Estimation of the number of people with Down syndrome in Latin America and the Caribbean

SUPPLEMENTARY MATERIALS

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Supplementary Methods 1: Number of potential and actual live births (LBs) of children with Down syndrome (DS)

S1A. Estimates of nonselective LBs of children with DS

Estimates from 1950 onwards of the number of live births (LBs) in the general population, by maternal age in single years, is available at the World Population Prospects (WPP) of the United Nations.[1] For each country/territory in Latin America and the Caribbean, we estimated the nonselective LB prevalence of children with Down syndrome (DS)–i.e., the potential LB prevalence that would have occurred without DS-related elective terminations of pregnancies, by applying the model of maternal-age specific chances for a LB of a child with DS that was developed by Morris et al.[2]

For 1936–1950, information on the distribution of maternal ages in the general population is available in the Demographic Yearbooks (DYB) of the United Nations for some of the countries/territories in this region (14 in total) and for some of the years of birth.[3] However, in the early 1950s, for many countries/territories in this region, this source appears to report lower numbers of LBs in general population than estimated by the WPP, likely because birth registrations were incomplete. This appears also to be the case before 1950.

Previously, de Graaf et al. designed a procedure to estimate the number of LBs in the general population, the nonselective number of LBs of children with DS, and the nonselective LB prevalence for DS before 1950. This was based on the female population in 5-year age groupings in 1950 and 1955 and the age-specific fertility in 1960, 1955, and 1950 (data available at WPP), projecting backward in time.[4] We used this procedure to estimate nonselective prevalence for 1915–1950.[4] Before 1915, we assumed that prevalence was similar to our 1915 estimate.

In the table below, for 1936–1950, we compare the model estimates of annual number of LBs of children with DS—and the LB prevalence estimates for DS—with the estimates on the basis of the DYB.[3] For 10 out of the 14 countries/territories with DYB data, the model and the DYB estimates of LBs with DS have a less than 15% difference. For 4 countries/territories the difference in estimated LBs with DS is more than 20%; however, for these 4 countries/territories the difference in DS LB prevalence estimates is 10% or less. This implies that the difference in the estimated number of LBs of children with DS for these countries/territories is explained by a lower estimated number of total LBs in the general population. We assume that this is most likely due to incomplete registration. According to the DYB in only 4 out of the 14 countries/territories the registration of LBs in the general population is considered complete.

Estimates of number of LBs with DS and DS LB prevalence 1936–1950; model versus DYB

Complete registration according to DYB	Country/ territory	Period	Predicted annual number of LBs with DS (model)	Average annual number in DYB	Predicted LB prevalence (model)	LB prevalence on the basis of DYB	Difference in LBs	Difference in prevalence
incomplete	Bolivia	1938–1947	318	319	26.1	33.5	0%	-22%
incomplete	Chile	1936–1950	515	490	23.3	28.4	5%	-18%

incomplete	Colombia	1937–1948; 1950	992	778	21.4	23.6	28%	-9%
incomplete	Dominican Republic	1941–1946; 1948–1950	221	197	20	24.1	12%	-17%
incomplete	El Salvador	1946–1950	176	161	18.7	19.6	9%	-5%
incomplete	Guatemala	1946–1950	308	319	20.9	23.6	-3%	-11%
complete	Jamaica	1946–1950	79	80	18	18.6	-1%	-3%
complete	Mexico	1936–1945	2197	2278	20.8	25.6	-4%	-19%
incomplete	Nicaragua	1936–1945	106	76	19.7	18.4	39%	7%
incomplete	Panama	1943; 1947–1950	60	41	18.1	16.8	46%	8%
incomplete	Peru	1940–1950	814	725	25.5	26	12%	-2%
incomplete	Puerto Rico	1943–1950	145	157	17.3	18.2	-8%	-5%
complete	US Virgin Islands	1936–1950	1.42	1.47	17.8	17.3	-3%	3%
complete	Venezuela	1939–1940; 1944–1950	421	349	18.8	20.9	21%	-10%

We have decided not to use the estimates on the basis of the 1936–1950 DYB data on maternal ages since

- The birth registration data in the DYB appear to be incomplete for most countries/territories;
- We don't know for sure whether the under-reporting is similar for all maternal ages. So even if we would only use the estimates of the birth prevalence (and not the absolute numbers), these might be off;
- The DYB data are unavailable for many of the countries/territories in the region, and if available, often, only for some of the years;
- The advantage of using the model projections instead is that every country/territory has been estimated following the same procedure.

Note: The numbers of LBs of children with DS before 1950 have almost no effect on the estimates of DS population prevalence as of 2020, as there are only few people with DS of 70 years or older.

S1B. Estimates of actual LBs of children with DS

In the majority of countries/territories in Latin America and the Caribbean, terminations of pregnancy are not permitted, unless in circumstances of rape, incest, or a mother's life being in jeopardy. Only in some of the countries/territories, terminations are allowed in cases of a fetal anomaly.[5] We assumed that in countries/territories in which termination is not permitted in cases of a fetal anomaly, there will be no (or only very few) Down syndrome related selective abortions.

