Survival Modeling of Disease Consequences and Post-disease Syndromes

Michal Haindl(✉)

Institute of Information Theory and Automation, Czech Academy of Sciences,
Pod Vodárenskou věží 4, 182 08 Prague, Czechia
haindl@utia.cas.cz
http://www.utia.cas.cz

Abstract. We present a survival model for human maladies, which leave victims with permanent health damages requiring life-long medical observation and treatment. The model allows national health authorities to prepare sufficient medical specialists with adequate capacity in specialized clinics, vaccinations, spas, or rehabilitation facilities. We test the model on Czech Polio (Poliomyelitis Anterior Acuta) victims' data. COVID-19 or Long Covid-19 and the treatment of their wide range of ongoing health problems, where these conditions can last weeks, months, or years, can benefit from Polio and COVID-19 RNA virus similarities.

Keywords: survival model · permanent disease consequence · Poliomyelitis anterior acuta · post-disease syndromes

1 Introduction

Numerous infectious or no-infectious human maladies leave victims with permanent health damages requiring life-long medical observation and treatment. Such maladies are ancient humanity problems such as Poliomyelitis, newly detected malady COVID-19, and several others. National health systems have to be prepared not only with a sufficient number of medical specialists but also with adequate capacity in specialized clinics, vaccinations, medicaments, spas, or rehabilitation facilities. Apart from this, aging patients need age-based modified treatment, and the same holds for novel emerging treatment methods and drugs replacing older therapies. Thus, it is crucial to predict the number of corresponding patients in the coming several years and their age structure.

Our model differs from usual standard survival models [1–4] for chronic diseases that model the survival rate of the patients to the survival rate expected in a group in the general population. We expect a similar survival rate of malady victims as the general population, but the model can be straightforwardly modified to accommodate such differences. The model is tested on Czech Polio victims' data, carefully registered during Polio pre-eradication years 1937–1960 in former Czechoslovakia. The primary computational challenges are the lack of necessary data to estimate necessary model parameters and what we have

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to overcome using additional simplifying model assumptions with all related shortcomings, such as less precise numerical estimates and the impossibility of gender-based simulations and some others.

Its importance is in Polio and COVID-19 similarities because the post-polio syndrome (PPS) treatment profits from 40 years of experience. Although over five thousand papers about poliomyelitis were published during the last twenty years [5], Polio or PPS research is not a priority anymore, probably due to widespread optimistic expectations about Polio eradication soon. Thus, only limited significant results were achieved, and the principal Polio problems, such as its treatment or PPS diagnosis, remain. Post COVID-19 syndrome includes symptoms common to PPS [6], i.e., weakness; fatigue and pain like myalgic encephalomyelitis/chronic fatigue syndrome, breathlessness, and cognitive disturbances. Another synonymical study [7] shows that countries using oral Polio vaccine (OPV) have a lower cumulative number of cases diagnosed with COVID-19 per 100,000 population by an average of 30% compared with those using only inactivated Polio vaccine (IPV). This result might suggest that OPV may either prevent SARS-CoV-2 infection at an individual level or slow down the transmission at the community level.

1.1 Polio Outbreak

Poliomyelitis is an acute illness that follows invasion through the gastro intestinal tract by one of the three serotypes of the Polio virus. The virus replicates in the gut and has a high affinity for nervous tissue. The infection is most frequently clinically inapparent, or symptoms may range in severity from fever to aseptic meningitis or paralysis. The cases of infections of the respiratory neurons can lead to death, with a mortality rate of approximately five to ten percent [8]. Poliomyelitis still has no cure, and most Polio survivors may suffer from PPS. Post-polio syndrome usually occurs 15–40 years after the infection and recovery, and there are neither laboratory nor diagnostic tests for PPS. No effective treatments can stop deterioration or reverse the deficits caused by the syndrome.

