The Covid-19 pandemic in Germany as an extended SIR model

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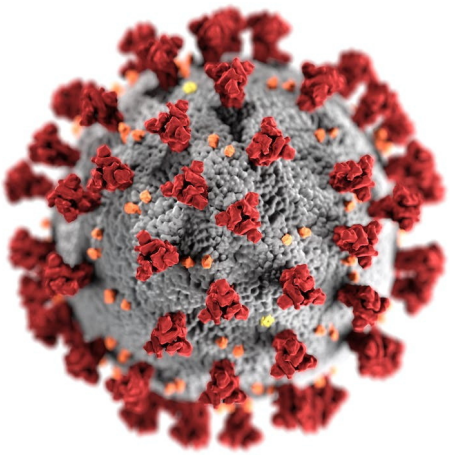

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1 Introduction

Deterministic SIR models are mathematical models that can be used to quantitatively describe the onset, spread and extinction of epidemic infectious diseases. They consist of chained differential or difference equations. In the simplest case, the SIR basic model, the individuals of an infected population are divided into three groups, which are designated *S* (Susceptible), *I* (Infected) and *R* (Resistant, also Removed). The variables *S*, *I*, *R* are on the one hand group designations. In the models, they also have the meaning of continuous or discrete time-dependent random variables, which reflect the number of individuals present in the respective group at a certain time or interval. In the early phase of the Covid-19 pandemic (corona pandemic), SIR models were used to model the course of infection and to estimate the likely success of possible control measures (Wangping et al., 2020; Cooper et al., 2020).

The equations of the SIR models can be solved numerically and then provide bell curves or saturation curves, which can be hyperbolic or sigmoidal, depending on the variables considered and the basic conditions. Under certain conditions, damped oscillations can also be generated, but there are no concrete indications of their occurrence with Covid-19. A single infection wave can already be simulated well with the basic model. Covid-19, however, is a succession of infection outbreaks, with several partly overlapping waves of infection following one another, caused by different types of viruses that have emerged from their precursors through mutations. This behavior cannot be represented by conventional SIR models. This paper describes how the basic SIR model can be extended to reflect the overall course of the corona pandemic in Germany.

Based on the discrete form of the model, it is assumed that in each time step of the pandemic mutations in the virus genome are generated with low probability, which results in escape mutants of the virus bypassing the host's immune system and spreading together with and independently of their precursors in the host population. While the original form of the virus is eliminated by the development of resistance, an escape mutant for which there is initially no resistance can spread unhindered in the population and generate a new wave of infection. Eventually, it is also captured by the immune system and the new wave subsides.

This results in a system of chained difference equations, where each chain link consists of the basic equations of the classical SIR model. The equations can be solved numerically, whereby the parameters must be selected in such a way that the model reflects the observed infection processes as well as possible. With modern spreadsheet software, this task can be accomplished relatively easily and without taking too much time. The required data basis is provided by the PCR tests and corona deaths collected and published weekly by the German Robert Koch Institute (RKI), which is responsible for disease surveillance.

The results show that the model can depict the course of infections and deaths, with no systematic deviation from the data in the case of morbidity and only a slight systematic deviation in the case of mortality. Its informative value goes beyond merely tracing the course of the epidemic. It confirms the plausibility of the basic assumptions made about the mechanism of disease spread. It provides epidemiological indicators such as morbidity and mortality, which can be used to compare the different virus variants that cause the disease and to characterize and classify the pandemic as a whole in comparison to other causes of death. It is able to narrow down the temporal origin of Covid-19 and retrospectively provides an evidence-based assessment of the success of pandemic control by showing how protective measures must change the morbidity and mortality kinetics of the pandemic if they are effective.

2 The disease

2.1 Origin and spread

COVID-19 (coronavirus disease 2019) is a viral infectious disease that was first observed in December 2019 in *Wuhan*, a city with over a million inhabitants in the Chinese province of *Hubei*, developed into a pandemic in China and then spread worldwide. Covid-19 is a zoonotic disease. These are infectious diseases that occur naturally in vertebrates and can be transmitted from animals to humans and vice versa. The World Health Organization (WHO) classified COVID-19 as a "public health emergency of international concern" at the end of January 2020. In February 2020, it defined the acronym "COVID-19" as the official name (CO for corona, VI for virus, D for disease and 19 for the year of the first description). In March 2020, the WHO classified the disease as a pandemic due to its global spread.

2.2 The pathogen

The pathogen, SARS-CoV-2 (severe acute respiratory syndrome coronavirus type 2), is a betacoronavirus. Coronaviruses are enveloped single-stranded RNA viruses (ribonucleic acid viruses). The viral envelope is a spherical outer layer consisting of lipids, a phospholipid bilayer of the original host cell and viral proteins embedded in it. The genome is a single-stranded RNA molecule almost 30 kb (kilobases) long. The virion (virus particle) is 60 - 140 nanometers in size.

2.3 Transmission, symptoms and course of the disease

According to current knowledge infection occurs predominantly through droplet infection. Transmission by smear infection through contact with contaminated surfaces is considered less likely. The time from infection to the appearance of the first symptoms (incubation period) of COVID-19 is five to six days on average. Covid-19 has a broad, non-specific spectrum of symptoms, which often resemble a flu-like infection in milder cases. The clinical picture of the disease is similar to that of atypical pneumonia, which, unlike common pneumonia caused by pneumococci or staphylococci, is caused by viruses, fungi or obligate intracellular bacteria. The course of the disease is non-specific and can vary greatly. The most common symptoms are fever, dry cough and fatigue. Less common are other symptoms such as headache, sore throat and aching limbs or temporary loss of taste and smell. According to studies conducted in China, 55 to 85% of those infected have noticeable symptoms and/or show recognizable signs or typical symptom combinations of COVID-19 disease. The rest are symptom-free (asymptomatic) but can pass on the virus. Around 80% of symptomatic patients have a mild course that does not require hospitalization. In around 14% of cases, the course of the disease is more severe, and in around 5% it is so severe that the patient has to be ventilated in an intensive care unit (Ma et al., 2021). The mortality rate of corona patients who are actively (invasively) ventilated is quite high at 50% or more (Budweiser, 2021). The highest risk of becoming seriously ill is for seniors over 70 and people with pre-existing conditions. The median age of corona deaths is 83 years, which is higher than the general life expectancy of 81 years (Corona Fakten & Fragen, 2023).

2.4 Long Covid

Surviving a Covid-19 infection can have long-term health consequences. This is referred to as Covid-19 long-term syndrome (long covid), also known as post-Covid syndrome (PCS). The symptoms are non-specific, similar to Covid-19 symptoms and, like these, can affect almost all organ systems. Like Covid-19 patients, many PCS sufferers also have concomitant diseases (cardiovascular disease, diabetes, etc.). Given the current state of PCS research, it is not possible to make a reliable PCS diagnosis in individual cases, as causes other than Covid-19 cannot be ruled out with certainty. In the case of symptoms that occur weeks, months or years after a Covid-19 infection and are also relatively non-specific, statistical proof of a connection with a previous Covid-19 disease is also hardly possible. It is necessary to rely on the detection of organic, histological (tissue samples) or biochemical properties that are only or almost only observed after a Covid-19 infection. In principle, the detection of antibodies directed against SARS-CoV-2 in the serum of PCS patients is suitable for this purpose. However, the latter must not have been vaccinated. They should also not have any autoimmune diseases, as antibodies may be present in the serum of these patients that cross-react with the available antibody detection tests. The higher the proportion of people vaccinated against SARS-CoV-2 in the global population, the more difficult it will be to obtain representative statistical samples that meet both requirements (Anaya et al., 2021; Scheibenbogen et al., 2023).

3 Key figures of epidemic infectious diseases

In order to characterize epidemics and compare them with each other and with non-epidemic diseases in terms of their danger, epidemiology uses certain indicators, the most important of which are morbidity, mortality and lethality.

Morbidity

Let G be the size of the German population, which forms the basic population, and $I(t)$ the number of infected persons. The morbidity Mb of G is the fraction of individuals in the population who are infected with the disease at a given time t:

$$Mb(t) = I(t) / G \tag{1}$$

Mortality

The weekly mortality Mw of Covid-19 is the fraction of individuals in the population that die of the disease within a calendar week (Cw):

$$Mw = Tw / G \tag{2}$$

Tw corresponds to the number of corona deaths in the total population reported to the RKI per calendar week. If the recording period is extended to the entire course of a pandemic by cumulating the number of weekly deaths, waves of infection caused by individual virus mutants and epidemics caused by other pathogens can also be compared in terms of mortality. When mortality is mentioned in the future and nothing else is said, weekly mortality is always meant. The reference period for statistical comparisons of different causes of death, including non-epidemic causes, is usually 1 year.

Lethality

Let I be a group of infected persons and T the number of deaths who die or have died from the disease. The lethality L is the quotient of the two values:

$$L = T / I \tag{3}$$

L can be determined by following the fate of each infected person in a selected group until the last of them has either recovered from or died of the disease. Where such data are missing, the lethality of the disease is initially unknown. However, the lethality of an epidemic that follows an SIR model can be calculated using the model. We will return to this when considering the first corona wave.

The lethality defined according to (3) is also referred to as the infection fatality rate (IFR). In epidemiology, the term case fatality rate (CFR) is also used. To determine the CFR, only those infected people who have clear clinical symptoms such as a cough or fever are counted. As many infections with Covid-19 remain asymptomatic, IFR and CFR can differ greatly. It is then important to ensure that the same lethality definitions are used when comparing the lethality of Covid-19 with that of other diseases. Only IFR is used here.

Pervasiveness

When assessing the overall health and economic burden that a pandemic can cause, its degree of spread (also known as pervasiveness) is also important. It corresponds to the spread of the pandemic at a certain point in time, whereby, in contrast to morbidity, cases in the past are also counted. To determine the pervasiveness, it is necessary to know the total number of people infected since the beginning of the epidemic. For SIR-faithful infection histories the pervasiveness can also be calculated using an SIR model.

Prevalence

Let S be the size of a statistical sample from a population of infected individuals and J the number of those, who are infected. The prevalence Pv of the sample is the fraction of infected individuals:

$$Pv = J / S \tag{4}$$

A sample is representative if its prevalence is identical to the morbidity of the population from which it originates, i.e. if $Pv = Mb$. If, in addition, all samples were taken at exactly the same time, the sample provides the morbidity, i.e. the prevalence of the disease in the population at the time the sample was taken. This is also referred to as point prevalence. With very large samples, such as the weekly corona tests published by the RKI, synchronous sampling is not possible. Prevalences determined on this basis therefore represent a temporal average taken over the entire collection period. As long as the time interval of sample collection (approx. 1 week) remains small compared to the period of infection waves (approx. 3 months), the mapping of infection kinetics is not significantly impaired by this circumstance; however, it reduces the data quality and in this respect underlines the value of representative samples planned and evaluated according to the rules of mathematical and medical statistics for epidemic tracking.

7-day incidence

Another key figure for characterizing the infection kinetics of Covid-19 is the 7-day incidence. The nationwide 7-day incidence *In*, which is of exclusive interest here, is calculated using the formula

$$In = 100{,}000 \cdot (J / G) \tag{5}$$

Where J is the total number of infections reported nationwide within a period of 7 days and confirmed by a positive PCR test and G is the population of Germany at the time of data collection. It is therefore the proportion of positives in the population multiplied by 100,000. The test results are passed on by the test laboratories to the responsible health authorities, registered by them and transmitted to the RKI. In the 14th calendar week (*Cw*) of 2020, when the first corona wave had reached its peak, 37,649 positive PCR corona tests and a total of 417,646 tests were reported to the RKI. The positive rate Pr was then 9.01%. The total population of Germany during this period was 83,020,000. This corresponded to a 7-day incidence of $100{,}000 \cdot 37{,}649 / 83{,}020{,}000 = 45$. In general, with $100{,}000 = k$ and $J = PR \cdot S$

$$In = k \cdot Pr \cdot S / G \tag{6}$$

If the PCR tests used to evaluate the sample are error-free and the sample is also representative, the positive rate of the sample, the prevalence of the sample and the morbidity of the population are the same: $Pr = Pv = Mb$. Thus

$$In = k \cdot Mb \cdot S / G \tag{7}$$

Significance of prevalence and 7-day incidence

A comparison of the informative value of prevalence and incidence shows the following: The positive rate of a sample and thus the prevalence is independent of the size of the sample. Although the morbidity of a population can be determined more accurately with large samples than with small samples, the statistical expected value of the prevalence is the same for all sample sizes as long as the morbidity does not change. Even multiple testing of the same test subjects does not change the expected value of prevalence, as it increases J and S in the same proportion.

The situation is different for incidence. As can be seen from the definition equation (7), the 7-day incidence is directly proportional to the size of the sample. Samples of different sizes taken from a population of constant morbidity can therefore have completely different incidences. If we resolve (7) according to Mb, we obtain

$$Mb = (In/k) \cdot (G/S) = (In/k) \cdot Dz \tag{8}$$

with $Dz = G / S$. Dz is the dark figure of the incidence. It indicates the factor by which the incidence divided by k must be multiplied in order to obtain the morbidity of the population. For $G/S = 1$, i.e. the case that the entire population is tested, $Mb = In / k$. Then and only then does the incidence provide the morbidity of the population, except for the constant factor k. In testing practice, S is always smaller, usually very small compared to G. Dz then becomes so large that the attempt to calculate the morbidity from the 7-day incidence without taking it into account gives a completely unrealistic picture of the extent of the pandemic. In the numerical example above, the dark figure is 199 (83,020,000 / 417,646). Without the correction, (8) then results in a morbidity of 0.045% (45 / 100,000), whereas in reality it is 9%.

While representative samples can provide a reliable picture of the spread of epidemic infectious diseases, this is not the case with the 7-day incidence. At best, it can be used to determine whether the number of infected people in a population is rising, stagnating or falling, but if the positive rates of the tests are known, it is not needed for this either. The latter was the case from the outset, as not only the number of positive but also the number of negative tests from each sample and therefore the positive rate was recorded from the outset and published by the RKI, albeit not in a prominent position. Despite its low informative value, the 7-day incidence was used as a decisive criterion by political decision-makers when evaluating preventive measures against the spread of Covid-19.

4 Quality criteria for laboratory diagnostic test procedures

The symptoms of Covid-19 disease are not very specific and are similar to those of other respiratory diseases. For this reason, the reliable detection of a corona infection is based on laboratory diagnostic methods, of which those based on the principle of reverse transcriptase polymerase chain reaction (RT-PCR), or PCR for short (Wikipedia 1, 2023; Wikipedia 2, 2023), are the most common. The corona PCR test reacts to the presence of two nucleotide sequences known as primers in the E gene and RdRp gene of the virus genome. The former encodes a protein of the viral envelope, the latter the viral RNA polymerase, which replicates the RNA genome of the virus during its replication cycle. During the test procedure, the sequence segments of the virus genome located between the primers are copied by the revertase contained in the test mixture, transcribed into DNA and amplified until a concentration is reached that can be detected biochemically. The first PCR tests for the detection of SARS-CoV-2 came onto the market just a few months after the start of the Covid-19 pandemic. The test not only detects current infections, but also inactive viruses and remnants of the virus genome that originate from infections that have already been overcome and are located in the intact genome between the two copies of each primer pair. Despite this disadvantage, it has remained the most sensitive and reliable method for detecting SARS-CoV-2 to date. The corona cases published by the RKI are all PCR-confirmed infections. In order to be able to quantitatively characterize the reliability of a diagnostic test procedure, three main criteria are used in medical laboratory diagnostics: sensitivity, selectivity and the positive or negative predictive value.

4.1 Sensitivity, selectivity and predictive value

The sensitivity *Em* of a test is the probability that an isolate from an infected person will give a positive test result. Mathematically, *Em* is the quotient of the number of true positive (*Rp*) and the sum of the true positive and false negative (*Fn*) individual samples of a statistical sample from an infected population:

$$Em = Rp/(Rp+ Fn) \tag{9}$$

If a test detects all (*Rp* = 1, *Fn* = 0) infected isolates, it has a sensitivity of 100%, if it detects half (*Rp* = 0.5, *Fn* = 0.5), it has a sensitivity of 50%, if it detects none (*Rp* = 0, Fn = 1), it has a sensitivity of 0.