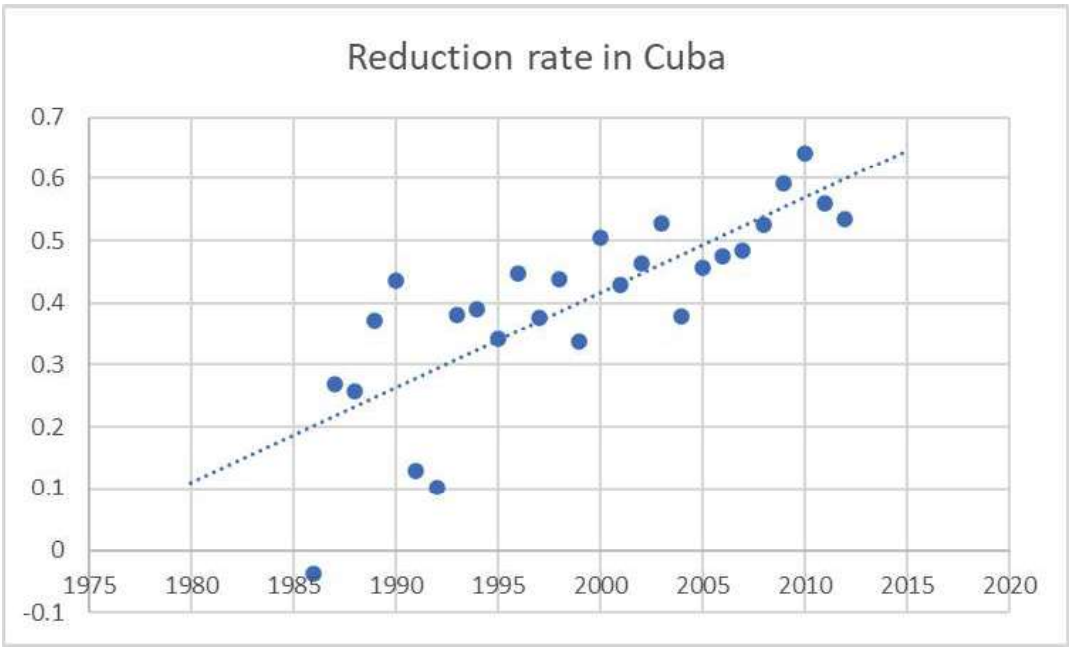
Regarding Latin America and the Caribbean, there are some studies based on birth certificate data, which are not a reliable source for estimating LB prevalence for DS. However, for Argentina and for South America as a whole, there is more reliable birth surveillance information available from the National Network of Congenital Anomalies of Argentina (RENAC) and from the Latin American Collaborative Study of Congenital Malformations (ECLAMC). On the basis of RENAC data, covering around 26% of all births in Argentina, DS LB prevalence was estimated at 17.26 per 10,000 LBs for 2009–2015.[6] This is 10% lower than our model prediction of 19.26 per 10,000. This difference might be the result of illegal selective abortions, or it might be explained by under-reporting in the RENAC data and/or by differences in maternal ages between regions inside Argentina. On the basis of ECLAMC data for Argentina, covering around 9% of all LBs in this country, DS LB prevalence was estimated at 19.6 per 10,000 LBs for 1994–2007.[7] This is 7% higher than our model prediction of 18.4 per 10.000 LBs for the same period. For South America, as of 2012, ECLAMC estimates DS LB prevalence at 17.7 per 10,000 LBs.[8] Our model predicts a similar estimate of 17.9 per 10,000 LBs.

These studies appear to corroborate our assumption that, in these countries, Down syndrome related selective abortions are indeed rare. Thus, in our modeling, we have assumed that, in countries/territories that do not permit terminations for fetal anomaly, the actual DS LB prevalence will be equivalent to the nonselective DS LB prevalence, as estimated on the basis of maternal ages in the general population.

There are 18 countries/territories (out of 50) in the region that allow elective terminations for fetal impairment. Only 4 have a relatively large population (Cuba, Puerto Rico, Panama, Mexico). The other 14 are small or very small.

Cuba

For Cuba, we found information on LB prevalence for DS from 1986–2011 from The International Centre on Birth Defects and for 2012 from Méndez-Rosado (2014).[8,9] We compared these data with our modeled expected rates (on the basis of maternal ages) to estimate reduction percentage by year of birth. The linear regression line in the figure below hits 0% in 1972 and 72% in 2020. For 1986–2012, we have used the actual LB prevalence data; for 1972–1985 and 2013–2020, we have implemented the reduction rates as produced by the regression equation.



Puerto Rico

For Puerto Rico, only prevalence data at birth are available, in which LBs, natural loss, and elective terminations are pooled, which makes it impossible to know the LB rates for DS. As an alternative, as the Puerto Rico population is predominantly Hispanic, we have applied the estimates of reduction for Hispanics in the U.S. from earlier studies, estimates available up to 2010.[10]

For 2011–2018, we constructed the number of DS LBs in Hispanics in the U.S. on the basis of data from the National Birth Defects Prevention Network (NBDPN).[11] For 2019–2020 we combined the data from the National Birth Defects Prevention Network (NBDPN) with data (available from 1989 onwards) from the National Vital Statistics Reports on the number of children who have DS reported on their birth certificate.[12–25] This made it possible to estimate the extent of under-reporting of babies with DS by ethnicity in the birth certificates up to 2018. We have projected the extent of under-reporting on the birth certificate data 2019–2020, thus making it possible to estimate the LB prevalence of DS in Hispanics. Nonselective prevalence could be estimated on the basis of data on maternal ages in Hispanics in the US, available from the Centers for Disease Control and Prevention (CDC).[25]

U.S. Virgin Islands

We have estimated reduction in the U.S. Virgin Islands on the basis of their ethnic composition, applying the U.S. equivalents for each ethnic group, and using the same sources as reported above for Puerto Rico.