Most patients are children $1 \sim 6$ years old and about 7% more males than females. However, acute flaccid paralysis (AFP) surveillance only detects clinical disease, and as poliovirus infection is asymptomatic, most Polio infections are undetected. Some countries also perform environmental surveillance, which mainly involves testing sewage samples for the presence of Poliovirus.

Transmission is through contact with an infected person's feces or pharyngeal secretions. The incubation period ranges from three to 21 days. Poliovirus replicates for extended periods, and it can be excreted for three to six weeks in feces and two weeks in saliva.

Immunization with inactivated Poliomyelitis Salk vaccine (IPV) was introduced in 1956 and later replaced with the live attenuated oral Polio Sabin vaccine (OPV 1962). In only 40% EU countries is vaccination against Polio compulsory; outside the EU, it is 45%. Elsewhere, vaccination is only recommended. There is a real threat of a Polio epidemic in under-vaccinated European or other populations, given that there are still about a thousand AFP cases worldwide

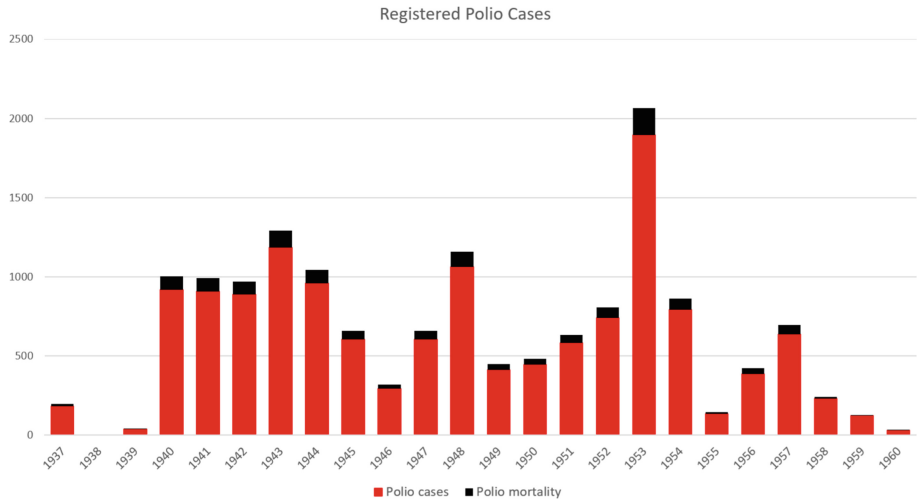

Fig. 1. The number of Polio cases 14 076, with a median of 595 per year, Polio mortality 1 267 (median 54 per year) in the Czech part of Czechoslovakia from 1937 to 1960.

yearly. Poliomyelitis, either the wild virus or recent prevailing vaccine-associated paralytic Poliomyelitis (a reverse mutation of the attenuated virus back to its pathogenic forms), remains endemic in only a few developing countries despite large expenditures since 1998 of the Global Polio Eradication Initiative (GPEI) of the World Health Organization. However, several countries or subnational territories ([9] Birmingham District) are at high or intermediate risk of Polio transmission due to suboptimal population immunity, inadequate surveillance [10] or voluntary vaccination.

Countries with successful Polio eradication efforts, such as former Czechoslovakia, which was the first country in the world to eradicate Polio (Poliomyelitis Anterior Acuta) already in **1960** [11,12], have a problem estimating the number of Polio survivors and Polio-affected people in their population in recent years. For most countries exist, only very rough scale indicators India 863 000, England and Wales 44 000, France 50 000, etc. This missing data is because health authorities do not track a statistic for such in a country long-term non-existent illness in their countries. Such negligence has not only a negative consequence on the medical and social care of still-living Polio victims but can be dangerous in possible future epidemics.

The model can be similarly used for other illnesses (Long Covid, stroke, EBV viruses, boreliosis, etc.) with permanent or long-duration damages. Our motivation is twofold:

- to estimate the number of disease/Polio AFP victims in every specified year, including their age structure, and simultaneously
- to estimate a curve with the overall number of disease/Polio survivors as a function of the year.