The selectivity *Tr* of a test is the probability that an isolate from a healthy person will give a negative test result. *Tr* is the quotient of the number of true negatives (*Rn*) and the sum of the true negatives and false positives (*Fp*) in a statistical sample from an infected population.

$$Tr = Rn/(Rn + Fp) \tag{10}$$

If a test detects all (*Rn* = 1, *Fp* = 0), it has a selectivity of 100%, if it detects half (*Rn* = 0.5, *Fp* = 0.5), it has a selectivity of 50%, if it detects none (*Rn* = 0, *Fp* = 1), it has a selectivity of 0. *Em* and *Tr* are prevalence-independent quantities that depend only on the biochemical properties of the test.

The positive predictive value *Vp* of the test is the proportion of true positives out of the total number of positives:

$$Vp = Rp/(Rp +Fp) \tag{11}$$

It corresponds to the probability that a positive isolate actually comes from an infected person.

The negative predictive value *Vn* of the test is the proportion of true negatives out of the total number of negatives:

$$Vn = Rn/(Rn + Fn) \tag{12}$$

It corresponds to the probability that a negative isolate actually comes from a non-infected person.

In contrast to *Em* and *Tr*, the predicted values are prevalence-dependent. Their practical significance lies in the fact that they provide a measure of the certainty with which an infection can be detected (*Vp*) or excluded (*Vn*) in a test person. If tests are used to determine the prevalence of a disease, their positive predictive value is the most important factor.

The sensitivity and selectivity power of a test can only be determined empirically by testing an infected population of which the size of all four possible groups *Rp*, *Fp*, *Rn*, *Fn* is reliably known. The lack of such test populations and of studies conducted primarily to standardize PCR corona tests and to determine their quality led to lively, sometimes heated discussions about the value and benefits of corona mass tests in the early phase of the corona pandemic, some of which are still ongoing today (Borger et al., 2020).

4.2 Analytical and clinical test quality

When assessing the sensitivity and selectivity of PCR-based corona tests, a distinction must be made between their analytical and clinical quality. The former refers to the test procedure itself, the quality of the reagents used and the biochemical and biophysical conditions under which the test is performed. In the case of the reagents, the nucleic acid sequence of the PCR primers used is particularly important, as this is decisive for the specificity of the test; in the case of the test conditions, the primer concentrations, the melting temperature set for the PCR cycles and the number of cycles are particularly important.

The analytical quality of the PCR corona test is very good under optimal conditions. Sensitivity and selectivity are close to 100%. Most PCR tests detect 500 - 5000 viral RNA molecules/ml sample fluid and hardly react with non-viral RNA or the RNA of other viruses. The clinical reliability of PCR diagnostics is lower. The clinical significance of a corona test, i.e. the answer to the question of whether a person tested is infected or not, depends not only on the analytical reliability of the test, but also on the biological and technical conditions during the collection, storage and transportation of the samples. It can make a difference whether a sample is taken from the nasal or pharyngeal mucosa and whether the infection is at an early or later stage. Contamination can already occur during sample collection, and the low stability of RNA molecules can lead to the SARS-CoV-2 RNA contained in the samples being partially or completely degraded by the time the sample reaches the test laboratory if they are not cooled sufficiently or stored for too long. The clinical reliability of the tests is therefore significantly lower than the analytical reliability and is unlikely to be more than 80% on average. The selectivity is less impaired and is 98 - 99% even under clinical test conditions (Johe S., 2023; Jarrom J. et al., 2023).

4.3 Prevalence and positive rate of samples

Knowing the sensitivity and selectivity of a corona test used to analyze a statistical sample from an infected population, the prevalence of the disease and the predictive values of the test can be calculated from the positive rate of the sample. In a sample of size *S* from an infected population, let *H* be the healthy, *J* the infected, *P* the test-positive and *N* the test-negative individuals. The following relationships then apply between these variables and the 4 groups *Fp*, *Fn*, *Rp* and *Rn*:

$$J = Rp + Fn \tag{13}$$

$$H = Rn + Fp \tag{14}$$

$$N = Rn + Fn \tag{15}$$

$$P = Rp + Fp \tag{16}$$

$$J + H = N + P = S \tag{17}$$

Substituting (13) and (14) into the defining equations (9) and (10) for *Em* and *Tr* yields

$$Rp = Em \cdot J \tag{18}$$

$$Rn = Tr \cdot H \tag{19}$$

From (16) and (18) we now obtain

$$Fp = P - Em \cdot J \tag{20}$$

and from *(15)* and *(19)*

$$Fn = N - Tr \cdot H \tag{21}$$

Finally, by inserting the right-hand sides of (18) and (21) into the defining equation (9) for *Em*

$$Em = Em \cdot J/(Em \cdot J + N - Tr \cdot H) \tag{22}$$

Solving (22) for J yields

$$J = (Tr \cdot H - N)/(Em - 1). \qquad (23)$$

From *(17)* we have $H = S - J$ and $N = S - P$, thus

$$J = [Tr \cdot (S - J) - (S - P)] / (Em - 1)$$

$$J = (Tr \cdot S - Tr \cdot J - S + P) / (Em - 1)$$

$$J \cdot (Em - 1) = Tr \cdot S - Tr \cdot J - S + P$$

$$J \cdot Em - J + Tr \cdot J = Tr \cdot S - S + P$$

$$J \cdot (Em - 1 + Tr) = Tr \cdot S - S + P$$

$$J = (Tr \cdot S - S + P) / (Em - 1 + Tr)$$

and using $J = Pv \cdot S$ and $P = Pr \cdot S$

$$Pv \cdot S = (Tr \cdot S - S + Pr \cdot S) / (Em + Tr - 1)$$

$$\boldsymbol{Pv = (Pr + Tr - 1) / (Em + Tr - 1)} \qquad \textbf{(24)}$$

This provides a formula for calculating the prevalence from the positive rate of the sample and the key figures *Em* and *Tr* of the test.

The predictive values defined in equations (11) and (12) can also be calculated if the prevalence is known. For the positive predictive value, inserting the right-hand sides of (18) and (20) into the defining equation (11) gives *Vp*:

$$Vp = Em \cdot J / (Em \cdot J + P - Em \cdot J)$$

$$Vp = Em \cdot J / P = Em \cdot Pv \cdot S / PR \cdot S$$

$$Vp = Em \cdot Pv / Pr \qquad (25)$$

Formula (24), when solved for Pr yields

$$Pr = Pv \cdot (Em + Tr - 1) - Tr + 1,$$

which, used in (25) for the positive predictive value, gives the formula

$$\boldsymbol{Vp = Pv \cdot Em / [Pv \cdot (Em + Tr - 1) - Tr + 1)]} \qquad \textbf{(26)}$$

With decreasing prevalence, *Vp* decreases slowly at first and then faster and faster. For $Em = 0.80$ and $Tr = 0.99$, *Vp* is still 90% at a prevalence of 10% (positive rate 8.9%) and only 45% at a prevalence of 1% (positive rate 1.79%). Then 55% of the positive tests are false positives. With a positive rate of 1%, *Pv* and *Vp* both have the value zero. Only noise is then measured. At low prevalences, as they occur at the beginning and end of each wave of infection, the sensitivity and specificity of the diagnostic tests used must be taken into account, if a realistic picture of the course of infection is to be obtained.

5 Course of the epidemic

5.1 Morbidity

The data provided by RKI (RKI 1, 2023) form the basis of the course of the epidemic shown in Figure 1. The data have been published weekly during the pandemic and always refer to a calendar week (*Cw*). In addition to the number of laboratory-confirmed PCR tests reported each week, the tables also contain the total number of tests and the proportion of positives, the quotient of these two variables.

We consider the weekly tests submitted to the RKI as statistical samples whose prevalence can be calculated from the positive rate and the quality criteria *Em* and *Tr* of the PCR test according to formula (24). *Em* and *Tr* are not the same for all tests, as the test is not standardized and many laboratories that do not consistently use the same test kits and test conditions participate in the tests. We assume that the clinical quality of the tests has an average sensitivity of 80% and a selectivity of 99%.

Hundreds of thousands of samples from test centers and laboratories across the country cannot be taken, evaluated and forwarded to the RKI simultaneously. The nationwide prevalence of Covid-19 determined for each calendar week therefore represents an average value of the point prevalence in the calendar week in question. We assume that this value is approximately representative of the morbidity *Mb* of the population. It should therefore apply to every calendar week in the entire observation period:

$$Mb(Cw) \approx Pv(Cw)$$

The nationwide morbidity curve of Covid-19 (Figure 1, green solid line) shows 10 more or less clearly separated waves. Waves 6 and 7 overlap so much that it should not be assumed without further ado that these are 2 different virus mutants in close succession. However, the mapping quality of the pandemic with the SIRTM model (see below) is significantly better if this is assumed.

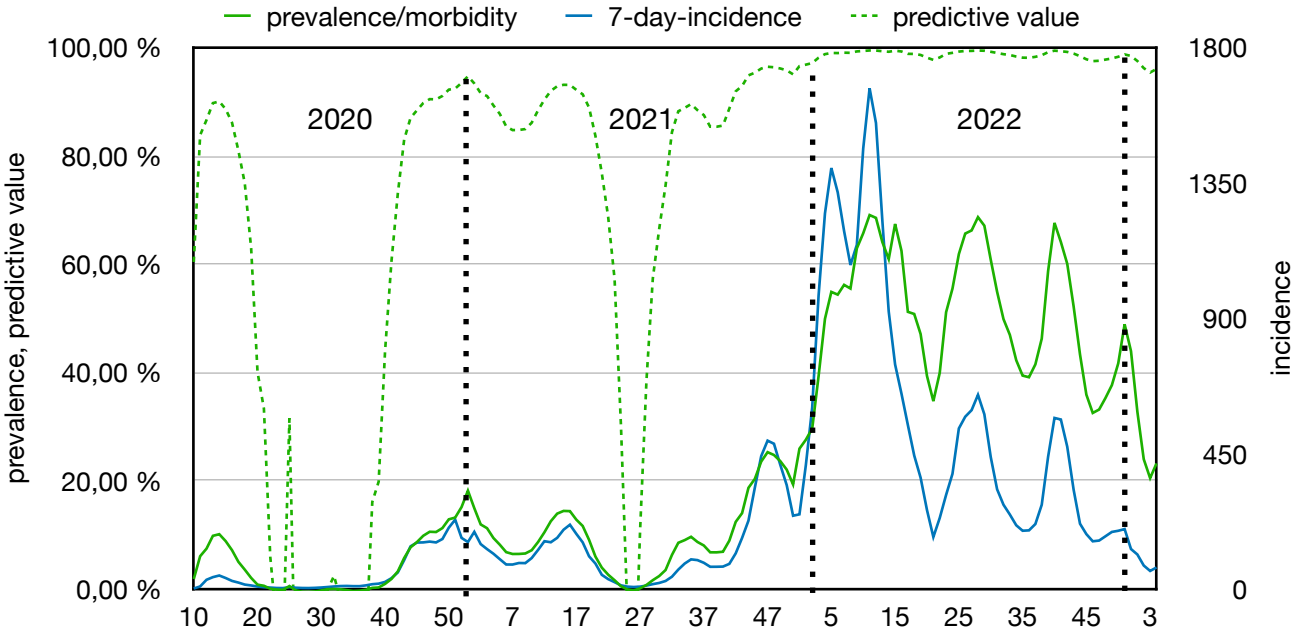

Figure 1: The corona years in Germany. Prevalence, 7-day incidence and predictive value. The positive predictive value of the RT-PCR test is close to 100% at the peak of the waves and decreases very quickly with decreasing prevalence. At a prevalence of 10% it is 90%, at 1% only 45%. A comma is used as a decimal symbol for percentages in graphics and some tables.

The lowest wave of infection reaches its maximum in *Cw* 35/2021 with a morbidity of 9.7%, the highest in *Cw* 15/2022 with a morbidity of 67%. The maximum of the first wave in *Cw* 14 lies in between at 10.1%. This means that at the peak of the first, fourth and seventh waves, 9.7%, 10.1% and 67% of the population were infected with at least one virus variant. What is striking is the massive increase in morbidity, which be-

gins shortly after the fourth wave around *Cw* 37/2021 and ends with the peak of the seventh wave. The subsequent waves are lower, but much higher than the first, and at the end of the observation period the morbidity is still 23.2%. At the beginning of 2023, therefore, twice as many German residents were currently infected with SARS-CoV-2 compared to the peak of the first wave.

The positive predictive value of the PCR test can be calculated using formula (26) for *Em* = 80% and *Tr* = 99% and is shown in the graph as a dashed green line. It is close to 100% at the peak of the waves and decreases very rapidly with decreasing prevalence. At a prevalence of 10% it is 90%, as mentioned above, and at 1% it is only 45%. At values below 1%, there are almost only false positives among the test-positive specimens. Only noise is then measured.

5.2 7-day incidence

The 7-day incidence (Figure 1, blue line) roughly follows the morbidity. It is not immediately apparent from the graph that it rises with increasing sample size, but this becomes clear if you look at the period from *Cw* 20 to *Cw* 40, during which the number of tests rose very sharply (Figure 2). As the scatter diagram shows, the morbidity here shows only random fluctuations. The incidence, on the other hand, increases linearly with the number of tests.

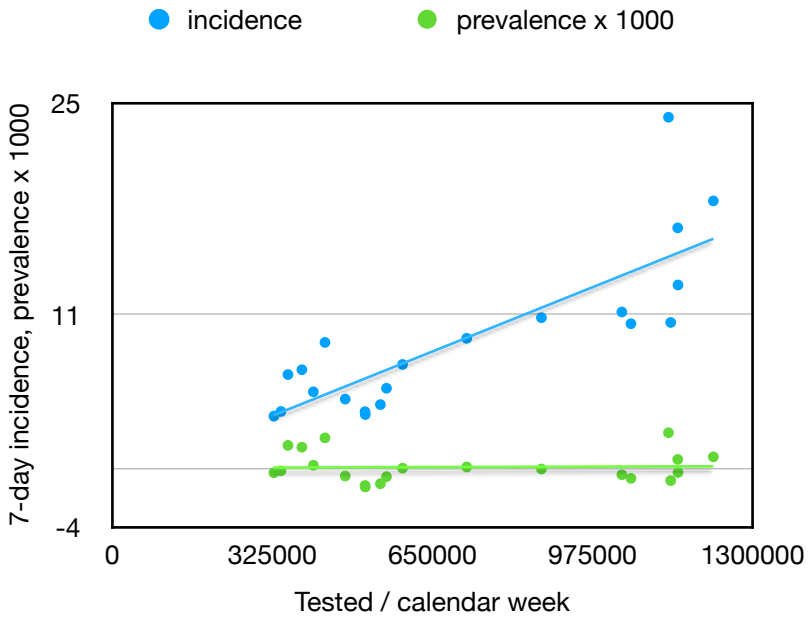

Figure 2: Corona PCR tests, 7-day incidence and prevalence in 2020, calendar week 20 - 40. Prevalences are multiplied by 1000.

5.3 Mortality

The weekly corona deaths registered nationwide by the RKI (RKI 2, 2023) roughly follow the morbidity (Figure 3), although this does not mean that Covid-19 is the primary cause of death in every case. What is striking is the massive increase in weekly mortality during the second wave, which is not accompanied by a corresponding increase in morbidity.