Aruba and Bonaire

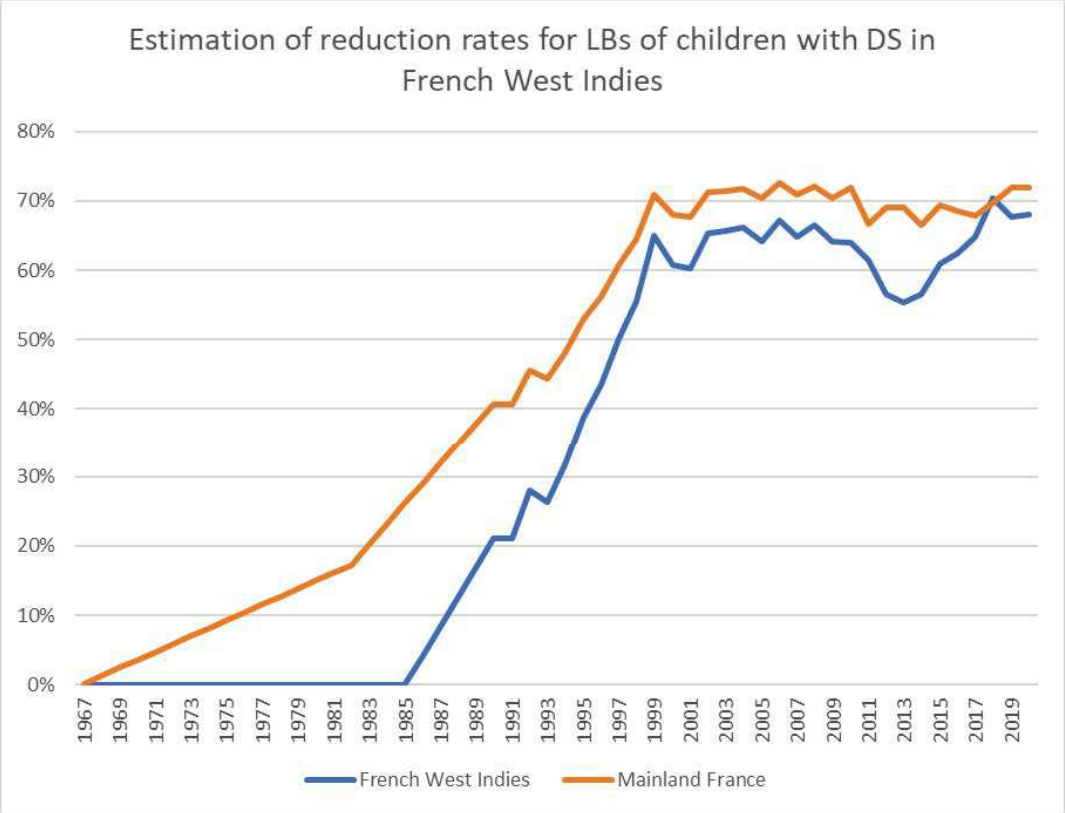
For Aruba, which is officially a Dutch municipality, we applied the reduction rates from 1967 onwards, as these were estimated for the Netherlands.[4,26] For Bonaire, we did this from 2010 onwards, as earlier abortion was illegal.

Falkland Islands

The Falkland Islands are a British overseas area. We applied the reduction rates as these were estimated for the UK.[4]

French West Indies: Guadeloupe, Martinique, Saint Martin, and Saint Barthélemy

These are French overseas territories. For 2009–19, data on LBs with DS were available from Eurocat for French West Indies.[27] We estimated non-selective prevalence on the basis of maternal ages and estimated reduction rates for this period. We plotted these rates against the reduction rates for mainland France in the same period. The reduction rates were slightly lower in the French West Indies. We used the regression equation to predict the French West Indies reduction rates for earlier and later years. In the figure below, the results are presented. For 2009–19 the rates based on Eurocat are presented; for earlier years and for 2020, the results on the basis of the regression.



French Guiana

We applied the reduction rates as constructed for French West Indies to French Guiana. Like in French West Indies, abortion is legal and prenatal screening for DS is offered to all pregnant women.[28] In comparison to mainland France, reduction in French Guiana (like in the French West Indies) is probably lower, as the uptake of prenatal screening is lower. The uptake was 91% in mainland France, versus 65% in French Guiana, as of 2021.[29]

Barbados, the Bahamas, Belize, Guyana, Panama, Saint Vincent and the Grenadines, and Mexico

The Barbados Down Syndrome Association, in an electronic communication with the first author on September 13, 2024, said that selective terminations for DS, though legal, are very rare in their country. As a best guess, we have modeled reduction rates at 5% for 2000–2009 and at 10% for 2010 and onwards.

We have applied the same rates to the Bahamas, Belize, Guyana, and Panama, Saint Vincent and the Grenadines, countries for which we have not been able to find data. For Mexico, we have modeled a lower reduction rate of 3% since 2007, as between 2007–2020 abortion in case of a fetal anomaly was only legal in one region of the country.

Supplementary Methods 2: Modeling survival in DS

S2A. New approach to constructing survival curves for DS

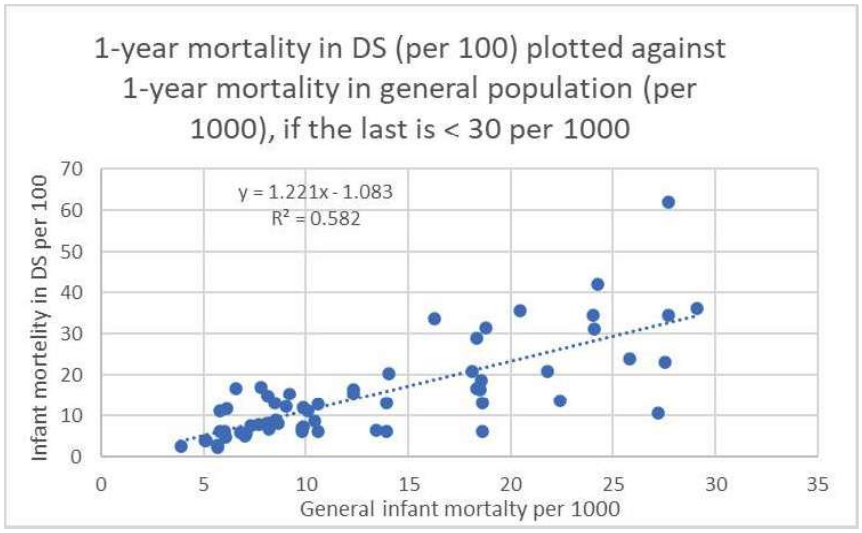
Based on multiple historical studies from developed countries, de Graaf et al. had previously constructed DS-specific survival curves by year of birth.[4,10,30,31] These curves were adapted for different U.S. ethnic groups, based on the relationship between 1-year mortality in these ethnic groups in the general population and the 1-year mortality in children with DS during the period 1983–2003. This relation was projected back in time.[10] The same procedure was followed for different U.S. states and countries in Europe, and for Australia, New Zealand, and Canada.[4,30–32] It was expected that a lower 1-year survival in the general population is indicative of a less well-developed medical care system, which will also negatively affect the survival of children with DS.