Such a curve allows us to estimate a perspective for a disease/Polio association and a country requiring medical capacity for post-disease/post-polio syndrome treatment.

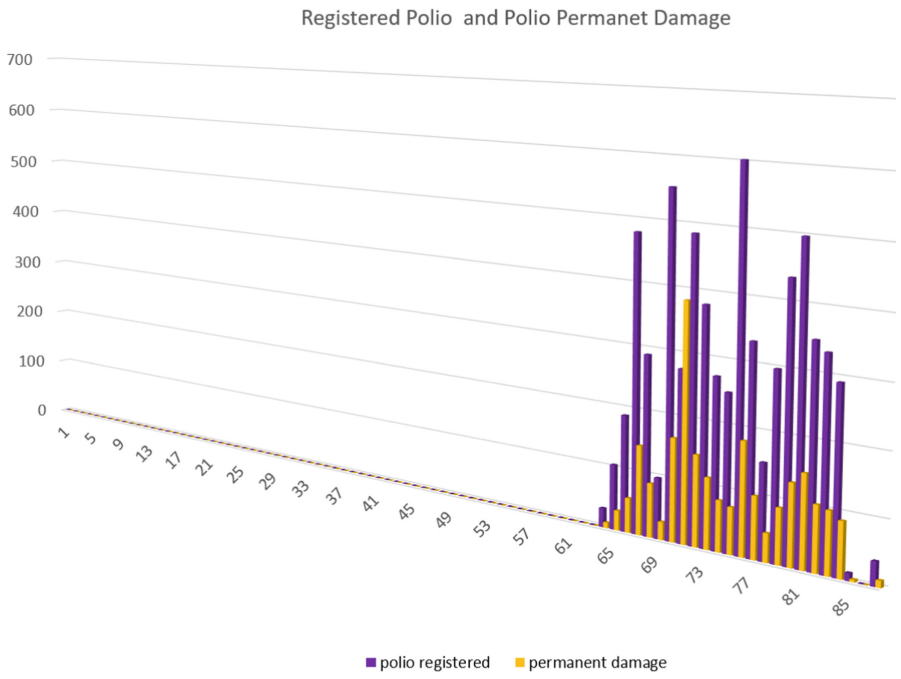

Fig. 2. The age-based Polio victims with permanent damage in 2023.

2 Survival Model

Our survival model is cumulative due to different years when people acquire an illness and suffer from the post-illness consequences. The temporal dependence is related to the aging of past malady victims modified by the appropriate mortality rates. Our malady survival model is as follows:

$$ {}^{w}PV(a,\beta) = \sum_{i=1 \wedge \beta - b_i = a}^{n} {}^{w}\delta_{a,\beta-b_i} \prod_{j=f_{k,y}}^{a} (1 - {}^{w}\pi_{j+f_{k,y}}) \left(1 - \frac{{}^{w}m_y}{{}^{w}p_y}\right) \quad , \quad (1) $$

$$ {}^{m}PV(a,\beta) = \sum_{i=1 \wedge \beta - b_i = a}^{n} {}^{m}\delta_{a,\beta-b_i} \prod_{j=f_{k,y}}^{a} (1 - {}^{m}\pi_{j+f_{k,y}}) \left(1 - \frac{{}^{m}m_y}{{}^{m}p_y}\right) \quad , \quad (2) $$

$$ n = \sum_{i=Y_{first}}^{Y_{last}} {}^{m}p_i + {}^{w}p_i \quad , \quad (3) $$

where ${}^{w}PV(a,\beta)$ is the number of a-year-old illness victims (w - woman, m - men) living in the year β, $\delta_{a,\beta-b_i}$ is the number of illness victims a-years-old without a mortality reduction, p_y is the number of registered malady victims in the y-th year, m_y is the number of illness incurred deaths in the y-th year, b_k $k-$th is the illness victim's born year, $f_{k,y}$ $k-$th illness victim year y of acquired illness.