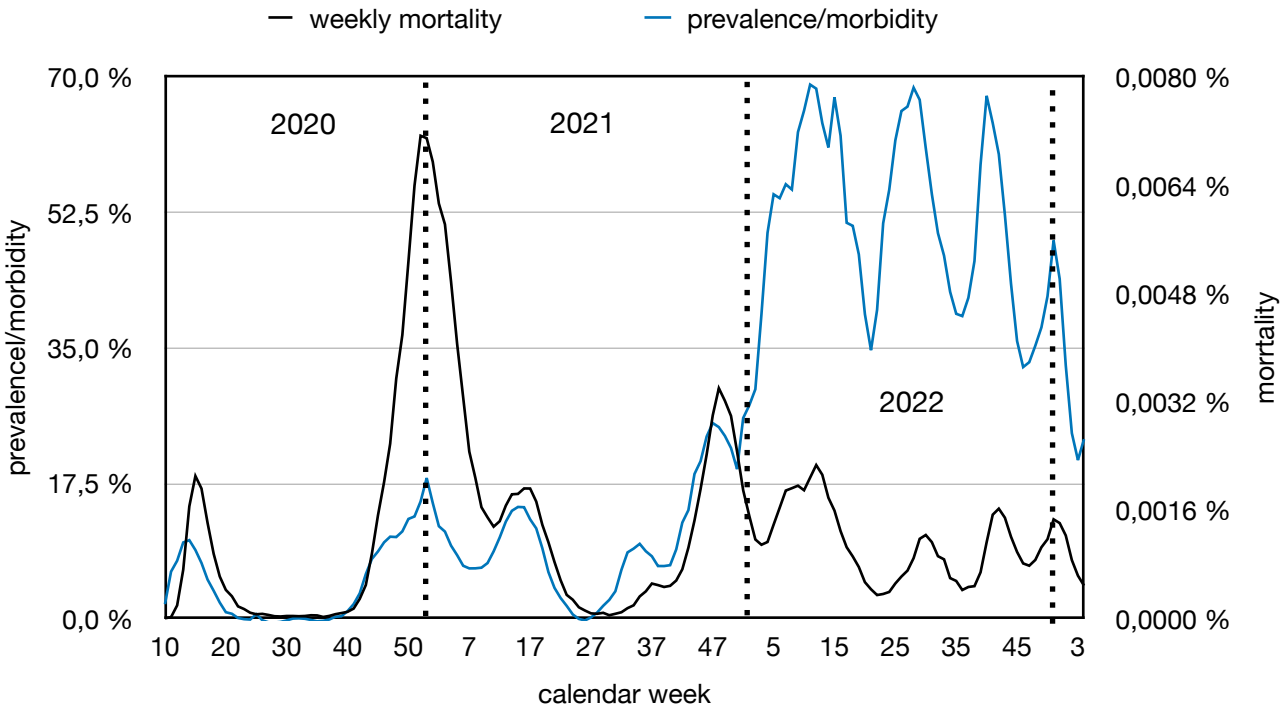

Figure 3: The corona years in Germany; morbidity and weekly mortality. The latter follows morbidity with a time lag of approx. 1 *Cw*.

6 The first corona wave in the SIRT model

SI models are mathematical models that attempt to quantitatively describe the spread of diseases in the population. Many are quite complex. Probably the simplest ones assume a fixed population size, which forms the basic population and which is divided into only two groups, the susceptibles, who are still healthy but susceptible to the disease, and the infected, who are already suffering from the disease. In the case of infectious diseases, which can be fatal on the one hand and in which those who have recovered acquire permanent resistance on the other, there are two further groups, the resistant and the infected, who die from the disease. The latter leave the population.

6.1 Model structure

A simple SIR model is described below, which will be referred to in future as the SIRT model and consists of a population *G*, which forms the basic population, and the 3 subpopulations *S*, *I*, *R*. If an infected person dies of the disease, he or she moves to the group of the dead *T* and thus leaves the population (Figure 4). We make the following assumptions: At each time step, in this case each calendar week, a certain percentage of susceptibles become infected with the disease, while another percentage of infected individuals recover and simultaneously acquire complete and lasting resistance to the disease. The resistant individuals remain in the population but, as the resistance is permanent, they no longer have any influence on the spread of the disease. A further proportion *T* of those infected die from the disease. For a susceptible person to become infected, they must encounter an infected person. If susceptibles and infected persons can move independently of each other, the probability of a susceptible person meeting an infected person by chance and becoming infected is proportional to the product of the total number of susceptibles and the total number of infected persons in the population. The increase in the number of infected persons in a *Cw* is then $a \cdot S_t \cdot I_t$, where *a* is a constant proportionality factor. At the same time, some of the infected people recover and move into the group of resistant people. The loss is proportional to the number of infected people and is $b \cdot I_t$. Another part $c \cdot I_t$ of the infected dies of the disease and leaves the population. This loss is compensated by births, whereby the newborns, since they are not infected and the resistance is not inherited, are exclusively included in the group of susceptibles.

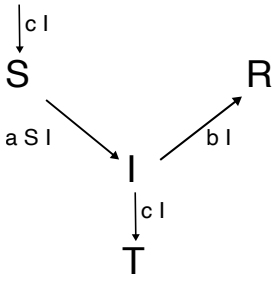

Figure 4: Flow diagram of the SIRT model. The inflow/outflow terms of the equation system are written unsigned on the reaction arrows.

6.2 Basic assumptions and equations

To describe the infection kinetics, we thus obtain a system of difference equations with the discrete variables *S*, *I*, *R*, *T*, *D* and the constants *a*, *b*, *c*:

$S_{t+1} = S_t - a \cdot St \cdot It + c \cdot I_t$

$I_{t+1} = I_t + a \cdot St \cdot It - b \cdot I_t - c \cdot I_t$

$R_{t+1} = R_t + b \cdot I_t$

$T_{t+1} = c \cdot I_t$

$D_{t+1} = D_t + c \cdot I_t$

D_t is the cumulative number of corona deaths at time *t* since the beginning of the pandemic. As the loss of infected people due to the deceased is compensated for by the influx of newborns, the size of the population remains constant. If *G* remains constant and *S* and *I* are known, *R* can be calculated as the difference to *G*. The third difference equation is then

$R_{t+1} = G - S_{t+1} - I_{t+1},$

and you have the equation system

$S_{t+1} = S_t - a \cdot S_t \cdot I_t + c \cdot I_t$ (1)

$I_{t+1} = I_t + a \cdot S_t \cdot I_t - b \cdot I_t - c \cdot I_t$ (2)

$$R_{t+1} = G - S_{t+1} - I_{t+1} \quad (3)$$

$$T_{t+1} = c \cdot I_t \quad (4)$$

$$D_{t+1} = D_t + c \cdot I_t \quad (5)$$

In this system, I_t corresponds to the morbidity and T_t to the weekly mortality of the population.

If D and R are known, the lethality of the disease can also be determined. By definition, the lethality L_t of Covid-19 at time t

$$L_t = D_t / Ik_t$$

Ik_t is the cumulative number of infections counted since the start of the pandemic. The latter is equal to the sum of those who have become resistant and those who have died at this point in time, as in the model every infected person either becomes resistant or dies. This means that

$$Ik_t = (R_t + D_t)$$

$$L_t = D_t / (R_t + D_t) \quad (6)$$

In the calculation, the number of deaths in the denominator of the quotient is of little significance due to the low weekly mortality. The formula implies that the lethality of the disease changes over the course of the pandemic. In the first few days of the pandemic, when there are infected people but no deaths, the lethality is 0 and begins to increase as the pandemic progresses. Since D and R, as will be shown, both approach a limit value, the resting state of the system, this also applies to L. Once the pandemic has subsided and the resting state of the system has been reached, the lethality no longer changes. The limit value of L is therefore a measure of the lethality of the disease.

The pervasiveness V_t corresponds to the spread of the pandemic at a certain point in time, whereby in contrast to morbidity, past cases of those who have become resistant are also counted:

$$V_t = I_t + R_t = G - S_t \quad (7)$$

We set

$$S_t + I_t + R_t = G = 1 = 100\% \quad (8)$$

All values thus become relative numbers between 0 and 1 or percentages.

Iterative solution of the equation system

Equations (1) - (5) are recursion formulas with which, starting from certain initial values S_0, I_0, R_0, T_0, D_0, the values of the variables in Cw_{t+1} can be calculated for each Cw from those of the preceding Cw_t. Initial values and model parameters must now be selected so that the calculated values of the variables I and T come as close as possible to the observed values of morbidity Mb and weekly mortality Mw and reflect the actual course of the epidemic as closely as possible. When the pandemic begins, there are still no resistant cases and no deaths, which means that $R_0 = 0$, $T_0 = 0$ and $D_0 = 0$. However, there must be at least one infected person in the population for Covid-19 to spread. One infected person among 83 million, the approximate population of Germany during the corona years, corresponds to an initial value I_0 of 1 / 83 million, i.e. $1.2 \cdot 10^{-8}$. By using this value as the starting value of I_0, one accepts the idea that the pandemic is due to a single individual who migrated into the population months before the first PCR tests or who emerged there by mutation from an endemic and previously inconspicuous SARS-Cov-2 strain. If R_0, T_0, D_0 and I_0 are known, S_0, the missing starting value for the susceptibles, results from the conservation law (7). It will be shown that the first wave of the corona pandemic can be mapped well if the start event is moved to week 32 of 2019 and the values 1.7, 1.05 and 0.00021 are used for the parameters a, b and c. The following then applies for the first calculation step

$$S_0 = 1 - 1.2 \cdot 10^{-8} - 0$$

$$I_0 = 1.2 \cdot 10^{-8}$$

$R_0 = 0$

$T_0 = 0$

$D_0 = 0$

$S_1 = S_0 - 1.7 \cdot S_0 \cdot I_0 + 0.00021 \cdot I_0$

$I_1 = I_0 + 1.7 \cdot S_0 \cdot I_0 - 1.05 \cdot I_0 - 0.00021 \cdot I_0$

$R_1 = 1 - S_1 - I_1$

$T_1 = 0.00021 \cdot I_0$

$D_1 = D_0 + 0.00021 \cdot I_0$

Due to the considerable computational effort involved, it would now be quite unattractive to try to perform the iteration with a pocket calculator, especially when you consider that good parameter values are initially unknown and the calculation process has to be run several times until a combination is found with which the data can be reproduced approximately correctly. Modern spreadsheets make most of this work superfluous. Not only can the difference equations be solved numerically, but the resulting curves can also be displayed graphically. The use of spreadsheets for modeling epidemics and related dynamic processes has been described in detail several times (e. g. Ableitinger, Ch., 2008), which is why details are omitted here. With *Numbers*, *Apple's* spreadsheet application, which is used here throughout, the following picture emerges for the course of the first corona wave:

6.3 The first wave of infection

Morbidity

The pandemic (Figure 5) begins around *Cw* 32/2019 with the immigration of an infected person into the population or the mutation of an endemic, previously harmless coronavirus strain in a previously healthy individual, who thus becomes a carrier. This is followed by a lag phase lasting several months, during which the virus can spread unnoticed, as the symptoms of the disease, if they occur at all, are non-specific and cannot

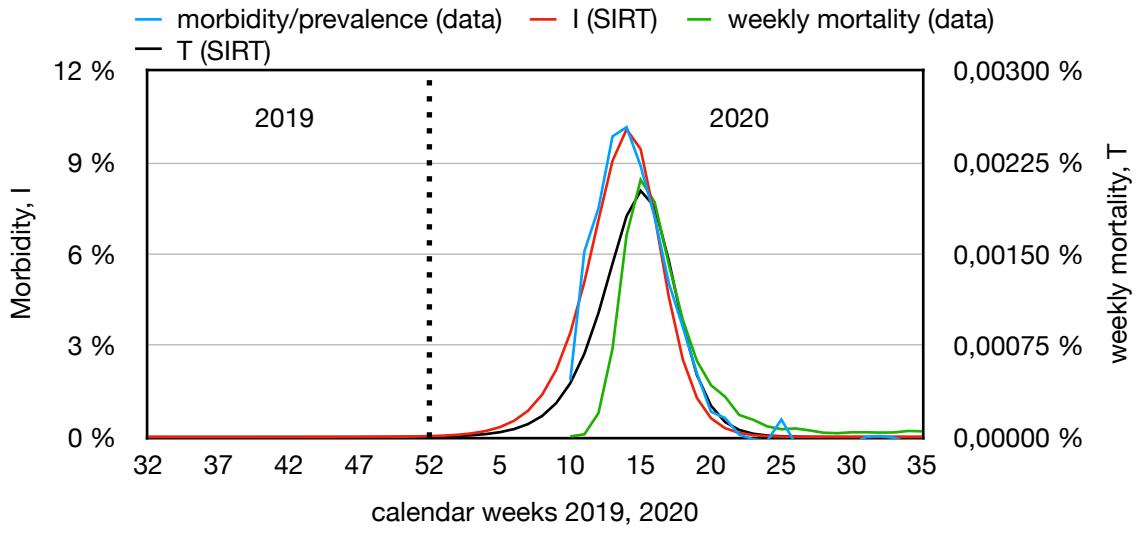

Figure 5: The first Corona wave (*Cw* 32/2019 to *Cw* 35/2020). Curve approximation with the SIRT-Model. Parameter values: $a = 1.70$, $b = 1.05$, $c = 0.00021$. Initial values: $S_0 = 1 - 1.20 \cdot 10^{-8}$, $I_0 = 1.02 \cdot 10^{-8}$, $R_0 = 0$, $T_0 = 0$, $D_0 = 0$.

be reliably distinguished from those of other respiratory diseases. With the introduction of PCR technology in *Cw* 10/2020, the disease will be detectable by laboratory diagnosis. The morbidity of the population has reached approx. 2% at this point. The spread now follows a bell curve, which reaches its maximum in *Cw*

14/2020 at a morbidity of 10% and then begins to fall. In *Cw* 20/2020, morbidity is less than 1%. In the model, it continues to fall asymptotically towards zero and has fallen below the initial value in *Cw* 38/2020. The pandemic ends.

Mortality

Weekly mortality (Figure 5) follows morbidity with a time lag of approx. 1 *Cw*, which roughly corresponds to the average duration of the disease. The maximum is reached at 0.0020% in week 15.

Resting state

The course of the curve (Figures 6, 7) shows that all variables converge towards limit values. It can also be formally proven that these exist (e. g. Schramek P., 2022). However, the homologous differential equations must then be used and analyzed instead of the difference equations, but this is not absolutely necessary here, especially since the convergence can be seen. The resting positions against which the variables converge are in the vicinity of 30% (*S*), 0% (*I*), 70% (*R*), 0% (*T*), 0.013% (*D*). During the first corona wave, 70% of the population became infected and either became immune or died. The lethality of the first virus type is 0.019% and its pervasiveness was 70%.

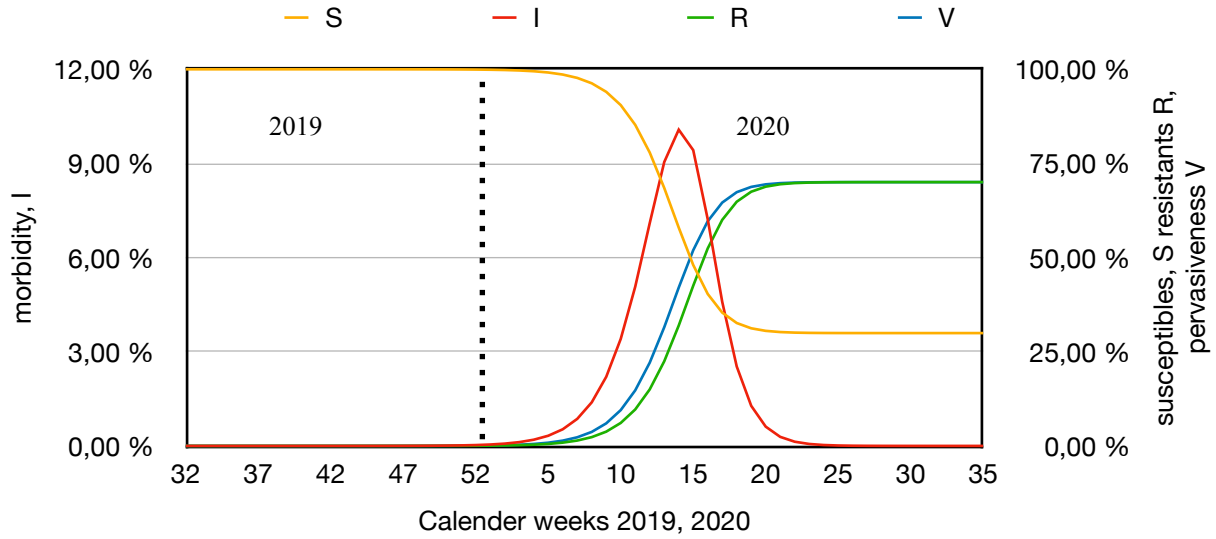

Figure 6: The first corona wave in the SIRT model. Setting the equilibrium. The system converges towards a stable resting state. Once this is reached, there are no more new infections and the population consists only of susceptible and resistant individuals. *S* susceptibles, *I* infected (morbidity), *R* resistants, *V* pervasiveness. Initial and parameter values as in Figure 5.

