6
7
7
5
5
5
4
4
4
3
1
0
0
0
number (left axis)
population prevalence per 10,000 inhabitants (right axis)

Bahamas

Based on our model, we expect there to be around 367 individuals (95% CI: 329–404) with DS living in the Bahamas, as of 2020 (9.0 per 10,000 inhabitants). In absence of elective terminations, this would have been 381 (95% CI: 343–429). The figures below provide more details and historical information on LBs and population. However, the reader should be aware that the uncertainty is large given the small numbers.