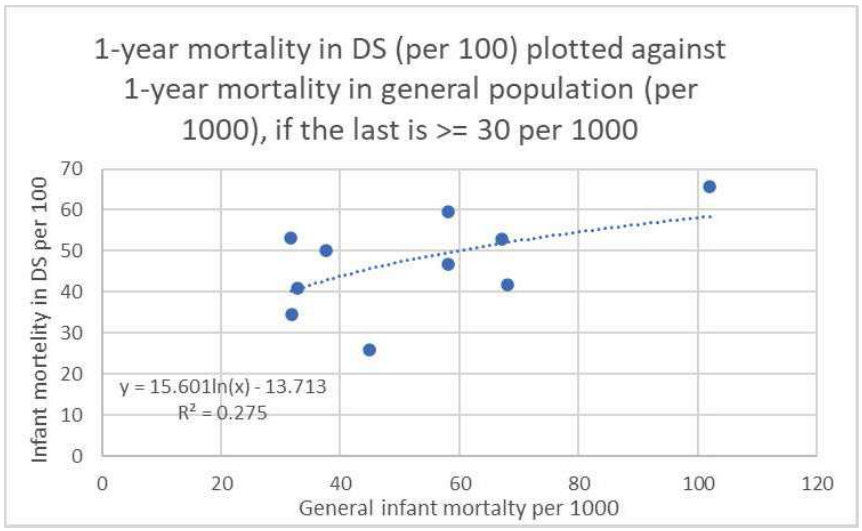
Basically, in these studies, the mortality rates were predicted by year of birth, and then adapted on the basis of the infant mortality in the general population in the specific country/territory. However, infant survival in the general population in many countries/territories in Latin America and the Caribbean is much lower than we had encountered in these earlier studies. It might be that some of the Latin America and Caribbean values are out of range for our adaptation procedure.

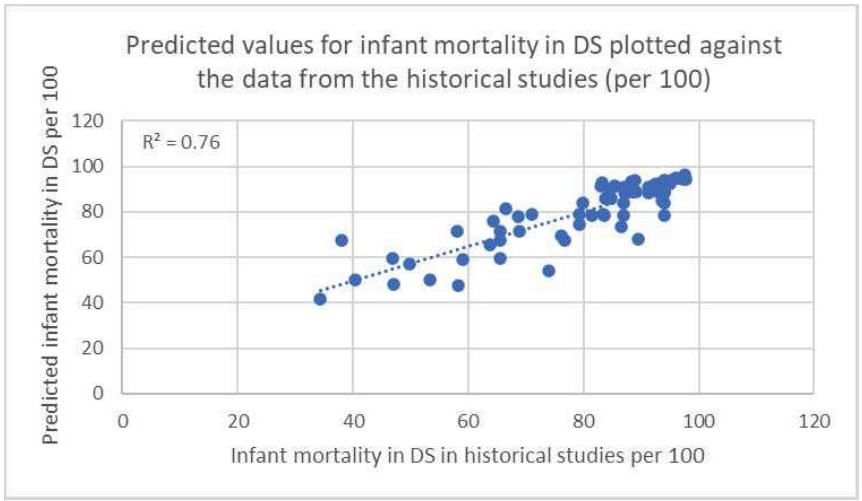
An alternative procedure to predict 1-year survival in DS

For the current study, we wanted to explore if an alternative procedure could be developed. Instead of constructing 1-year survival estimates for people with DS based on year of birth and subsequently adapting these on the basis of 1-year survival in the general population, we wanted to directly base our 1-year survival estimates for people with DS on 1-year survival rates in the general population. We used the same historical studies that de Graaf et al. used.[4,10,30–32] However, instead of looking at the relation between year of birth and survival, we looked directly at the relation between 1-year survival in the general population and 1 year survival in DS.

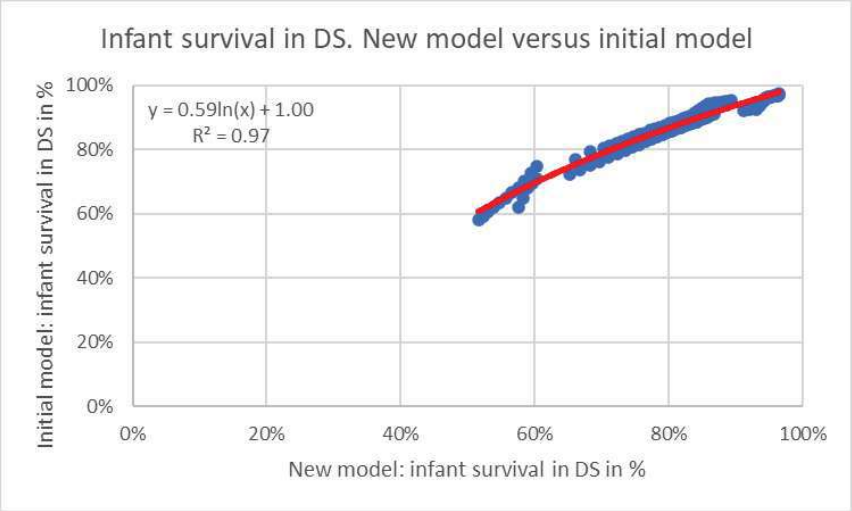
For our earlier studies, we had collected data from multiple historical studies on infant mortality in children with DS, including the country and period of time for each study.[4,10,30–32] The World Population Prospects (WPP) of the United Nations provides estimates of 1-year mortality in the general population.[1] We plotted mortality in DS from the historical studies (y-axis) against 1-year mortality in the general population (x-axis). In predicting the y-values on the basis of the x-values, we had a better fit if we made the regressions separately for values of general infant mortality above and below 30 per 1000 (figures below). If alternatively, we use all data (above and below 30 per 1000 together), a logarithmic regression has the best fit, with R^2=0.73. If we predict separately for above and below 30 per 1000, the predicted values for infant mortality in children with DS (all data pooled after the regression) correlate stronger with the empirical data (R^2=0.76), see the third figure below.