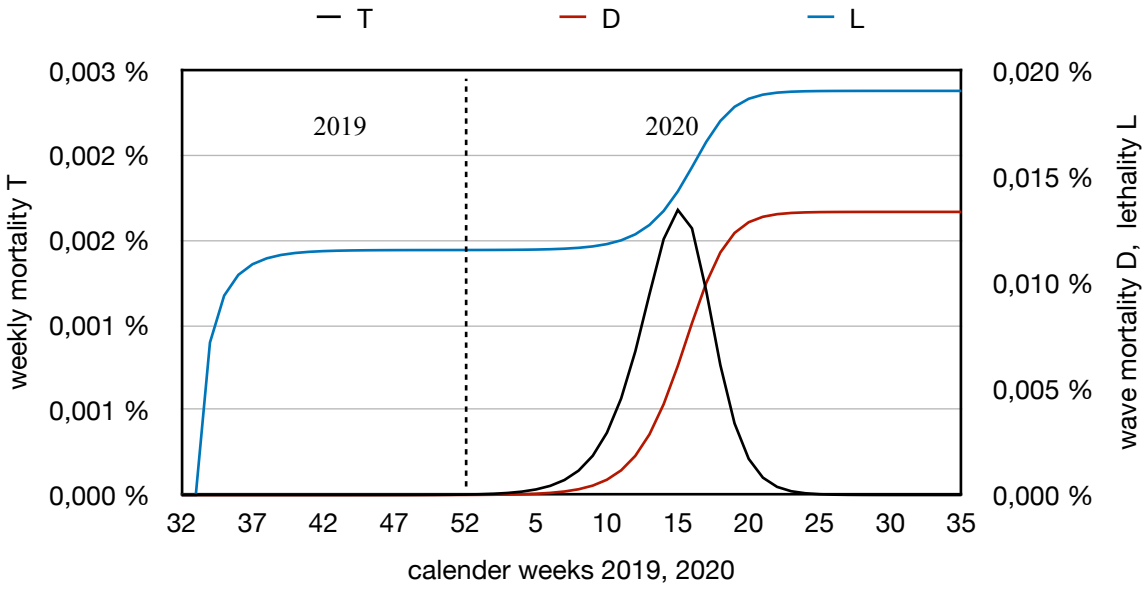

Figure 7: Weekly mortality *T*, wave mortality *D* and lethality *L* of Covid-19 in the first corona wave in the SIRT model. Once the quiescent state is reached, 0.013% of the population has died and the lethality of the wave is 0.019%. Initial and parameter values as in figures 5 and 6.

7 The SIRTM-Model

7.1 Model structure

7.2 Basic assumptions and equations

So far, only the first wave of the corona pandemic has been considered. However, the latter is a consequence of waves of infection caused by different subtypes of the SARS-CoV-2 virus, which differ due to mutations in the spike protein gene of the virus. They change the immunogenic properties of the viral envelope and thus enable the virus to undermine the immune protection built up against infections that have already been overcome. If we want to map not only individual waves of infection, but the entire pandemic, we must take this ability of the virus into account. We make the following simplifying assumptions:

1. As already described, the pandemic begins with the immigration of an infected person into the population or the mutation of an endemic, previously harmless coronavirus strain in a previously healthy individual, who thus becomes a carrier.
2. At each stage of the pandemic, mutations in the replication cycle of the virus cause a small proportion of infected individuals to become carriers of one or more SARS-CoV-2 escape mutants. In the latter case, the mutations do not have to be identical, i.e. they do not have to occur at the same position in the nucleotide sequence of the spike protein gene. It is sufficient if they have the common property of being able to undermine the resistance built up by their host due to an infection that has already been overcome. This enables them to multiply unhindered until the immune system reacts.
3. Each new type of virus is created by mutation(s) in the population of its immediate predecessor.
4. Once the disease has been overcome, each virus type generates a complete resistance specific to it, which is maintained at least until the end of the observation period.
5. Each individual can be infected by more than one virus strain.
6. The virus strains circulating in a population spread independently of each other.
7. The values of all model parameters remain constant throughout the pandemic.

The resulting SIRTM model of the corona pandemic is a system of difference equations chained with the mutation term $d_n \cdot I_{n,t}$ (n = 2,...10), where each chain link consists of equations (1) - (5) of the SIRT model (Figure 8):

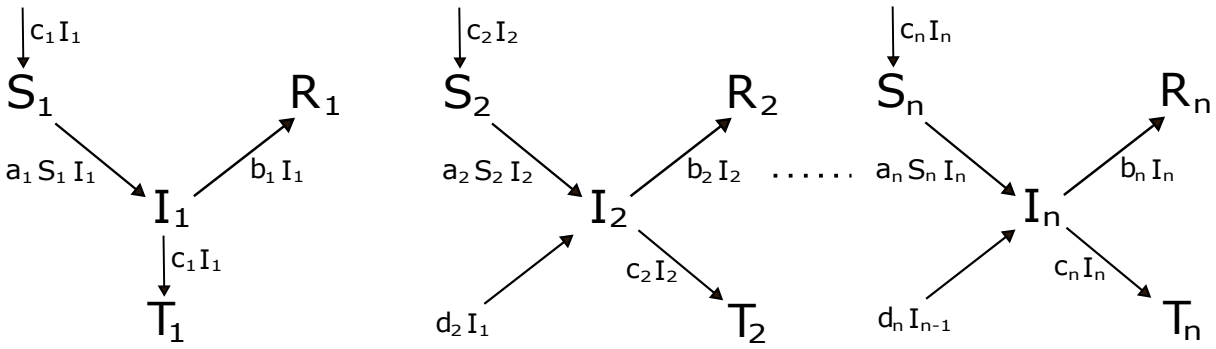

Figure 8: Flow chart of the SIRTM model.

The following equations result from the flow diagram:

$$S_{1,t+1} = S_{1,t} - a_1 \cdot S_{1,t} \cdot I_{1,t} + c_1 \cdot I_{1,t}$$

$$I_{1,t+1} = I_{1,t} + a_1 \cdot S_{1,t} \cdot I_{1,t} - b_1 \cdot I_{1,t} - c_1 \cdot I_{1,t}$$

$$R_{1,t+1} = 1 - S_{1,t+1} - I_{1,t+1}$$

$$T_{1,t+1} = c_1 \cdot I_{1,t}$$

$$D_{1,t+1} = D_{1,t} + c_1 \cdot I_{1,t}$$

$$S_{2,t+1} = S_{2,t} - a_2 \cdot S_{2,t} \cdot I_{2,t} + c_2 \cdot I_{2,t}$$

$$I_{2,t+1} = I_{2,t} + a_2 \cdot S_{2,t} \cdot I_{2,t} - b_2 \cdot I_{2,t} - c_2 \cdot I_{2,t} + d_2 \cdot I_{1,t}$$

$$R_{2,t+1} = 1 - S_{2,t+1} - I_{2,t+1}$$

$$T_{2,t+1} = c_2 \cdot I_{2,t}$$

$$D_{2,t+1} = D_{2,t} + c_2 \cdot I_{2,t}$$

……

$$S_{10,t+1} = S_{10,t} - a_{10} \cdot S_{10,t} \cdot I_{10,t} + c_{10} \cdot I_{10,t}$$

$$I_{10,t+1} = I_{10,t} + a_{10} \cdot S_{10,t} \cdot I_{10,t} - b_{10} \cdot I_{10,t} - c_{10} \cdot I_{10,t} + d_{10} \cdot I_{9,t}$$

$$R_{10,t+1} = 1 - S_{10,t+1} - I_{10,t+1}$$

$$T_{10,t+1} = c_{10} \cdot I_{10,t}$$

$$D_{10,t+1} = D_{10,t} + c_{10} \cdot I_{10,t}$$

7.3 Calculation of the pandemic course

SARS-CoV-2 mutants differ essentially only in the sequence of the envelope proteins, with the spike protein gene playing the decisive role in the infectivity of the mutants. The commonly used PCR tests do not distinguish the virus mutants because the nucleotide sequences of the PCR primers used are not located in the spike protein gene, but in genes whose sequence has been much more conserved in evolution than that of the spike protein gene.

The tests are positive if an individual sample is infected with at least one virus variant and provide an overall morbidity, which is made up of the proportions of the individual virus variants circulating in the population at the time of sampling. However, if multiple infections occur, the overall morbidity cannot simply be determined by adding the morbidity of the individual waves. If you try to do this, you will quickly realize that you will not get a particularly good representation of the data if the waves overlap considerably. An example: In *Cw* 28/2022, the maximum of the 8th wave, the overall morbidity according to the PCR data was 69%, the morbidity of virus variant 7 was 11% and that of variant 8 was 63%. The addition of both values yields 74%. The reason for the difference is simple: people infected with both virus variants are only counted once during testing, but belong to both waves and are therefore added together twice when the individual values are added. The overall morbidity is overestimated, and the error is greater the higher the proportion of those infected twice in the total number of infected people.

This can be avoided if the morbidities are interpreted as infection probabilities. A morbidity of 69% means that there is a 69% probability that a PCR sample from a randomly selected individual in the population will be positive. When testing each individual sample, 4 elementary events can occur:

i_7:The sample is infected with virus variant 7.
$\bar{i}_7$: The sample is not infected with virus variant 7.

i_8: The sample is infected with virus variant 8.
$\bar{i}_8$: The sample is not infected with virus variant 8.

In addition, 2 compound events can occur:

$i_7 \cup i_8$: i_7 or i_8; the sample is infected with variant 7 or 8 or both.
$\bar{i}_7 \cap \bar{i}_8$: The sample is not infected by either type of virus.

$\bar{i}_7$, $\bar{i}_8$ are the counter-events of i_7 and i_8. $\bar{i}_7 \cap \bar{i}_8$ is the counter-event of $i_7 \cup i_8$. Since a single sample cannot be infected and uninfected at the same time, i.e. an event cannot occur together with its counter-event, the two are incompatible (disjunct) and their probabilities of occurrence always add up to 1.

$$W(i_7) + W(\bar{i}_7) = 1 \quad (1)$$

$$W(i_8) + W(\bar{i}_8) = 1 \quad (2)$$

$$W(i_7 \cup i_8) + W(\bar{i}_7 \cap \bar{i}_8) = 1 \quad (3)$$

We have assumed that the virus mutants circulating in a population, once created, can spread independently of each other, i.e. that i_7 and i_8 and thus also the counter-events are stochastically independent. The probability W that a sample is not infected is then, according to the product rule of probability calculation, the product of the individual probabilities:

$$W(\bar{i}_7 \cap \bar{i}_8) = W(\bar{i}_7) \cdot W(\bar{i}_8) \quad (4)$$

The probability W that a sample is infected follows from (3) and (4)

$$W = W(i_7 \cup i_8) = 1 - W(\bar{i}_7) \cdot W(\bar{i}_8). \quad (5)$$

From this and from (1) and (2) follows

$$W = 1 - (1 - W(i_7)) \cdot (1 - W(i_8))$$

and by replacing W with the total morbidity I and $W(i_7)$, $W(i_8)$ with the morbidities I_7, I_8 of the 7th and 8th wave of infection

$$I = 1 - (1 - I_7) \cdot (1 - I_8). \quad (6)$$

With the figures given above for I_7 and I_8 from *Cw* 28/2022 of 11% and 63%, the total morbidity in this *Cw* is now 67%, which is much closer to the PCR data (69%) than the addition of I7 and I8 (74%).

The product rule for the probability of two stochastically independent random events can be generalized. The following applies to the probability of the joint occurrence of n independent events in a random experiment

$$W(i_1 \cap i_2 \cap i_3 \ldots \cap i_n) = W(i_1) \cdot W(i_2) \ldots W(i_n), \quad (7)$$

which gives the final formula for the total morbidity generated by the 10 corona waves in our model:

$$I = 1 - (1 - I_1) \cdot (1 - I_2) \ldots \cdot (1 - I_{10}) \quad (8)$$

Just as multiply infected persons are only counted once in the PCR tests, multiply infected corona deaths are also only counted once. For the total weekly mortality, the following therefore applies by analogy with (8)

$$T = 1 - (1 - T_1) \cdot (1 - T_2) \ldots \cdot (1 - T_{10}) \quad (9)$$

The following applies accordingly for individuals that have become resistant to at least one virus subtype

$$R = 1 - (1 - R_1) \cdot (1 - R_2) \ldots \cdot (1 - R_{10}) \quad (10)$$

and for deceased persons who have been infected at least once since the start of the pandemic

$$D = 1 - (1 - D_1) \cdot (1 - D_2) \ldots \cdot (1 - D_{10}). \quad (11)$$

As with the first wave, the following applies to the overall lethality of the pandemic

$$L = D / (R+D) \quad (12)$$

and for the pervasiveness

$$V = I + R \quad (13)$$

If the variables of the SIRTM model are interpreted as probabilities, the previously unconsidered proportion S of uninfected persons susceptible to all virus variants can also be calculated. In a sample, let S_i be the proportion of individuals susceptible to the ith virus variant and s_i the event that a tested individual is susceptible to this variant. Then the probability of s_i

$$W(s_i) = S_i, \ (i = 1,2,..n)$$

Because of the assumed stochastic independence of the s_i, the multiplication theorem (7) then applies to the probabilities and thus

$$S = W(s_1 \cap s_2 \cap s_3 ... \cap s_n) = W(s_1) \cdot W(s_2) ... \cdot W(s_n)$$

thus

$$S = S_1 \cdot S_2, ... S_n \quad (14)$$

The index t is omitted from these formulas for the sake of simplicity. They can be used to calculate the values of overall morbidity, overall weekly mortality and overall lethality of the pandemic resulting from the superimposition of the individual waves. These terms are meant in future when referring to the entire pandemic only in terms of morbidity, mortality and lethality. When iteratively solving the equations of the SIRTM model, it is now important to select the model parameters in such a way that the calculated values for I and T match the data as closely as possible. The parameter values and curves found are summarized in Table 1 and Figures 9 and 10.

wave	model parameters			
	a	*b*	*c*	*d*
1	1.755	1.1	0.00021	-
2	0.61	0.33	0.00052	0.00006
3	1.24	0.69	0.00009	0.000000023
4	1.92	1.23	0.00005	0.00000001
5	0.91	0.38	0.00013	0.04
6	0.78	0.16	0.0023	0.00045
7	0.75	0.12	0.000033	0.0011
8	0.72	0.1	0.000013	0.00006
9	0.95	0.17	0.000023	0.00000033
10	1.12	0.37	0.000035	0.00005

Tab. 1: Model parameters of the SIRTM model for mapping the Covid-19 pandemic 2020 - 2022. *d* is the fraction of the population of the respective virus type that forms immune escape mutants per calendar week. For the 10 virus types, this results in an average mutation rate of 5.87 - 10^{-4} / *Cw*.