$$ {}^{wd}PV(a,\beta) = d_w \, {}^{w}PV(a,\beta) \ , \tag{4} $$

$$ {}^{mu}PV(a,\beta) = u_m \, {}^{m}PV(a,\beta) \ , \tag{5} $$

where ${}^{wd}PV(a,\beta)$ is the number of a-year-old women with permanent damage in the year β, ${}^{mu}PV(a,\beta)$ the number of a-year-old men with undetected illness infection in the year β, n number of all illness victims between years $\langle Y_{first}; Y_{last}\rangle$, ${}^{w}\pi_j, {}^{m}\pi_j$ is the average women/men percentual mortality in age category j, d_w the percentage of permanent damage, u_w percentage of unregistered infections. The product computes the overall survival percentage in the corresponding year range. The mortality rate can be further specialized [3,13] if more detailed survey data are available, for example, for local region-based submodels or life conditions.

For illnesses with possible post-malady syndromes, such as post-polio syndrome, which appears decades after the initial infection, we estimate the number of victims suffering from such a syndrome:

$$ {}^{wd}PS(a,\beta) = {}^{wd}PV(a,\beta) \cdot {}^{m}\gamma \cdot e(a,\beta) \ , \tag{6} $$

$$ {}^{mu}PS(a,\beta) = {}^{mu}PV(a,\beta) \cdot {}^{w}\gamma \cdot e(a,\beta) \ , \tag{7} $$

$$ e(a,\beta) = \begin{cases} 0, & \text{if} \quad a \notin \langle Y_f; Y_l\rangle \ ; \\ f\left(a,\mu,\sigma,Y_f,Y_l\right) & \text{otherwise.} \end{cases} \ , \tag{8} $$

$$ f\left(a,\mu,\sigma,Y_f,Y_l\right) = \frac{1}{\sigma} \frac{\varphi\left(\frac{a-\mu}{\sigma}\right)}{\Phi\left(\frac{Y_l-\mu}{\sigma}\right) - \Phi\left(\frac{Y_f-\mu}{\sigma}\right)} \ , \tag{9} $$

$$ \varphi\left(x\right) = \frac{1}{\sqrt{2\pi}} \exp\left\{-\frac{1}{2}x^2\right\} \ , \tag{10} $$

$$ \Phi\left(\zeta\right) = \frac{1}{2}\left(1 + erf\left\{\frac{\zeta}{\sqrt{2}}\right\}\right) \ , \tag{11} $$

where ${}^{wd}PS(a,\beta)$, ${}^{mu}PS(a,\beta)$ is the number of post-malady syndrome suffering women/men a-year-old with permanent damage in the year β, ${}^{\circ}\gamma$ is a percentage of malady victims who will acquire post-malady syndrome during their lives and $e(a,\beta)$ is a random variable realization from the truncated normal distribution (9) constrained to be in the interval $\langle Y_f; Y_l\rangle$ which is the age year range when a post-malady can appear. $\mu = 1, \sigma = 10$ are mean value and standard deviation of the truncated normal distribution, $\varphi\left(\circ\right)$ is the probability density function of the standard normal distribution and $\Phi\left(\circ\right)$ its cumulative distribution function.