1-year mortality in DS (per 100) plotted against 1-year mortality in general population (per 1000), if the last is < 30 per 1000
y = 1.221x - 1.083
R² = 0.582
Infant mortelity in DS per 100
General infant mortalty per 1000
0
10
20
30
40
50
60
70
0
5
10
15
20
25
30
35


1-year mortality in DS (per 100) plotted against 1-year mortality in general population (per 1000), if the last is >= 30 per 1000
y = 15.601ln(x) - 13.713
R² = 0.275
Infant mortelity in DS per 100
General infant mortalty per 1000
0
10
20
30
40
50
60
70
0
20
40
60
80
100
120


Predicted values for infant mortality in DS plotted against the data from the historical studies (per 100)
R² = 0.76
Predicted infant mortality in DS per 100
Infant mortality in DS in historical studies per 100
0
20
40
60
80
100
120
0
20
40
60
80
100
120

The next step was checking if the predicted values for survival in children with DS for countries that had in recent years a relatively high general infant survival were in line with the predictions made on the basis of the initial model of de Graaf et al.[10,30–32] In our earlier studies these turned out to work well for these countries. We checked for a mixture of different countries (the UK, Brazil, Argentina, and Mexico) for the years 1990 onwards. The initial model produced slightly higher values for survival in DS. We plotted the values of the initial model (y-axis) against the new model (x-axis). We used the regression equation from the figure below to transform the new model's values for infant survival in DS from 1990 onwards into slightly higher values. The values up to and including 1987 were unchanged. The values of 1988 and 1989 were interpolated between the value of 1987 and the new value of 1990 in order to construct a smooth series of data.



For empirical data on survival of children with DS in South America, we found one source: ECLAMC reported an overall mean survival at age one year of 74% in 360 LBs of children with DS, born during 1988–1992 in 23 cities in 5 South American countries (Argentina, Brazil, Chile, Paraguay, and Uruguay).[33] As these are countries for which we have estimated different values for 1-year survival of children with DS, we have weighted our data for the number of hospitals from each country/territory. For instance, Argentina had 15 out of the 33 hospitals, and we allocated 15/33 or 45% to our estimate for Argentina. The weighted average of our model for these 5 countries between 1988–1992 was 72%. Without the transformation to higher values from 1990 onwards, this would have been 65%, which means that the estimates after this transformation have a better fit with the ECLAMC data.

Predicting 5- and 10- year survival in DS

Using data on survival rates in DS from historical studies, de Graaf et al. fitted a linear relation between 1-year survival in DS and 5-year and 10-year survival, respectively.[4] In a recent study, de Graaf et al. concluded that quadratic equations had a slightly higher fit.[32] In the current study, we will use these quadratic projections. However, if predicted 1-year survival rates are lower than 33%, the quadratic equations project values for 5- and 10- year survival higher than the 1-year rates. This is not possible. We have decided to use the initial linear equations for years in which 1-year survival is below 33%. In addition, we have minimized the value of 1-year survival in DS at 20%, as we consider that already to be very low. At the other side of the value range, 1-year survival values above 98% would yield 5-year and 10-year survival rates higher than 98%. Thus, the highest possible value for 1-year survival that our model would accommodate is 98%. We have maximized the 1-year survival at 98%.

Survival beyond 10 years of age

For modeling survival rates beyond 10 years of age from 1950 onwards, de Graaf et al. made use of the average of (highly similar) survival curves for DS from 7 different historical studies.3,5–7 If the 1-year survival rate for DS was <60%, de Graaf et al. used a more hazardous curve based on Penrose.[4,10,30–32] In the current study, we followed the same procedure.

For their study on the Canadian population of people with DS, de Graaf et al. concluded that, in developed countries, mortality rates for all years between 10–30 years of age seem to be lower than modeled from the 1990s onwards.[32] They halved for everyone born from 1980 onwards (10 years of age or older in 1990) the constructed mortality rates in the model for all years between 10–30 years of age, thus making the line between 10–30 years of age more horizontal. We followed the same procedure for the ones born from 1980 onwards, but only if in a country/territory the predicted 1-year survival for the corresponding year of birth was >80%.

To summarize, we apply the earlier model of de Graaf et al. with one large and two small adaptations.[4,10,30,31] We have estimated 1-year survival following another procedure; we have used quadratic equations (instead of linear) to predict 5- and 10-year survival rates for DS; we have assumed a better survival between 10–30 years in countries/territories with a 1-year survival >80% for the corresponding year of birth.

S2B. Sources for infant mortality in the general population

Mortality rates in general population can be estimated on basis of combining two files from the World Population Prospects 2022:

- File MORT/01-1: Deaths (both sexes combined) by single age, region, subregion and country/territory, annually for 1950-2100 (thousands)[1]
- File FERT/03: Births by single age of mother, region, subregion and country/territory, annually for 1950-2100 (thousands)[1]

For the period before 1950, for some countries, data on 1-year mortality rates can be found at https://www.gapminder.org/data/ (accessed October 8, 2019). If these were not available, we have predicted 1-year mortality for 1945–1950, 1950–1955 and 1940–1945, etc., on the basis of the 1-year survival in 1950–1955, using the predictions as were developed by de Graaf et al. on the basis of survival data from European countries.[4]