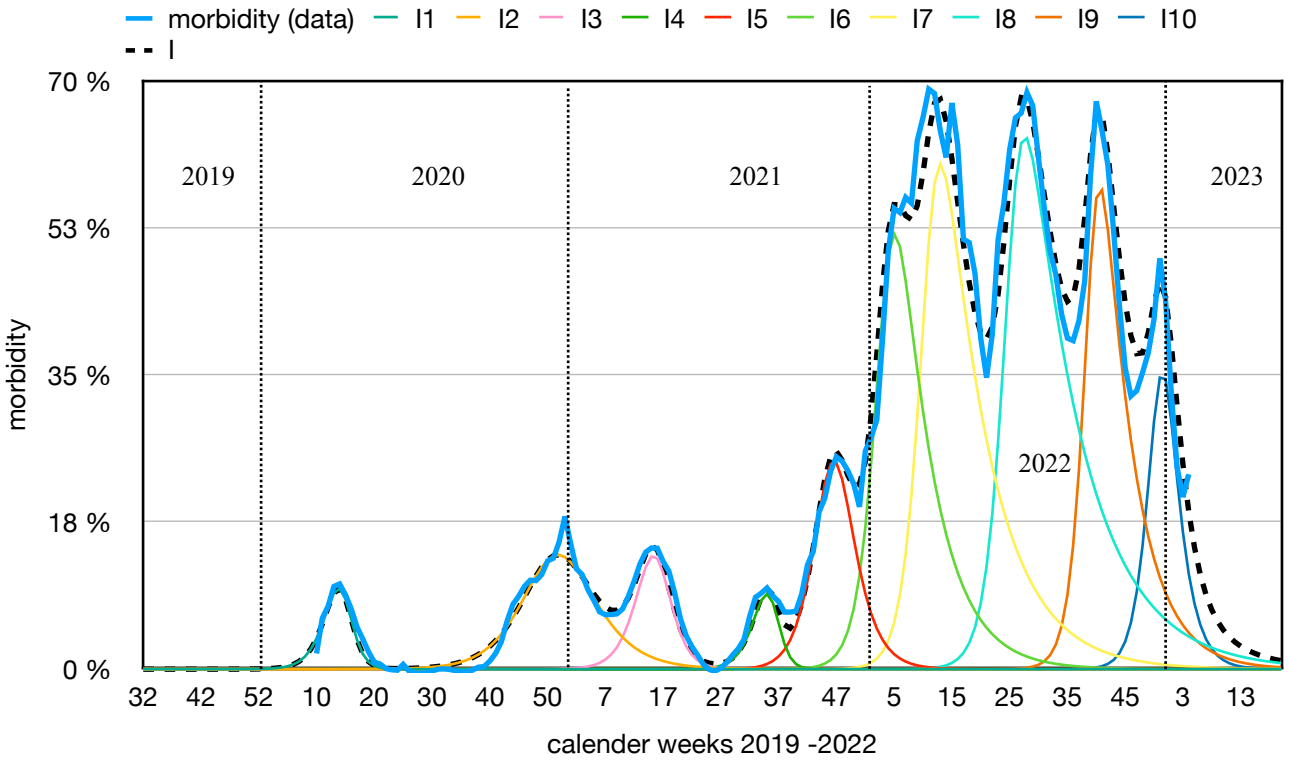

Figure 9: The first corona years (*Cw* 32/2019 - *Cw* 52/2022) in the SIRTM model. Total morbidity I calculated with SIRTM for 10 consecutive virus mutants. Parameter values see Table 1. Initial values: $S_{I,0} = 1 - 1.2 \cdot 10^{-8}$, $I_{I,0} = 1.2 \cdot 10^{-8}$, $R_{I,0} = 0$, $T_{I,0} = 0$, $D_{I,0} = 0$.

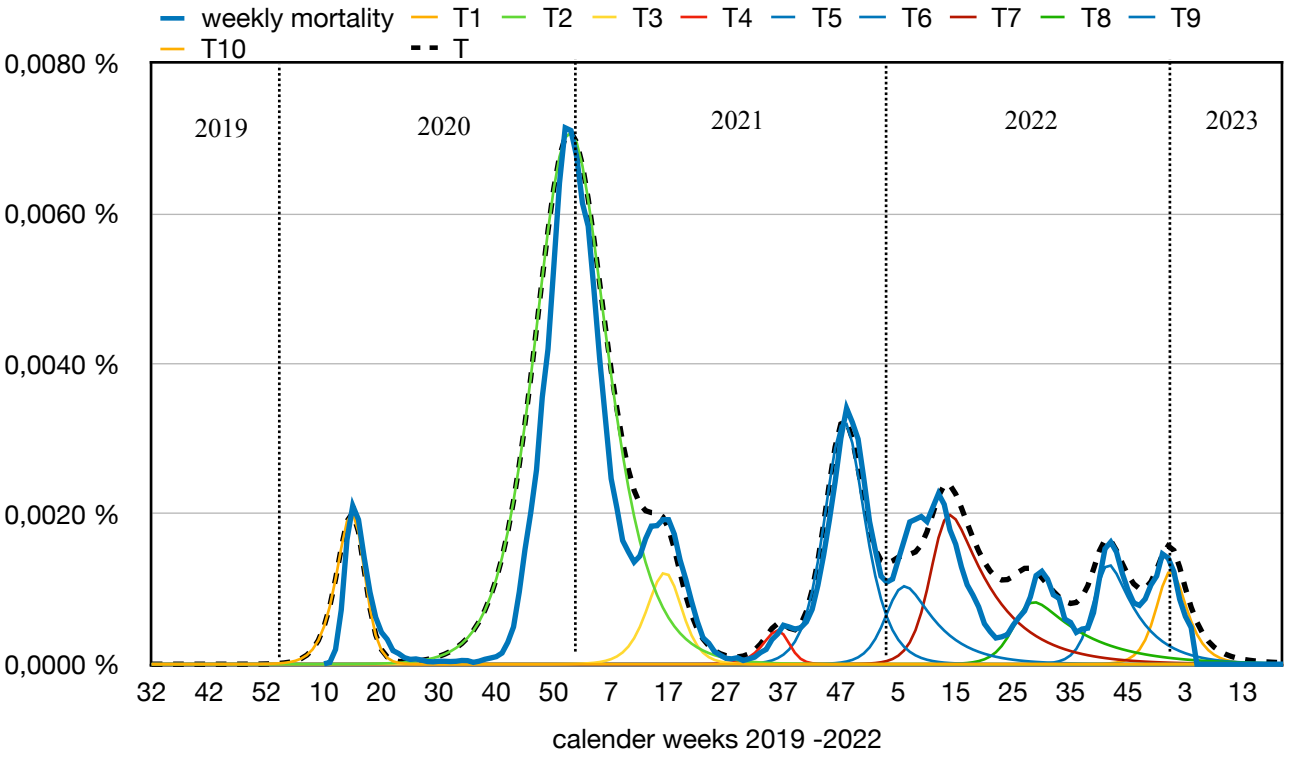

Figure 10: The first corona years (*Cw* 32/2019 - *Cw* 52/2022) in the SIRTM model. Total mortality T calculated with SIRTM for 10 consecutive virus mutants. For parameter and initial values, see Figure 9.

8 Model and reality

8.1 The quality of the image

Visual comparison of the curves

If we compare the sum curve of morbidity calculated according to (8) with the PCR data (Figure 9), we see that the SIRTM model reflects the course of infection well. The deviations between the empirically determined course of infection *Mb* and the model function *I* appear to be random and show no signs of a systematic difference. In the case of mortality (Figure 10), the cumulative curve is slightly higher than the observed corona mortality. However, here too, the position and height of the maxima of the calculated and observed mortality curves are in good agreement. The deviations do not exceed 13% on average.

Linear regression analysis

A more precise assessment of the mapping quality is obtained using linear regression. This involves checking whether there is a linear relationship between two variables *X* and *Y* of the general form

$$Y = b + a \cdot X + \varepsilon \tag{15}$$

with

$$Y = \hat{Y} + \varepsilon \tag{16}$$

X is an independent, non-stochastic discrete variable that can take the values $x_1,...x_n$. *X* can be dependent on other variables, e.g. time, but not on *Y*. *Y* is a discrete observable random variable dependent on *X* with the values (realizations) $y_1, y_2,... y_n$. ε, $\varepsilon = \varepsilon_1, \varepsilon_2,... \varepsilon_n$, is an observation error that occurs when *Y* is measured. The ε_i are stochastically independent, non-calculable random variables and are called residuals. $\hat{Y}$, $\hat{Y} = (\hat{y}_1, \hat{y}_2, ...\hat{y}_n)$ is the "true" value of *Y* calculated with the regression corrected for the observation error. Equating the right-hand sides of (15) and (16) provides the equation of the regression line with the parameters *a* and *b*:

$$\hat{Y} = b + a \cdot X \tag{17}$$

In simple linear regression using the least squares method (Ziegenhagen U., 2023), the parameters *a*, *b* are selected so that the sum *QS* of the squares of deviation of the observed, erroneous values y_i from their true values $\hat{y}_i$ is a minimum:

$$QS = min \sum_{i=1}^{n} \varepsilon_i^2 = min \sum_{i=1}^{n} (y_i - \hat{y}_i)^2 \tag{18}$$

The result of the calculation not performed here is the following values for the regression coefficients *a*, *b*

$$a = \frac{\sum_{i=1}^{n} x_i y_i - \bar{x} n \bar{y}}{\sum_{i=1}^{n} x_i^2 - \bar{x} \sum_{i=1}^{n} x_i} \tag{19}$$

$$b = \bar{y} - a\,\bar{x}. \tag{20}$$

In our case, since the model is intended to represent the true morbidity, $Mb \approx I$ must apply as precisely as possible. The regression line should therefore have a slope of 1 and pass through the origin of the coordinates, i.e. $a = 1$, $b = 0$. The result can be easily visualized by using the spreadsheet to plot the observed morbidity and the morbidity calculated with the model in a scatter plot and drawing the regression line (Figure 11). In the case of morbidity, the spreadsheet provides the value 0.9899 for the slope *a* of the regression line and the value 0.0002 for the absolute term *b*. The equation of the regression line is thus

$$\hat{Mb} = 0.9899 \cdot I - 0.0002. \tag{21}$$

The model provides an almost perfect reproduction of the corona PCR data.

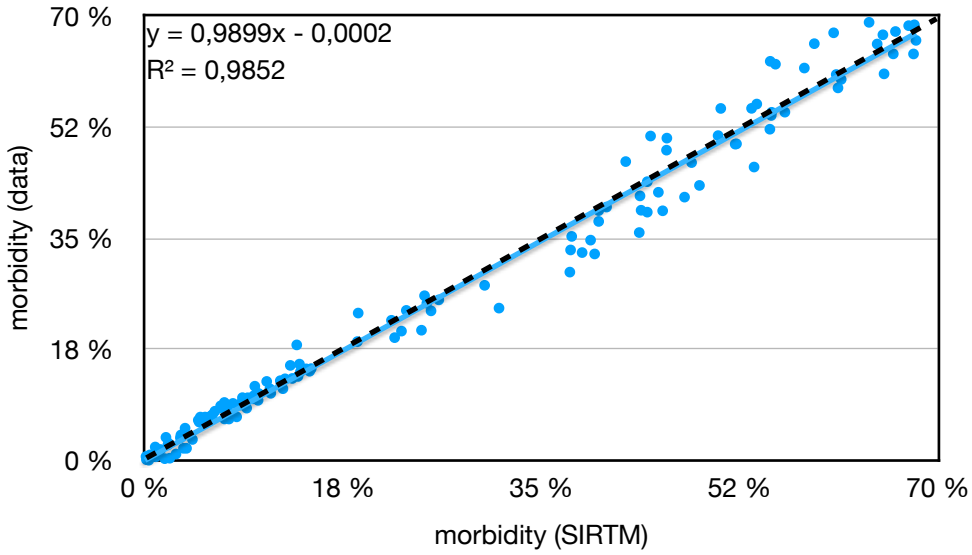

Figure 11: Regression analysis of the SIRTM model. The distribution kinetics of corona morbidity is fully explained by the model. The coefficient of determination has a value of 0.985. A systematic deviation of the regression line (blue) from the theoretically expected straight line through the origin with slope 1 (black) is not recognizable.

For mortality (Figure 12), the value for *a* is 0.8755 and for *b* $1.23 \cdot 10^{-6}$. The equation of the regression line is thus

$$\hat{Mw} = 0.875 \cdot T - 1.23 \cdot 10^{-6} \qquad (22)$$

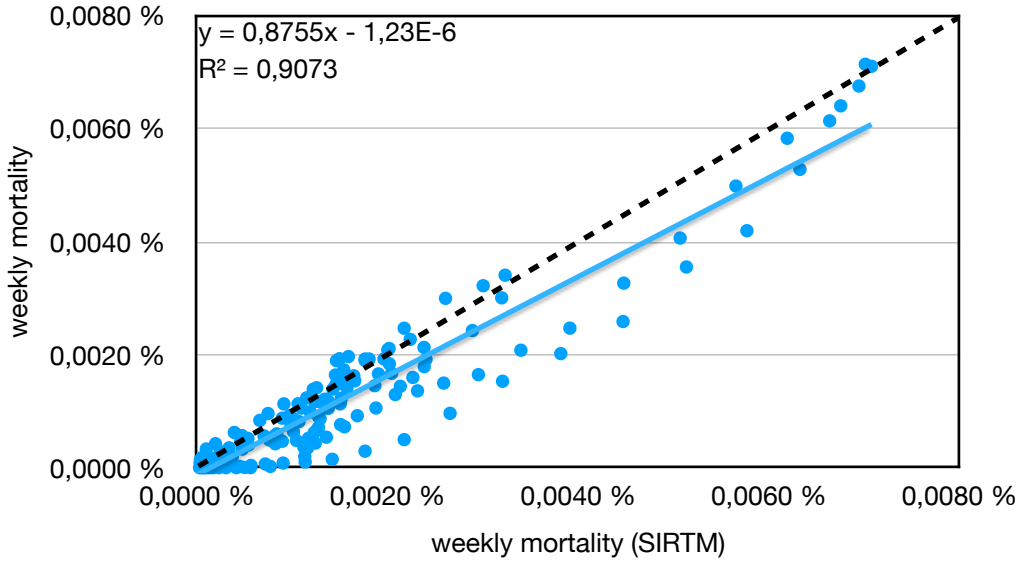

Figure 12: Regression analysis of the SIRTM model. The course of weekly mortality is largely explained by the model. The coefficient of determination has a value of 0.907. There remains a small (13%) unexplained systematic deviation from the theoretical line.

The absolute term b is completely negligible and the regression line practically passes through the origin. The slope is < 0.875 and is therefore well below the value of 1 that would be expected if the data were reproduced exactly by the model. However, the difference between the true values lying on the empirical regression line and the values calculated by the model is on average no more than 13%. The mortality trend is thus explained to about 90% by the model. The rest is a non-random systematic deviation of the model from the data, which is expressed in the different slopes of the regression line and the original line. This becomes particularly clear in the third corona year, where several waves of infection follow one another that are not clearly separated from one another. In this phase, the theoretical cumulative curve of weekly mortality is significantly higher than the data. This could be due to the fact that one of the basic assumptions of the model is violated, e.g. that successive virus mutants do not influence each other's growth. Refinements of the SIRTM model in this direction are conceivable, but would probably change the overall infection kinetics only slightly.

The coefficient of determination of morbidity and mortality

The coefficient of determination R^2 is a dimensionless measure between 0 and 1 that is often used to quantify the goodness of fit of a model. It is defined as follows:

$$R^2 = \frac{\sum_{i=1}^{n} (\hat{y}_i - \bar{y})^2}{\sum_{i=1}^{n} (y_i - \bar{y})^2} \qquad (23)$$

The y_i are the observed, $\hat{y}_i$ the true values of the dependent variable Y. $\bar{y}$ is the arithmetic mean of the y-values. Obviously, $R^2 = 1$ if $y_i = \hat{y}_i$ applies to all i, i.e. all observation points lie on the regression line. Then the relationship between X and Y is not random, but deterministic, and the model and data are in complete agreement. In reality, this condition is never fulfilled, as the observations scatter around the regression line. However, it is obvious that the smaller the residuals are, the closer R^2 must be to 1, i.e. that the limit value

$$\lim_{y_i - \hat{y}_i \to 0} R^2 = 1 \Big| \quad \forall i$$

exists. The smaller the residual sum of squares, the better the model.