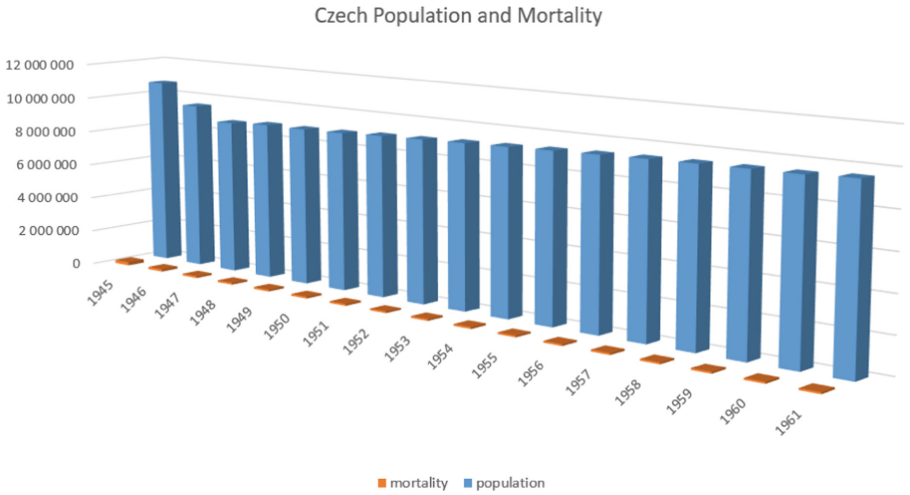

Fig. 3. Czech population and mortality between Polio years 1945–1960.

3 Czech Polio Model Assumptions

Several important data details about Polio victims in Czechoslovakia were not recorded, such as the victim's gender, acquired Polio age, etc. Hence, we have to inevitably use several mathematical assumptions for the Czech Polio model, which simplifies the modeling equations (1)-(5). Some of them (A 2, A 7, A 9) might affect the model precision, while others have only a minor effect (neglecting pre-1937 cases A 1, A 3, A10). Polio model simplifying assumptions:

A 1 no Polio victims were in Czechia before 1937, $Y_{first} = 1937, Y_{last} = 1960$,
A 2 every Polio victim was affected in his or her second year, $f_{k,y} = 2 \; \forall k, y$,
A 3 reported Polio victims are either long-period affected people or Polio fatalities,
A 4 Polio infected mortality is either a known number or 9% from reported Polio cases, ${}^{m}m_y = {}^{w}m_y$,
A 5 30% of Polio victims suffer permanent damages, $d_w = d_m = 0.3$,
A 6 only 1% from Polio-infected people were reported by physicians; the remaining cases were either undetected or wrongly assigned to other common infections, $u_w = u_m = 100$,
A 7 men and women's age-based mortality is identical, ${}^{w}\pi_j = {}^{m}\pi_j \;\; \forall j$,
A 8 Polio survivors' mortality is the same as the general population mortality,
A 9 average mortality numbers per age category corresponding to the year 2003, i.e., they are not related to each Polio survivor's birth date,
A10 no change of country residence for Polio survivors is assumed (immigration or emigration),
A11 40% of Polio victims (men and women ${}^{m}\gamma \approx {}^{w}\gamma$) will acquire post-polio syndrome between 15–40 years after Polio infection.

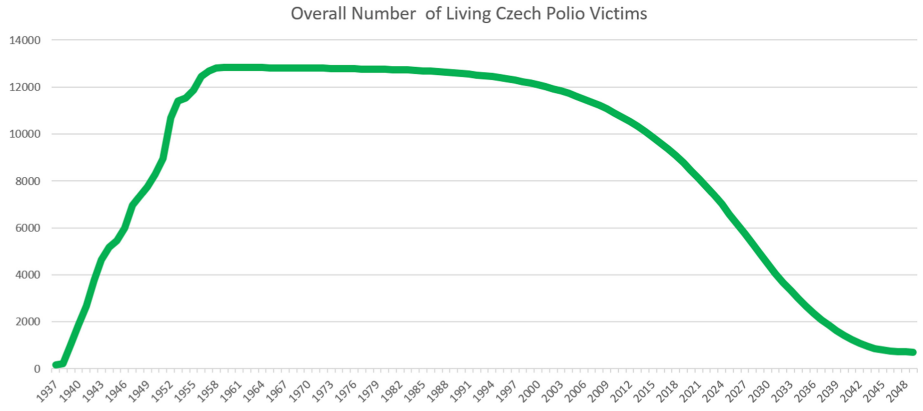

Fig. 4. Number of Polio survivors between the years 1937–2048.