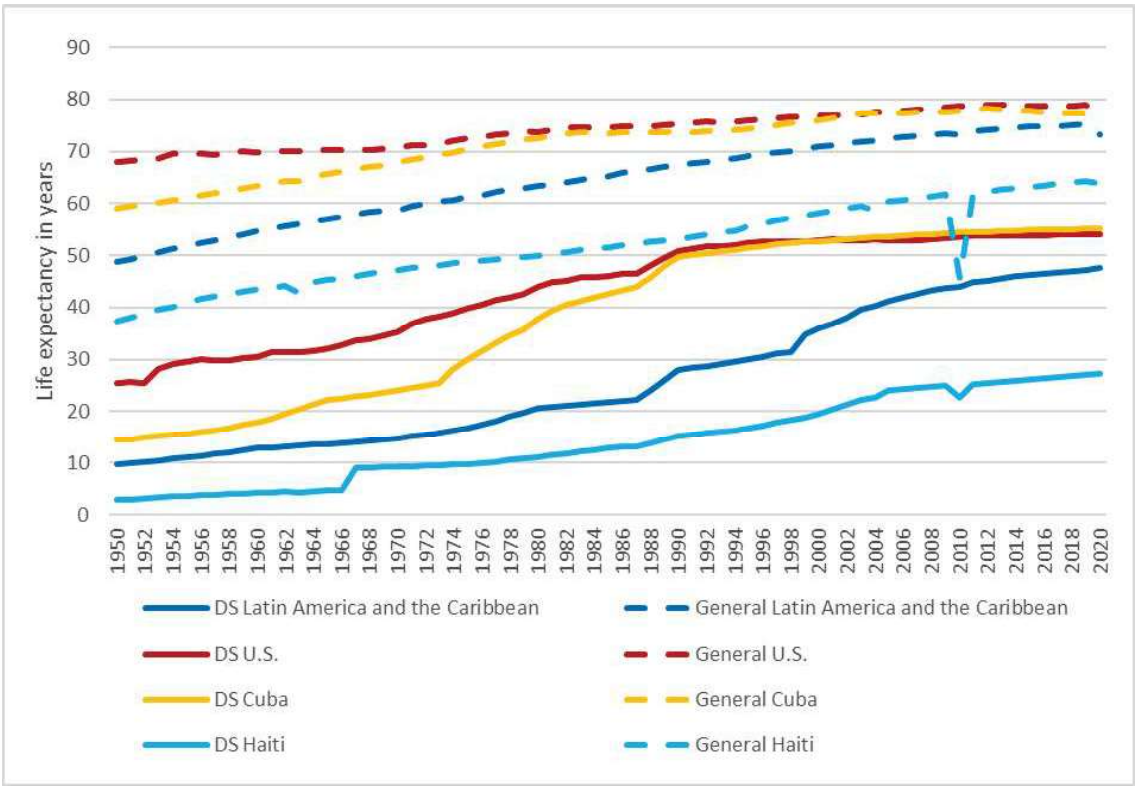
S2C. Changes in life expectancy

In the United States, the *mean* life expectancy for children with DS increased from an estimated 26 years in 1950 to 53 years in the 2010s (median 4 and 58 years, respectively).[10] In our modeling, survival curves for children with DS, based on their year of birth, were constructed, allowing us to estimate the corresponding mean life expectancies. In the Figure below, we have plotted the estimated mean life expectancies of people with DS by year of birth from 1950 to 2020 for Latin America and the Caribbean, the United States, Cuba (the country within Latin America and the Caribbean with the highest current survival), and Haiti (the country with the lowest survival). For comparison, we have also included the mean life expectancies of the general population, derived from the World Population Prospects.[1]

In Latin America and the Caribbean, the estimated mean life expectancy in DS increased from 10 years in 1950 to 48 years in 2020 (median 0 and 57 years, respectively). The gap between this region and the United States (mean life expectancy of 54, and median of 60 in 2020) is gradually narrowing. The figure below also highlights the significant differences in mean life expectancies within the Latin American and Caribbean region. After 2001, Cuba even surpassed the United States in this regard. At the other extreme, Haiti had a low mean life expectancy for children with DS: 3 years in 1950 and 27 years in 2020.

In the United States, and in Latin America and the Caribbean, the difference between the mean life expectancy in the general population and that for children with DS has significantly decreased. In the United States, this gap decreased from 43 years in 1950 to 23 years in 2020, while in Latin America and the Caribbean, it decreased from 39 years in 1950 to 26 years in 2020. In Haiti, this gap (34 years in 1950 and 36 years in 2020) remains substantial and has not yet narrowed.

Estimated mean life expectancy of people with DS and of the general population. The data for the general population are derived from the World Population Prospects[1]



Supplementary Methods 3: Validating the model

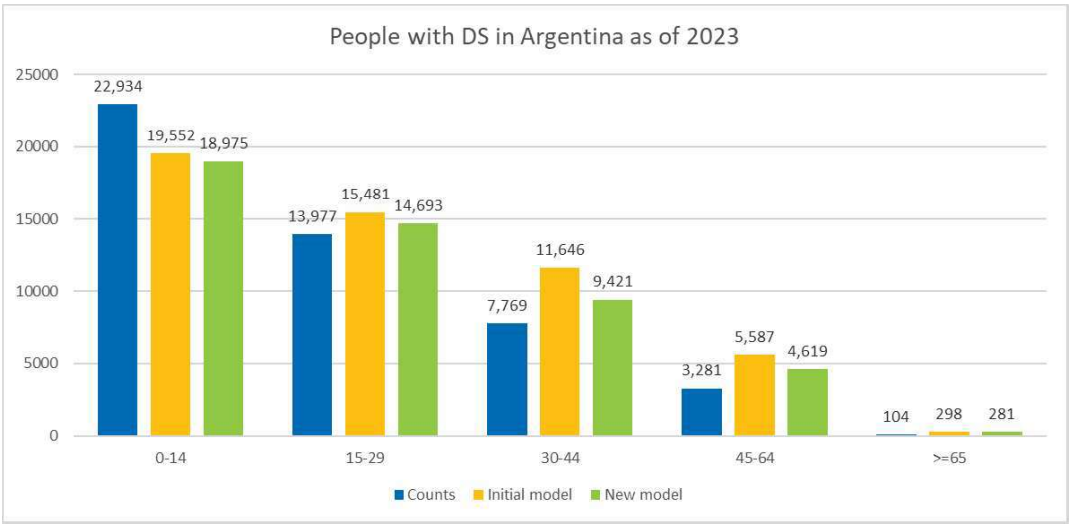
S3A. Comparison with population counts of people with DS

For Latin America and the Caribbean, counts of people with DS in the population are available from Argentina (as of 2023) and Cuba (as of 2002).[34,35]