If $R^2 = 0$, then the slope parameter a of the regression line has the value zero, and its equation consists only of the absolute term according to (17) and (20):

$$\hat{Y} = b + 0 \cdot X = b = \bar{y} \qquad (24)$$

This assertion is not self-evident. It must be assumed that the positive and negative residuals of the observation points cancel each other out as the sample size increases and add up to zero:

$$\lim_{n \to \infty} \sum_{i=1}^{n} \varepsilon_i = 0 \qquad (25)$$

Then and only then are the arithmetic mean values of the observation points y_i and those of the true points $\hat{y}_i$ equal and the following applies

$$\bar{y} = \frac{1}{n} \sum_{i=1}^{n} y_i = \frac{1}{n} \sum_{i=1}^{n} (\hat{y}_i + \varepsilon_i) = \frac{1}{n} \sum_{i=1}^{n} (\hat{y}_i) + \frac{1}{n} \sum_{i=1}^{n} (\varepsilon_i) = \bar{\hat{y}}$$

$$\bar{y} = \bar{\hat{y}} \qquad (26)$$

The coefficient of determination has the value zero if the numerator of its defining equation (23) is zero:

$$\sum_{i=1}^{n} (\hat{y}_i - \bar{y})^2 = 0 \quad \Leftrightarrow \quad R^2 = 0$$

From (26) then follows

$$\sum_{i=1}^{n} (\hat{y}_i - \bar{\hat{y}})^2 = 0$$

and from the regression equation (15)

$$\sum_{i=1}^{n} \left[(b + a\, x_i - \frac{1}{n} \sum_{i=1}^{n} (b + a\, x_i) \right]^2 = 0$$

$$\sum_{i=1}^{n} \left[(b + a\, x_i - \frac{nb}{n} - \frac{1}{n} \sum_{i=1}^{n} a\, x_i) \right]^2 = 0$$

$$\sum_{i=1}^{n} (a\, x_i - a\, \bar{x})^2 = 0$$

$$a^2 \sum_{i=1}^{n} (x_i - \bar{x})^2 = 0$$

Since negative signs cancel out when squaring, the sum of squares is always > 0. Consequently, if R^2 is zero, $a = 0$, which had to be proven. The regression line is then horizontal and there is no linear relationship between the variables *X* and *Y*.

For the coefficient of determination of morbidity, the spreadsheet provides the value 0.985 and for mortality the value 0.907. They are close to 1 and thus confirm the high mapping quality of the SIRTM model concluded from the purely qualitative comparative observation of the observed and calculated curve progressions and from the regression analysis.

8.2 The quality of data

Morbidity and prevalence

Our analysis of the corona pandemic assumes that the PCR-confirmed corona cases reported weekly to the RKI are random samples. As such, they must have the following properties:

1. the probability of being tested and reported to the RKI as a positive or negative test case is the same for everyone. In particular, infected persons are not tested more frequently or less frequently than healthy persons. In a corona sample, this requirement is only partially fulfilled. Each represents a different subset of the population and these subsets may contain individuals who differ significantly in terms of risk of infection or likelihood of being tested. For example, infected individuals are likely to be disproportionately represented in samples if the latter are predominantly from so-called vulnerable groups, such as residents of care facilities or professionals who use mass transportation on a daily basis and are therefore at higher risk of infection. However, in the case of very large samples, as is the case here, it can be assumed that regional or sociological-structural differences are balanced out and that the samples correctly reflect the nationwide corona morbidity.

2. everyone can be tested more than once. This assumption is mandatory simply because of the total number of tests. In the three years of the observation period, a total of 151,344,708 tests were registered and evaluated by the RKI, which, with an assumed population size of 83,020,000, means that every inhabitant of Germany was tested an average of 1.8 times.

3. the samples are sufficiently large. This is also true. In calendar weeks 10 - 19 of 2020, when the pandemic began, the RKI evaluated an average of 317,000 tests per week. In the period from *Cw* 1 - 10/2022, when

testing was at its peak, the weekly average was 2,619,000, and in the entire observation period 2020 - 2022 the average was 1,013,922. These values are orders of magnitude higher than the value of 1,000, which is usually considered the lower limit for population-representative studies (Planing P., 2023).

4. The time interval in which a sample is drawn is small compared to the entire observation period. The time unit for which the positivity rates of the samples were determined is one calendar week, i.e. 0.64% of the three-year observation period. The positivity rates hardly change by more than 10% from week to week, even in the steepest waves of infection. If the sampling interval were reduced, for example by grouping the individual samples by day rather than by week after the time of sample collection, this would smooth out the morbidity curve and improve the resolution; however, this would not change the overall picture of the pandemic. As a consequence of these considerations, it follows that the above assumptions are valid and the corrected prevalences calculated from the positive rates represent the morbidity trend in the population.

In addition to the imperfect representativeness of random samples, there are other effects that can reduce the informative value of RT-PCR-based corona diagnoses. A correctly positive PCR test only proves the existence of the SARS-CoV-RNA (more precisely: the partial RNA sequence of the virus genome located between the two PCR primers) in the body of the test person. As it can originate from previous infections, the test alone is not a reliable proof of the disease. This is particularly true for asymptomatic test subjects. A series of meta-studies on the spread of asymptomatic corona infections has now shown that up to 50% of the positive corona tests evaluated in the test laboratories come from asymptomatic test subjects, of whom an unknown but presumably high proportion do not develop symptoms, i.e. remain asymptomatic (Oran D. P. & Topol E. J., 2020; Ma et al., 2021). This does not change the accuracy of the data. However, since permanently asymptomatic infected persons are neither impaired by the infection themselves nor necessarily a burden on the healthcare system, a high proportion of asymptomatic infections reduces the danger of the pandemic.

The very high sensitivity of RT-PCR for a biochemical test, together with other factors such as the lack of global standardization and the resulting use of suboptimal test conditions (excessive cycle numbers, poor primer sequences, etc.), gave rise to fears in the initial phase of the pandemic that PCR detection would overestimate the spread of the disease and provide predominantly false, especially false positive, results. In retrospect, these fears have not been confirmed. The values for sensitivity (80%) and selectivity (99%) of the RT-PCR test used in the formulas (24, 26) to calculate the prevalences and their predictive values (Section 4.3) are only mean values, which may be exceeded or fallen short of in individual test laboratories. However, they originate from extensive meta-studies on the biochemical parameters of the test and can therefore be regarded as reliable. The nationwide course of Covid-19 suggested by the PCR data follows the wave pattern typical of seasonal periodically recurring respiratory diseases. There is no reason to attribute this pattern to the diagnostic technique rather than the pandemic.

Mortality

The corona deaths for each calendar week always relate to the total population and are not random samples. If not all those who have actually died from the virus are tested and reported to the health authorities as corona deaths, this leads to underreporting and an underestimation of mortality. This may have been the case in the early phase of the pandemic, when testing centers were set up and fewer tests were carried out. In the later stages of the pandemic, when sufficient testing capacity was available, this is probably no longer the case. Fatal infections are always preceded by a symptomatic phase that requires medical treatment, often followed by hospitalization. Since corona is always suspected in symptomatic respiratory diseases, testing has probably almost always been carried out in these cases. Underreporting to an extent that calls into question the cause of death statistics as a whole is therefore unlikely.

It is much more likely that the statistics overestimate the mortality of Covid-19. From the beginning of the pandemic, there were reasonable doubts as to whether Covid-19 was really the primary cause of death in all PCR-positive deceased persons who, for lack of better criteria, were counted as corona deaths. In a group of 355 corona-positive patients who died in Italy at a mean age of 79.5 years, 30% had ischemic heart disease, 35.5% diabetes, 20% active cancer, 24.5% atrial fibrillation, 6.8% had dementia, and 9.6% had suffered a stroke. Only 0.8% were healthy, 25.1% had one, 25.6% had two and 48.5% had three or more comorbidities (Onder et al., 2020). The median age of corona patients remains unchanged at 83 years (Corona Fakten & Fragen, 2023). Against this background, it is not surprising that some observers were quick to conclude that

for the majority of corona deaths, the actual cause of death was not the virus, but the decline in resistance due to age and comorbidities.

9 The image of Covid-19 in the SIRTM model

9.1 Key figures of the pandemic

Morbidity, mortality, lethality and pervasiveness are important measures that can be used to characterize epidemic infectious diseases in terms of their prevalence and danger and to compare them with each other and with other widespread diseases. With the SIRT model extended to include mutations, these figures can be determined both for each individual wave of infection and for the pandemic as a whole. They are summarized in Table 2 and Figure 13. As with the SIRT model, the variables of the SIRTM model also tend towards limit values as the pandemic progresses, which no longer change when the pandemic reaches a quiescent state.

wave	resistant	wave mortality	pervasiveness	lethality
1	68.9%	0.0131%	68.8%	0.0191%
2	76.7%	0.1211%	76.8%	0.1576%
3	76.9%	0.0100%	76.9%	0.0130%
4	67.2%	0.0027%	67.2%	0.0041%
5	90.5%	0.0310%	90.5%	0.0343%
6	99.6%	0.0124%	99.6%	0.0125%
7	99.9%	0.0275%	99.9%	0.0276%
8	99.2%	0.0129%	99.2%	0.0130%
9	99.7%	0.0134%	99.7%	0.0134%
10	96.7%	0.0091%	96.7%	0.0095%
all waves	100.0%	0.2538%	100.0%	0.2531%

Table 2: Key figures for the coronavirus waves 2020 - 2022. The figures are cumulative percentages calculated with SIRTM and relate to the entire observation period. Last line: The probability that every inhabitant of Germany was infected at least once during the years 2020 - 2022 is 100%, and 0.25% of the population died from/with Covid-19; see also Figure 13.

Morbidity

The maxima of the 10 infection waves represented by the model are between 8.9% (wave 4) and 61% (wave 8). A single wave can therefore infect more than half of the population. This becomes even clearer if you look not only at the maxima when comparing waves, but also at the total number of people infected per wave. When a wave of infection has subsided and a quiescent state has been reached, there are no more people infected with the virus variant in question in the population. The total number of people infected in the course of the wave is then the sum of those who have become resistant and those who have died from the infection. It lies between 67% (wave 4) and over 99% (waves 6 - 9).

Mortality

With the exception of the 2nd wave, the mortality of the infection waves is between 0.0027% (wave 4) and 0.031% (wave 5). It is significantly higher in the 2nd wave (0.12%), which can be most easily explained by the fact that the 2nd wave was caused by a particularly aggressive type of virus. However, as the other variants differ comparatively little in terms of mortality, this interpretation is not entirely satisfactory. The mortality of an infectious disease depends not only on the characteristics of its pathogen, but also on external factors such as the conditions under which it spreads, the population structure and the quality of treatment methods. If, as was particularly the case in the early phase of the pandemic (Onder G. et al., 2020), all deceased with PCR-positive findings are counted as corona deaths, there is a considerable observation error.

Lethality

With the exception of the 2nd wave, the lethality values of the 10 waves of the model are between 0.0041%

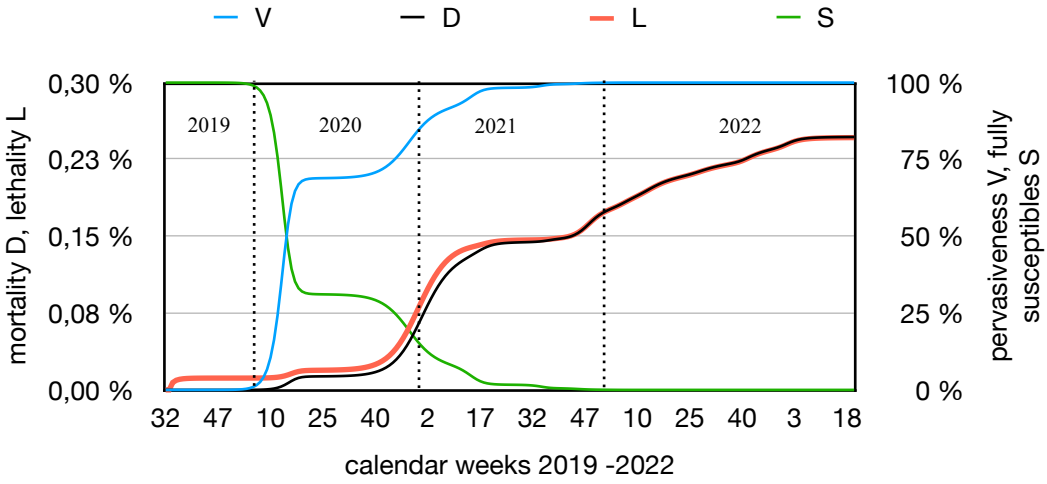

Figure 13: Epidemiological figures calculated with SIRTM for the first corona years in Germany. *D* mortality, *L* lethality, *V* pervasiveness, *S* susceptibles. By the end of 2022, the virus had infected the entire population. Statistically, everyone was infected at least once. There are no fully susceptibles and no more currently infected people. 0.25% of the population have died with/of corona.

(wave 4) and 0.034% (wave 5), whereby the 2nd wave also stands out here with a lethality of 0.16% (Table 2). Since mortality by definition refers to the population and lethality to the group of infected persons, the larger the latter, the less the two variables differ. If a virus has infected the entire population, mortality and lethality are the same.

Pervasiveness

According to formula (13), p. 22, the pervasiveness of Covid-19 at time t is the sum of those currently infected I_t and those who have become resistant R_t at this time:

$$V_t = I_t + R_t$$

where I and R are calculated with SIRTM according to formulas (8) and (10), p. 21. In *Cw* 5/2021, 90% of the population was infected with at least one virus variant, towards the end of the pandemic the entire population (Figure 13). Covid-19 has thus spread far more widely in the population than the wave maxima suggest and has already affected the majority of the population at an early stage. This finding cannot be derived from the incidences due to the unknown number of unreported cases.

9.2 When did the pandemic start?

The origin of Covid-19 is still unknown. The chronology of the disease begins in December 2019, when a high incidence of severe pneumonia of unknown cause was detected in the central Chinese city of *Wuhan* (WHO, 2020). There are currently two main competing hypotheses among experts (Berche, 2023). According to the first, SARS-CoV-2 is of natural origin. It was transmitted directly from bats to humans. This was followed by a silent latency phase with a low level of infection, during which the infection was able to spread unnoticed by the Chinese health authorities. There may have been an intermediate host, e.g. the raccoon dog (*Nyctereutes procyonoides*), which was traded on Chinese animal markets at the time. During the latency phase, the virus was able to adapt to humans as the final host through mutations. Scientists who hold this view consider it possible that a direct precursor of SARS-CoV-2 circulated in the population for years until it acquired the ability to effectively bind the ACE receptor of the host cells through mutations in the spike protein gene, thus triggering the pandemic.

The second scenario is that of a laboratory accident following a gain-of-function (GoF) experiment with SARS-CoV-2. Such experiments have been carried out not only in the virology research centers in *Wuhan*, but also in other laboratories around the world for years. The virulence of pathogens can thus be both reduced and increased. In GoF experiments, mutations are created, genes are removed from the virus genome or foreign genes are introduced into it. It is hoped that this will lead to a deeper understanding of virulence, which is a prerequisite for the development of antiviral drugs and vaccines. GoF experiments with pathogenic viruses are problematic insofar as it has been proven that viruses with only low pathogenicity can be transformed into hypervirulent forms. In the past, there have also been several cases of illness caused by genetically modified viruses from high-security laboratories (Jackson et al., 2001). This view is supported by the fact that there is still no evidence of an intermediate host more than three years after the start of the pandemic. It is also unclear why the disease started in *Wuhan*. The city of 12 million people is a long way from the bats' habitats. Nor have any secondary outbreaks of the disease originating from animal markets been observed in the early stages of the disease, which has been the case with other viral respiratory diseases. Finally, sequence comparisons and other molecular data suggest that SARS-CoV-2 is a relatively young virus that may not have emerged until the fall of 2019.