3.1 Czech Polio Model

The Czech Polio model after eleven simplifying assumptions (Sect. 3) is as follows:

$$PV(a,\beta) = p_{\beta-\alpha+1} \prod_{j=2}^{a} (1-\pi_{j+2}) \left(1 - \frac{m_{\beta-\alpha+1}}{p_{\beta-\alpha+1}}\right)$$
$$\forall \beta - \alpha + 1 \geq 1937 \ , \tag{12}$$
$$n = \sum_{\forall i} p_i \ , \tag{13}$$

where p_i is the number of registered Polio victims in the i-th year, m_i is the number of Polio deceased, π_j percentual mortality for age category j. The Czechia population is taken from [14]. Figure 3 illustrates the Czech population and mortality in the after-war Polio years in Czechoslovakia.

4 Results

The presented model was trained on the Czechia part of available Polio data carefully recorded in former Czechoslovakia from 1937 until Polio's complete eradication in 1960. Czechoslovakia was the first world country to eradicate Polio (**1960**). Figure 1 shows the number of recorded Polio cases yearly and the number of Polio-related deaths. The total number of Polio cases was 14 076, with a median of 595 per year. The recorded Polio mortality was 1 267, with a median of 54 per year. Figure 2 illustrates the age structure for Czech Polio AFP victims, both registered and with some permanent damage, in 2023. The total number of Polio victims surviving this year is 7 388; approximately another seven hundred thirty-one thousand Czechs suffered Polio without any visible consequences. There are also about 2 955 Polio victims suffering from

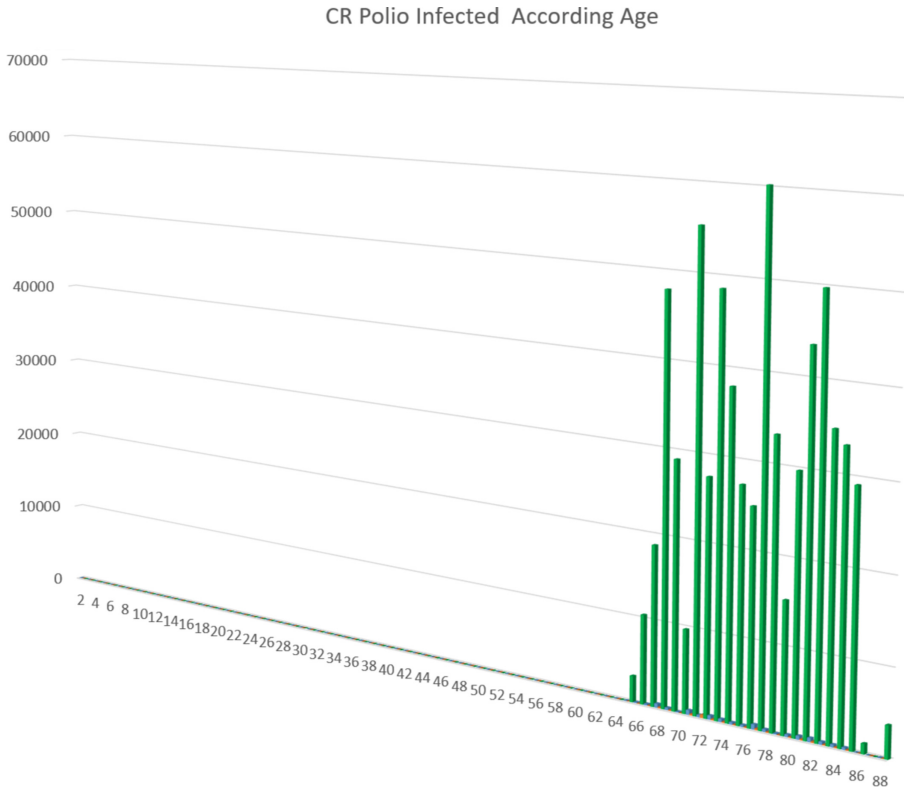

Fig. 5. The age-based overall number of infected Polio survivors.