Argentina

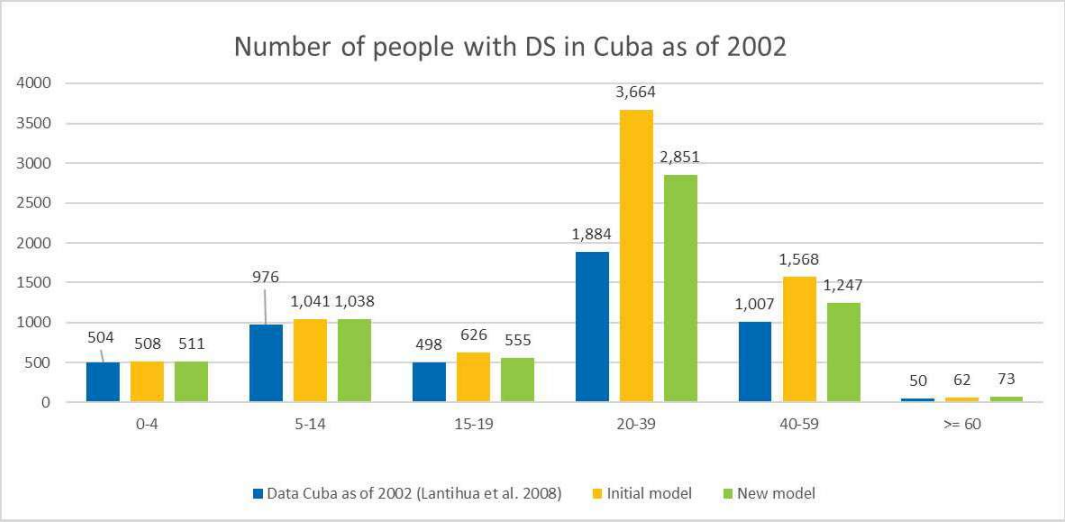
The data from Argentina are based on a national registry for people with disabilities. There is one complication: the authors of the report state that people can have multiple labels and that they counted labels, not people.[34] That raises the question if people with DS might have been double counted—for instance if they were labeled with both ICD-10 codes Q90 (Down syndrome) and 90.9 (Down syndrome, not specified). The full count of all label categories for DS (Q90; Q90.0; Q90.1; Q90.2; Q90.9) corresponds to 48,065 people; the largest single category (Q90) to 42,347. We don't know to what extent double counts may have occurred. However, one can conclude that there are at least 42,347 people with DS registered in Argentina as of 2023, and at most 48,065.

The initial model predicts 52,564 people with DS in Argentina as of 2023; the new model 47,988. Both models do not have a perfect match with the data, especially if we look at the age distribution (figure below). However, the new model appears to be more in line with the empirical data. However, there might be some double counting in the empirical data; though, at the same time, it is possible that not everyone with DS is enrolled in the register.



Cuba

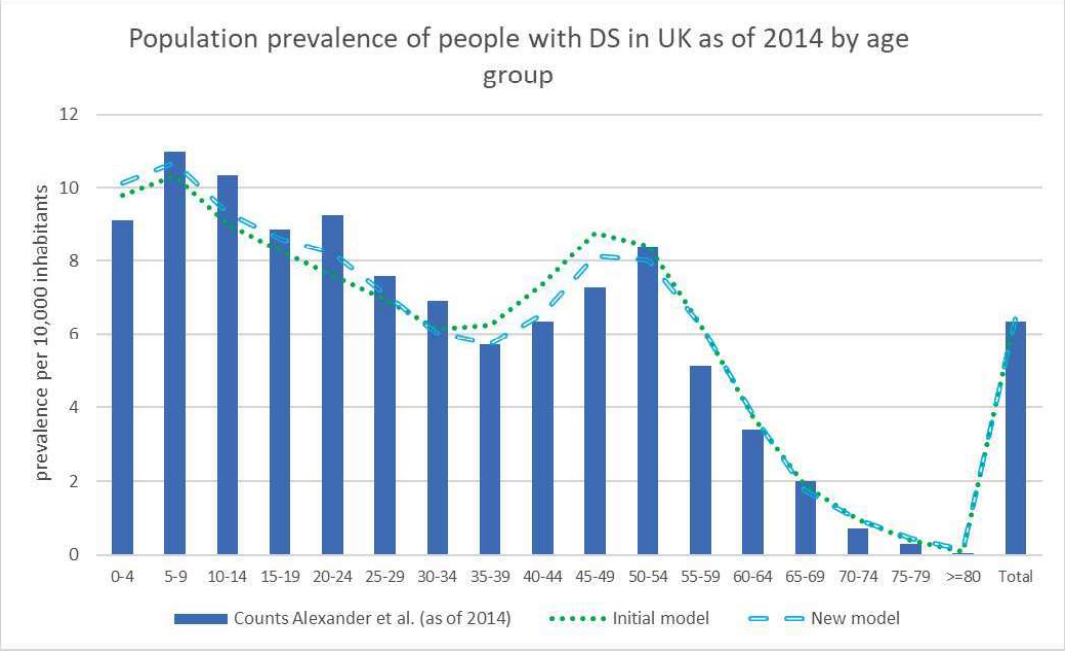
In Cuba, people with DS by age group were counted as of 2002.[35] Both the initial and the new model predict more people with DS, respectively 7,469 and 6,276, than were counted (4,919), but the new model is less off than the initial model (figure below). Especially the counts of the age group 20–39 (people born in the 1960s and 1970s) are smaller than predicted. Perhaps infant survival in DS in Cuba in that period was less favorable than modeled. Perhaps among refugees who left Cuba in the 1960s and 1970s, there were families with young children with DS. Perhaps the counts are not complete.