What these hypotheses have in common is that the disease first appeared in China, originated from a single or a small number of infected people and then spread around the world. The first case of infection in Germany was detected on January 27/2020 in an employee of the automotive supplier *Webasto* in the Bavarian municipality of *Gauting* (Redaktionsnetzwerk Deutschland, 2020). He is said to have been infected by a colleague who had traveled from *Shanghai*, who was then quickly declared "patient 0", i.e. the infected person who, against her will and without knowing it, became the first mother of all those infected with Covid-19 in Germany (Gortana et al., 2020).

Let's go back to the first wave of infection and its representation by the SIRT model. For the sake of simplicity, it assumes a homogeneous population and makes no assumptions regarding the geographical distribution of those infected. The hypothetical patient 0, who started it all, may therefore also have lived or be living in *Wuhan*. It is also plausible that in a fully networked world, infectious diseases can spread across the globe in a relatively short time, even if they originate from a single point and a single individual. However, to build up a wave of infection that starts from a single infected person, reaches a morbidity of 10% at its peak and infects a total of 70% of the population, a lag time of several months is needed in a population the size of Germany's. Its length, the time of the initial infection and thus also that of the entire pandemic can be calculated with the model by using the iterative calculation of the optimal parameter values of the SIRT or SIRTM model with the initial values of the first observation point (S_0 = 98.13%, I_0 = 1.87%, R_0 = 0, T_0 = 0, D_0 = 0) and then gradually reducing I_0 until the value is reached at which there is statistically only one infected person left in the population (1 / 83 020 000). The result is based on the parameters found for the first wave (Figure 5): The starting event should have occurred in *Cw* 32/2019 (August 5 - 11, 2019). This result can be easily reconciled with what has been known so far about the starting point and timing of the pandemic in China, especially if one considers that the assumed timelines can only be more or less well-founded estimates. In *Cw* 10/2020, the first calendar week for which PCR data are available, 69,493 tests with a positive rate of 2.48% were reported to the RKI, which corresponds to a morbidity rate of 1.87% corrected for the proportion of false positives. Based on one infected person in August 2019, the model provides a morbidity of 0.350% for *Cw* 5/2020, when the suspected patient 0 was detected. That is still 287,070 infected people. Given the mapping quality of the model, the idea that the pandemic could have started on January 27/2020 with the immigration of a single infected person is therefore unrealistic. Either this event took place many months earlier, or there was a creeping infiltration by infected people from China and/or other countries that lasted for months, which could not be recognized due to the unclear clinical symptoms and could not be detected biochemically because the corona PCR test did not yet exist.

9.3 Living with the virus

If, as has been assumed, every infected person who survives the disease acquires permanent complete immunity, all virus variants will die out sooner or later. SARS-CoV-2 can then only survive in the long term if new mutations regularly occur to which there is little or no resistance. However, these mutations do not always have to be completely new mutations that have not previously occurred in the entire infection tree. Using the SIRTM model, it can be calculated that 256 calendar weeks, i.e. 4.9 years, after the pandemic began with one infected person, there is statistically only one infected person left in the population. As resistance is not inherited, the proportion of resistant individuals in the population is now steadily decreasing due to the natural

mortality rate. At the same time, the proportion of susceptibles increases. So if the mutant that started the pandemic emerges again, sooner or later it will encounter a susceptible population.

Mutations that have phenotypically visible effects are also rare in viruses. In SARS-CoV-2, the mutation rate is estimated at $\approx 10^{-6}$ per nucleotide position and replication cycle. Since 1 ml of a saliva sample can contain $\approx 10^{7}$ viral nucleic acid molecules, more than one mutated RNA can occur in the sample for each position (Bar-On Y. M. et al., 2020). In this respect, the idea that the same mutation can occur several times in one and the same infection tree within a few years is plausible. If this is true, Covid-19 will not disappear as long as neither effective drugs nor reliable and safe vaccines are available that protect not only against known mutants but also against future mutants. Until then, we will have to live with the virus.

9.4 The risk potential of the disease

There is no absolute yardstick by which the dangerousness of a disease, activity or lifestyle can be measured. However, it makes sense to put the number of fatalities, as expressed in mortality and lethality, first in a comparative assessment.

Mortality

The mortality of the individual waves of Covid-19 infection is between 0.003% and 0.12% and averages 0.025% (Table 2). The annual mortality for the pandemic was 0.076% in 2020, the first coronavirus year, 0.098% in 2021 and 0.072% in 2022, i.e. an average of 0.082%. It is the difference between the mortality achieved at the beginning and end of each year. The overall pandemic has a mortality of 0.25% (Figure 13).

Lethality

The 10 SARS-CoV-2 mutants of the SIRTM model have a lethality of 0.0041% - 0.16%, on average 0.030%, and the entire pandemic has a lethality of 0.25% (Table 2). It follows from the definitions of mortality and lethality that both variables must converge towards the same limit value as the pandemic becomes more widespread, which is clearly shown in Figure 13. When interpreting the mortality, it should be borne in mind that it is based exclusively on the number of PCR-confirmed infections. It is therefore the infection fatality rate (IFR). When comparing the lethality of different diseases, however, the case fatality rate (CFR) is usually taken as the basis. This is the proportion of infected people who have clinical symptoms and die from the disease. In the case of Covid-19, the case fatality rate can be significantly higher than the infection mortality rate due to the large number of asymptomatic infections. However, there is as yet no reliable data on the former, mainly due to the ambiguous symptoms, which also occur in a similar form in other respiratory diseases, and the frequent equation or confusion of the two terms. An early study from China mentioned above came to the conclusion that almost half of the PCR-positive test subjects in random samples had no symptoms of the disease and did not develop any later (Ma Q. et al., 2021). If this is taken as a first indication, the lethality values must be at least doubled to come close to the case mortality. Even then, the lethality of Covid-19 is low compared to other infectious diseases (Table 3).

Rabies (untreated)	100 %
Sleeping sickness (untreated)	100 %
Creutzfeldt-Jakob disease	100 %
HIV	80 %
Avian flu	60 %
Tuberculosis (untreated)	60 %
Ebola	50 %
Marburg-Virus	50 %
SARS (2002)	9.6 %
SARS-CoV-2 (2019)	1.24 %

Table 3: Lethality (case fatality rate) of Covid-19 and other infectious diseases (selection). Statista 2018.

Pervasiveness

From the morbidity kinetics of Covid-19 (Figure 1), it can be deduced even without mathematical models that the virus must have spread quickly and affected large parts of the population. The maxima of the infection waves are between 9.6% (wave 1) and 60.0% (wave 7). They only reflect the current infections. PCR tests on recovered patients are, with rare exceptions, negative according to current knowledge just a few days after the last symptoms of the disease have subsided (Graf J., 2022), and those who have become resistant are not recorded. The degree of spread of the disease must therefore be far higher than the maxima of the

waves suggest. It can be calculated with SIRTM (Table 2). You can see: Even after the first wave of infection, 69% of the population is infected, and by the 6th wave, the virus has spread to the entire population. Seen in this light, the pandemic response, insofar as it was carried out with the intention of containing the disease, has failed to achieve its purpose.

Age structure of corona patients

The statistics for corona deaths have been broken down by age cohort, which shows that the median age of corona deaths is 83 years (Corona Fakten & Fragen, 2023). The general life expectancy in 2019 - 2021 was 78.5 years for men and 83.4 years for women, i.e. an average of 80.9 years (Demografie-Portal, 2023). This also suggests that Covid-19 is a disease whose primary cause is not the virus, but the weakening of the body's defenses due to age, concomitant diseases or other circumstances.

Excess mortality in the corona years

In population statistics, excess mortality is the percentage of deaths within a year that exceeds the mortality in an earlier reference year. There is still debate as to whether and to what extent there was a significant excess mortality in the coronavirus years compared to previous years and how this should be interpreted. The weekly mortality for the years 2015 - 2022 (Figure 14) reflect the typical course of seasonal respiratory diseases in all years, with a low level in summer and significant increases in the cold season. The highest peaks occurred in the winter of 2018, when a severe flu epidemic swept through the country, and in the winter of

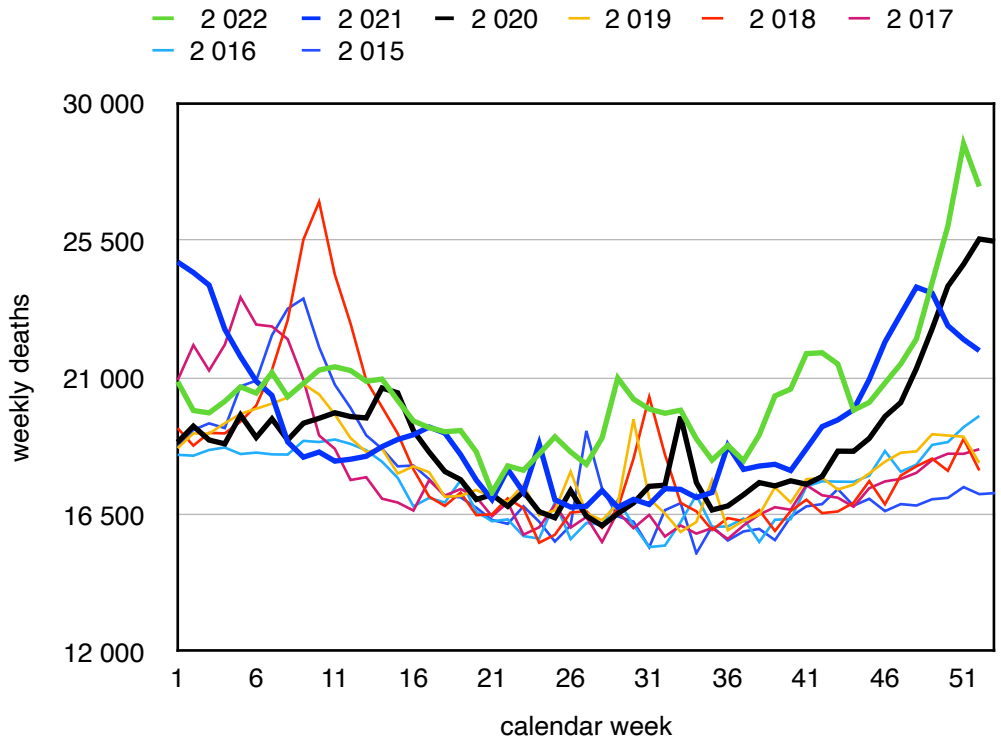

Figure 14: Weekly general deaths in Germany 2015 - 2022 in annual comparison. Statista, 2023.

2022, when Covid-19 reached its peak. The two peaks are comparable in terms of height. They differ by no more than 7%. Assuming a constant population, annual mortality in Germany has risen continuously since 2015. The trend is clear (R^2 = 0.78;). However, the individual values are within or slightly outside the standard deviation. (Figure 15). The average annual mortality rate of the previous 5 years is 1.14%, that of the corona years 1.25%. Although a notable excess mortality during the corona pandemic is recognizable, it is hardly statistically significant. If the previous year's trend is factored out, there is hardly anything left of it.

There is no doubt that Covid-19 is a respiratory disease that everyone affected should take seriously, especially because of the risk of subsequent pneumonia. But what about the risk potential of the disease for the population as a whole? As a comparison with 2018 shows, Covid-19 has caused hardly any more deaths, if any, than a severe flu epidemic. The proportion of corona deaths among those who died during the pandemic

ranges from 4.4% in 2020 to 7% in 2021, with an annual average of 5.3% (Table 4). If 5% of those who die in a year die from Covid-19, this also means that 95% die from other causes, some of which are diseases that are not contagious, but each of which causes several times as many corona deaths year after year. A threat to the population that goes beyond the widespread health risks or even an "epidemic situation of national significance", as the German Bundestag saw it when it amended the Infection Protection Act with regard to Covid-19 and thus wanted to justify massive state intervention in elementary personal rights, cannot be medically justified in this situation.

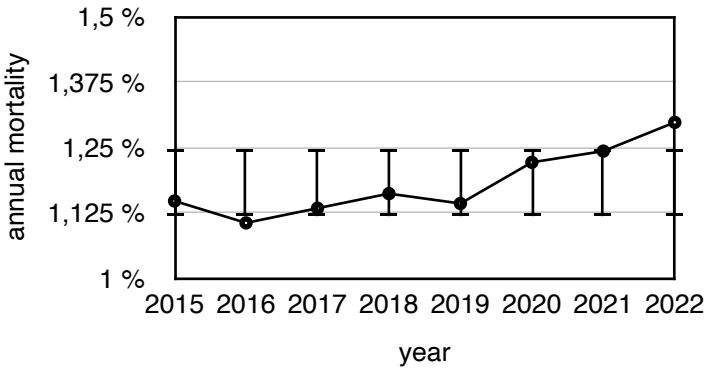

Figure 15. annual mortality 2015 - 2022 in Germany. The error bars show the standard deviation (± 5.6% of the mean). Statista, 2023.

In addition to the epidemic parameters discussed, such as morbidity, mortality, etc., there are other factors that can influence the demographic risk potential of a disease, such as the duration and severity of the course, possible long-term effects and, in the case of hereditary diseases, the probability of passing the disease on to offspring, which depends on inheritance. These influences cannot be assessed solely on the basis of morbidity and mortality trends. Attempting to do so would also miss a key objective: to derive from the SIRTM model a picture as realistic as possible of the success of pandemic control.

year	total deaths	annual mortality	Corona deaths (total)	Corona deaths (%)
2015	940708	1,147 %	-	-
2016	906 309	1,105 %	-	-
2017	929 351	1,133 %	-	-
2018	952 295	1,161 %	-	-
2019	936 772	1,142 %	-	-
2020	1 001 448	1,221 %	44239	4,42 %
2021	1 019 045	1,242 %	71298	7,00 %
2022	1 064 220	1,298 %	48512	4,56 %
mean 2015 - 2019	933087	1,138 %	-	-
mean 2020 - 2022	1028238	1,254 %	54683	5,32 %

Table 4: Total deaths and annual mortality from 2015 - 2022 and proportion of corona deaths in the corona years. RKI 2, 2023, Statista 2023.

10 Fighting the pandemic

„Ein großer Aufwand, schmählich! ist vertan.“
Faust II, letzter Akt

Following the example of China and recommendations from the World Health Organization (WHO), more or less rigid measures to combat the pandemic were ordered in many countries soon after the first Covid-19 cases became known, which can be divided into administrative (compulsory masks, school closures, etc.) and medical (vaccinations).

10.1 Lockdowns and compulsory masks

Lockdown measures, or lockdowns for short (Figure 16), were introduced in Germany in 3 phases: from 22.3. to 2.5. 2020, from 2.11. to 15.12.2020 and from 15.12.2020 to 25.5.2021. The obligation to wear protective masks covering the mouth and nose was introduced on 27.4.2020 and only lifted on 7.4.2023. The 1st lockdown included a far-reaching ban on contact, with restaurants, hairdressing salons and similar businesses being closed nationwide. Further restrictions followed. The chronology of the administrative measures to combat the pandemic is summarized in Figure 16 and Table 5 along with the individual measures.