PPS in 2023. This estimate is based on the unconfirmed assumption that only Polio victims with a significant disability can later acquire PPS. If this is not true and Polio-infected people without marked disability can get PPS, then the number of PPS is much larger, and the PPS problems are probably attributed to other medical causes. These graphs show that all Czech Polio victims are at the retirement age and the age when they can expect negative consequences from the post-polio syndrome. PPS is believed to be the result of a deterioration of nerve cells called motor neurons over many years that leads to loss of muscle strength and dysfunction. Only a Polio survivor can develop PPS, and about 40% of those who survive Polio will develop PPS. The graph in Fig. 4 indicates the expected number of Czech living Polio victims in each year between 1937 and 2048. If no new imported Polio cases exist, PPS treatment will not be needed until around 2045. Figure 5 shows the age structure of all estimated Czech inhabitants infected by the Polio virus, mainly without any permanent damages, although it is unknown if PPS cannot appear even in such initially undetected Polio infections. Figure 6 shows estimates of the age structure of PPS victims in 2023.

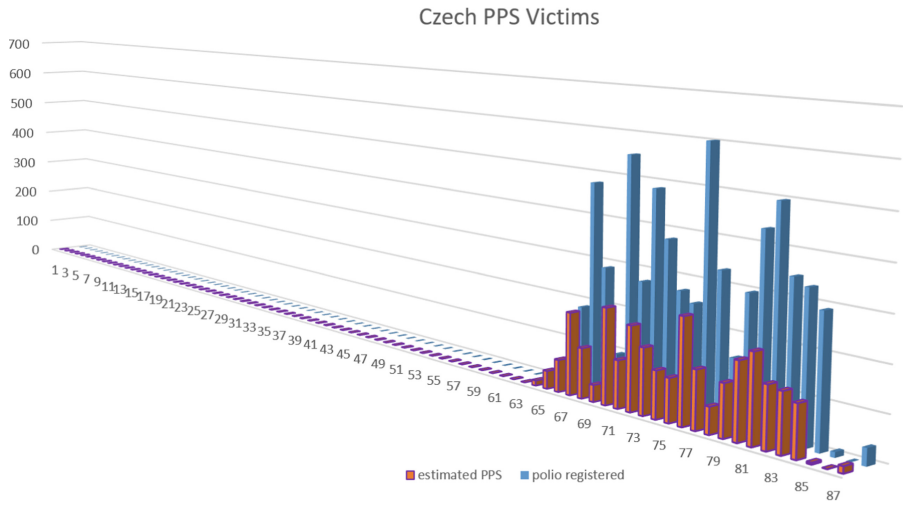

Fig. 6. The age-based structure of estimated PPS victims in 2023.

5 Conclusions

The presented survival model for human maladies, which leave victims with permanent health damages allows national health authorities to estimate the number of living disease victims every year, the number of permanently damaged disease victims, the number of living malady-infected people every year and thus prepare sufficient medical specialists with adequate capacity in specialized clinics, vaccination, medicaments, spas, or rehabilitation facilities.

The model is tested on known Poliomyelitis anterior acuta data from the Czech part of former Czechoslovakia from 1937 until Polio's complete eradication in 1960 to benefit from Polio and COVID-19 similarities. The total number of Polio acute flaccid paralysis victims surviving the year 2023 is 7 388; approximately another seven hundred thirty-one thousand Czechs suffered Polio without any visible consequences, and about 2 955 Polio victims suffer from PPS. If there will not be new imported Polio cases, around 2045, Polio cases will completely disappear from Czechia. The usual significant computational challenge is the need for more data to estimate necessary model parameters, which has to be overcome using additional simplifying model assumptions. Similarly, some necessary Polio details are unknown; thus, the corresponding simplifying assumptions must be accepted. The lack of all needed data resulted in inaccurate assumptions (A2, A7, A9), inevitably leading to rough, less precise numerical estimates and the impossibility of gender-based simulations. However, they still suffice for the necessary medical treatment planning.

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