United Kingdom

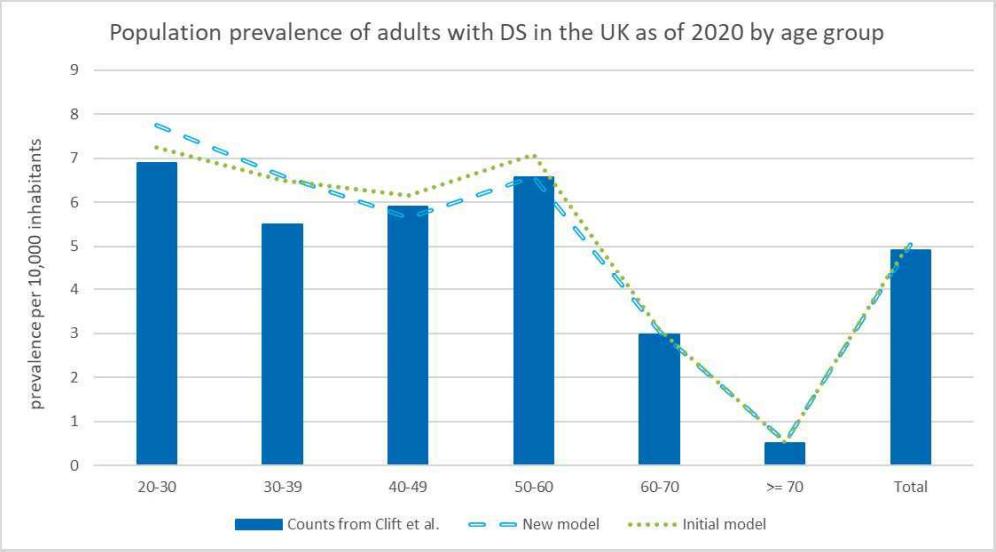
To check if the new model works better than the initial model, we have made some comparisons with empirical data for countries outside Latin America and the Caribbean. We chose countries that have recent and probably fairly complete data of people with DS by age group or data based on a large sample. This is the case for the UK, France, Australia, and the U.S.[31,36–38]

For the UK, Alexander et al. (2016) estimated the population prevalence of people with DS in the UK, as of 2014, using a large primary care database containing information on 2,476 individuals with DS in a total of 3.9 million individuals enrolled. In de Graaf et al., the results were compared with the initial model.[4,36] The new model appears to have a slightly better match (figure below).



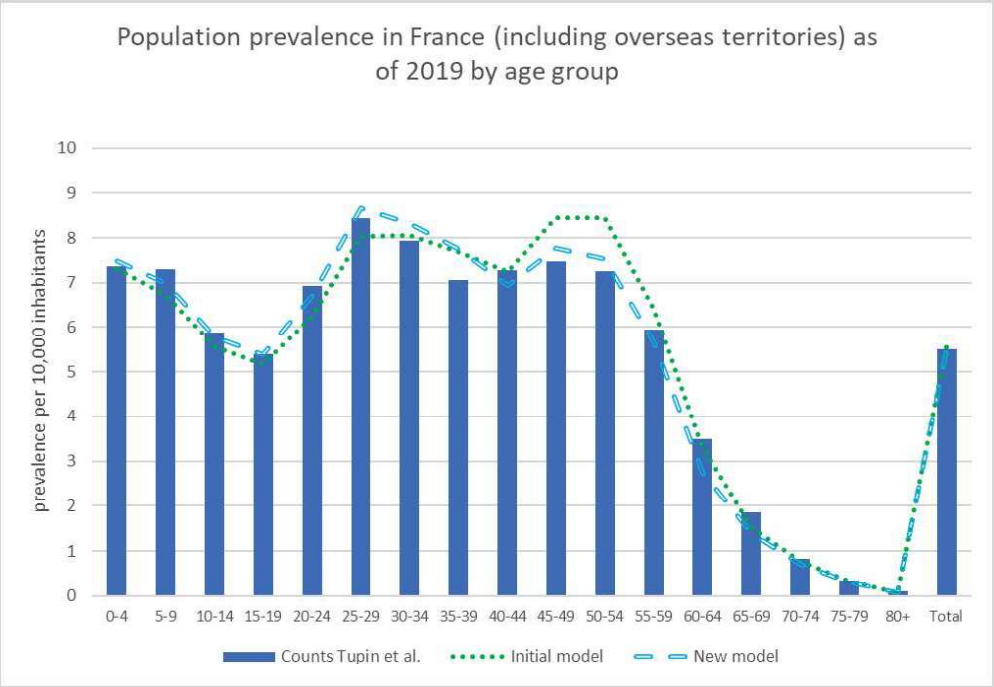
In another study, Clift et al. studied data from a population-level primary care database in England.[37] Out of 8.3 million adults in 2020, 4,053 had Down syndrome (4.91 per 10,000). Our new model

predicts an adult prevalence of DS of 5.05 per 10,000; the initial model 5.12 per 10,000. In the figure below, we compare the results by age group. The new model has a better fit for the range 40–60 years of age. Both models seem to overestimate the prevalence in the range 20–40 years of age. These are people born in the period 1980–2000. In the figure above, with data as of 2014, these people would be in the age range 15–35 years of age. Interestingly, for this age range, the figure above suggests that both models underestimate. We suggest that the difference with the situation in the figure below is explained by uncertainty in the empirical data, which are based on samples and not on the whole population.



France

Tuppin et al. studied the French national health database (SNDS) which contains the information of at least 98,5% of all people in France, including French overseas territories (FOT).[38] In the database, there were 36,464 people with DS enrolled. For comparison, we estimated the number of people with DS in France, and the overseas territories, as of 2019 (applying to the expected number of LBs of children with DS in Réunion the same reduction as we earlier did to the FOT in South America). The new model predicted 36,296 people with DS; the initial model 36,854. In the figure below, the numbers by age group are presented. The new model has the best fit.



Australia

In Australia, the National Disability Insurance Agency (NDIA) collects data on the primary and secondary disability for all participants in the National Disability Insurance Scheme (NDIS). On request of Down Syndrome Australia, the NDIA has provided data on the number of participants with Down syndrome identified as a primary or secondary disability, by age group for 2021.[31] In de Graaf et al., these numbers were compared with the estimates of the initial model.[31] Below, we add the estimates of the new model. People of 65 years of age and older are omitted, as one must be under 65 to enter the NDIS. In the youngest age groups, not all parents will have applied for access. That explains why the models seem to overestimate under 10 years of age. The new model has a slightly better fit, especially for people older than 40 years of age. Please note that this analysis is the sole responsibility of the authors of this study and has not been prepared in collaboration or partnership with the NDIA.