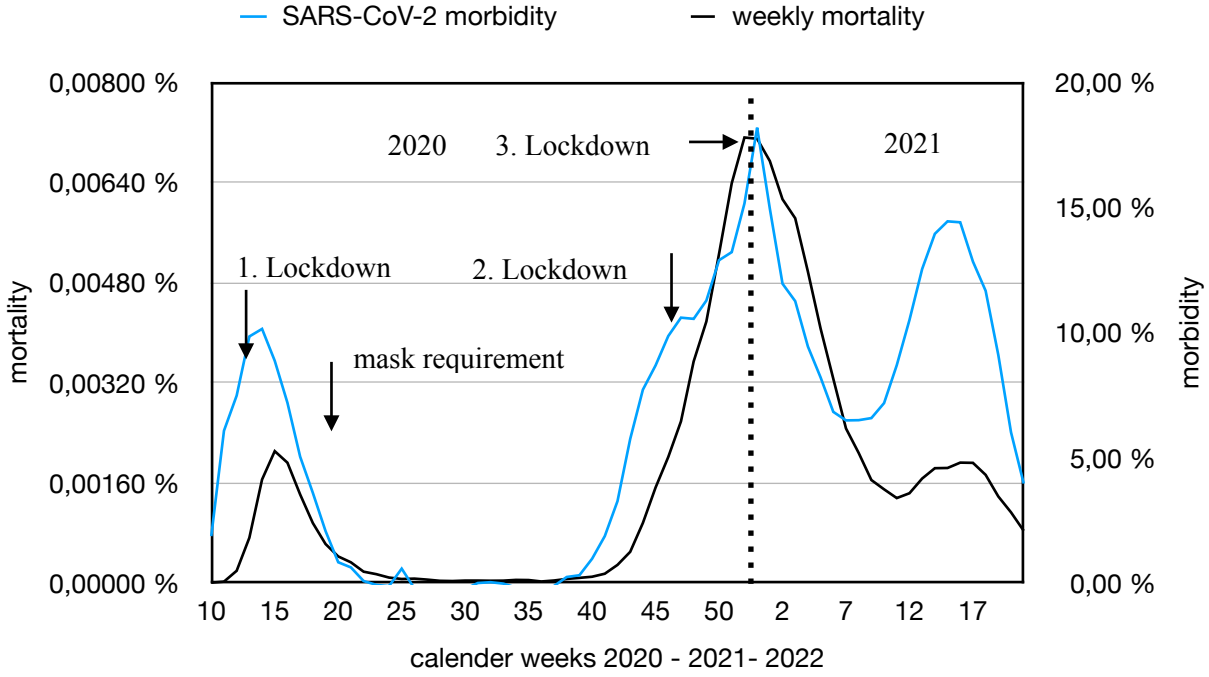

Figure 16: Lockdown measures, mask requirement and course of the epidemic 2020 - 2021. Franchy, 2023.

In contrast to vaccination, which can only have a delayed effect, lockdowns and compulsory masks, if they are effective and apply nationwide, inhibit the spread of the disease from the day they are ordered. This should be noticeable in the course of morbidity and, after a latency period corresponding to the average length of lethal disease progression, also in the development of weekly mortality. The expected effect can be illustrated with a simple simulation experiment (Figure 17).

The example shows the effect of a nationwide mask requirement starting in calendar week 13/2020. It is assumed that the mask requirement reduces the speed at which the infection spreads by half. The parameter a, which in the SIRT model determines the number of new infections per week during the first wave of the pandemic, then only has half the value. This violates the last basic assumption of the model, according to which all model parameters are constants. As a result, the calculated morbidity curve has a kink and can no longer reflect the actual morbidity curve from the time of the introduction of compulsory masking.

Type	Start	End	Measures
1. Lockdown	22.3.2020/*Cw*12	02.05-16.05.2020	Far-reaching ban on contact. Restaurants, hairdressing salons, beauty salons and similar businesses are closed nationwide.
Mask requirement	27.4.2020/*Cw*18	07.04.2023	The mask requirement is introduced. It initially applies on local public transport and soon also in stores. Initially, a simple mouth-nose cover is sufficient, but surgical or FFP masks will later become mandatory.
2. Lockdown	2.11.2020/*Cw*45	15.12.2020/*Cw*51	"Lockdown light": restaurants and tourism close, but schools and stores remain open this time.
3. Lockdown	15.12.2020/*Cw*51	25.05/2021/Cw17	Stores have to close, private travel is banned and contact restrictions are imposed for Christmas and New Year's Eve.

Table 5: Administrative pandemic control in Germany: lockdowns and compulsory masks. Franchy B., 2023.

If you now sift through the course of the epidemic in the expectation of finding discontinuity points of this kind that match the timing of the control measures, you will be disappointed. There is no correlation between epidemic progression and epidemic control. Morbidity follows the typical wave pattern of infectious respiratory diseases, completely unaffected by the measures. The model also provides a simple explanation for this:

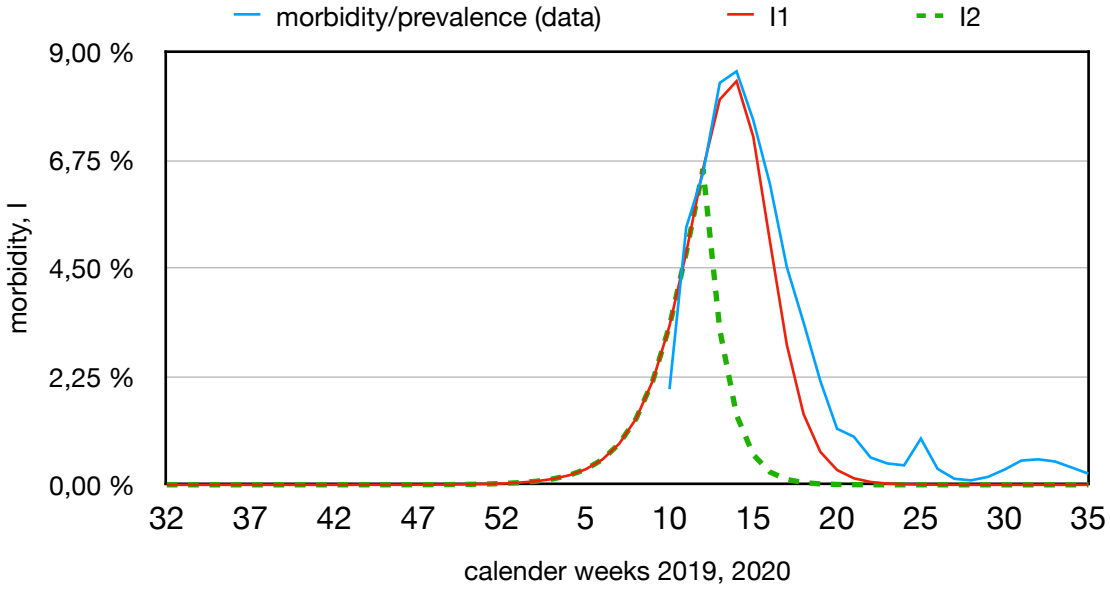

Figure 17: The first corona wave; SIRT simulation of the effect of a nationwide mask requirement starting in calendar week 13/2020. It is assumed that the mask requirement reduces the speed at which the infection spreads by half. *I1* course of infection without, *I2* with mask requirement. Parameter values: $a = 1.85$ up to calendar week 12/2021, $a = 0.9$ from calendar week 13/2021 to *Cw* 35/2021, $b = 1.2$, $c = 0.00025$.

when PCR testing began, the morbidity calculated from the positive rate was 1.9%. That is 1,577,000 infected people out of a population of around 83 million. At the end of the first wave, around 70% of the population had been infected at least once (Figure 6). Given this level of spread, it is quite possible that there was

already an infected person in almost every household at least some of the time during the first wave. It was therefore highly likely that people could become infected at home, where neither masks were compulsory nor contact restrictions were in place. The high initial value also explains why, despite considerable investment in the software used, it was never possible to trace a chain of infection back to its origin, isolate "patient 0" together with their contacts and thus stop or at least slow down the pandemic. By the time PCR testing began, it was long too late for that.

10.2 The vaccination campaign

The Covid-19 vaccination in Germany was and is part of the global vaccination campaigns against the COVID-19 pandemic and, like all vaccinations, aims to contain the disease or at least prevent severe disease progression, deaths and long-term consequences as far as possible. By spring 2021, several hundred vaccination centers had been set up in Germany. The federal states chose different approaches, from specially created vaccination centers to mobile vaccination teams. The first vaccinations in GP surgeries began at the start of 2021, followed by specialists, and pharmacies have also been allowed to offer coronavirus vaccinations since the start of 2022. By summer 2023, six SARS-CoV-2 vaccines had been used in Germany, with the mRNA vaccines *Comirnaty* (*BioNTech/Pfizer*) and *Spikevax* (*Moderna*) being administered most frequently (RKI 3, 2023). The majority of the population has now been vaccinated against Covid-19 more than once. As of May 2023, the Standing Committee on Vaccination (STIKO) at the Robert Koch Institute, which is responsible for vaccination recommendations, recommends basic immunity consisting of two vaccinations and a further antigen contact for all healthy people aged 18 - 59 years. This can be a vaccination or an infection. Members of vulnerable groups should receive an annual booster vaccination in addition to the basic immunity. Vulnerable groups include the over-60s, residents of care facilities, medical staff and others (RKI 4, 2023).

Given the extent and intensity with which the coronavirus vaccinations were advertised and carried out, the progressive vaccination of the population should be visibly reflected in a massive slowdown in the kinetics of infection. The actual course of the epidemic does not confirm this expectation (Figure 18). First of all, it is noticeable that morbidity and vaccination progress are completely different types of curves. The morbidity curve is wave-shaped. The curves that reflect the vaccination status of the population are sigmoid. The morbidity curve retains its wavy character throughout the 3rd corona year, although the vaccination status hardly changes, as more than 80% of the population has been vaccinated at least once. About 30 weeks after the start of vaccination, there is a sharp increase in morbidity. This correlates visibly with the progress of the first three vaccinations. However, the correlation is positive: the higher the vaccination status, the more widespread the disease.

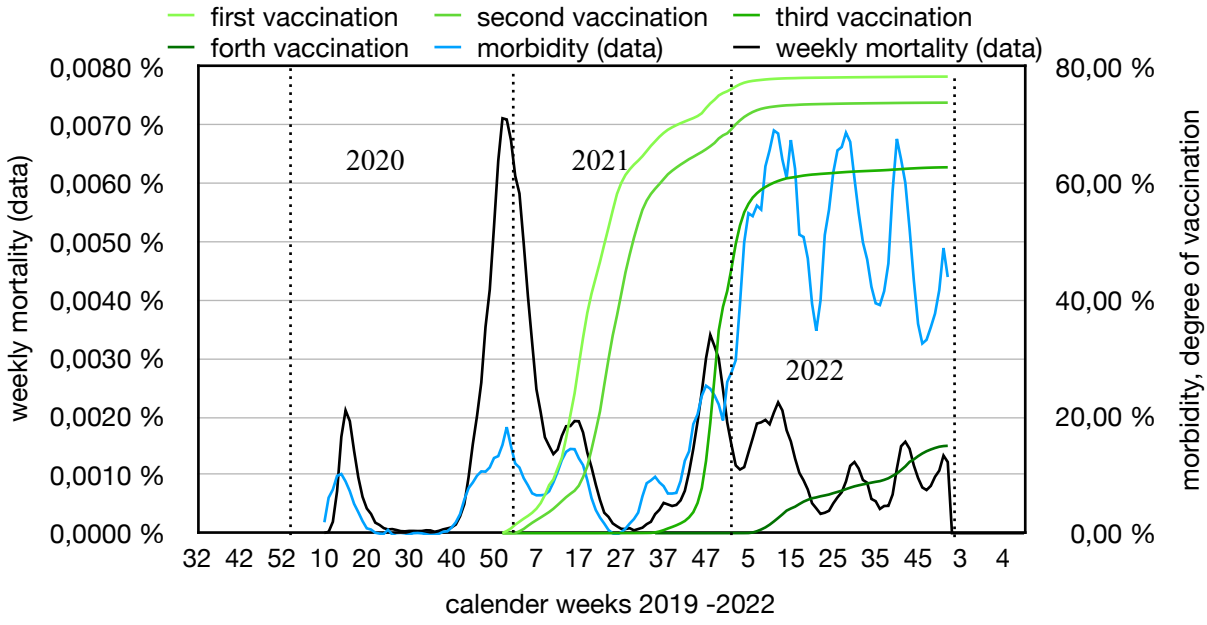

Figure 18: Morbidity, weekly mortality and vaccination status of the population in the 3 coronavirus years.

From a theoretical perspective, too, there is much to suggest that the vaccinations, if they have any influence at all, promote rather than inhibit the spread of Covid-19: 1. When vaccination began in early 2021, 86% of the population had been infected at least once and had either become immune or died (Figure 13). Vaccination was therefore only able to protect the remaining small proportion of the population that was still susceptible from the outset. 2. vaccines can so far only be developed against already known virus mutants and are only weakly effective or ineffective against newly emerging escape mutants that bypass the immune system. If they are used against them, however, they put a strain on the immune system by forcing it to produce the wrong antibodies, among other things, and thus promote the spread of the new virus variants. 3. mass vaccination with a vaccine that is only directed against one or a few mutants creates considerable selection pressure in favor of new vaccine-resistant virus types. The problem of resistance development is well known from other areas. One need only mention the prophylactic use of antibiotics in human medicine and animal husbandry or the use of certain total herbicides in plant production. The only difference is that in the latter cases it can take years or decades for a level of resistance to build up that makes the use of the active substance as a whole appear problematic, whereas with coronaviruses this can be the case after just months due to the high mutation rates of the virus genome.

Even if mass vaccinations cannot slow down the spread of the disease, there is still the possibility that they will at least protect against severe courses of the disease. If we now look at the course of weekly mortality from this perspective, this hope is not fulfilled either: the types of curves for mortality and vaccination progression are fundamentally different, and there is no correlation indicating a significant reduction in weekly mortality. The statistics show more corona-related deaths in 2021 and 2022, when vaccination took place, than in 2020, when vaccination was not yet available (Table 6).

year	Corona deaths	annual mortality	first vaccination	second vaccination
2020	44144	0,053 %	0 %	0 %
2021	71200	0,086 %	46,6 %	35,05 %
2022	47320	0,057 %	78,01 %	73,28 %

Table 6: Covid-19 annual mortality and vaccination status (annual average) of the first and second mass vaccination 2020 - 2022 (RKI2, 2023; RKI3, 2023).

The lethality of a disease, even if it remains untreated, does not depend exclusively on the properties of the pathogen, but also on the resistance of the population on which the lethality is measured. SARS-CoV-2 mutants that infect a population vaccinated with an effective vaccine should therefore show significantly lower lethality than those that infect an unvaccinated population with comparable pathogen properties. However, the lethality of the 10 mutants in the model is almost the same, with the exception of the second variant (Figure 19). This also does not speak in favor of the effectiveness of the vaccination.

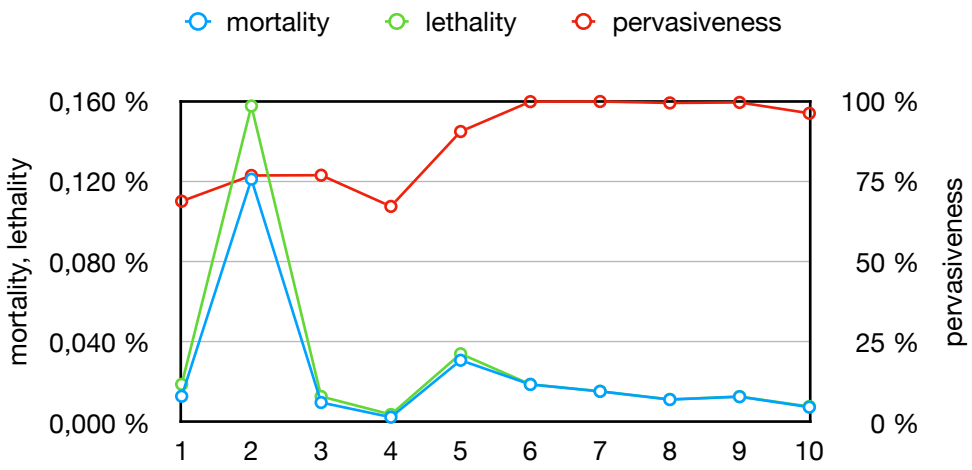

Figure 19: Mortality, lethality and pervasiveness of the 10 SARS-CoV-2 mutants of the SIRTM model.

Corona vaccines based on mRNA are suspected of having serious side effects, which are far more common overall than with conventional vaccines (Corona Fakten & Fragen, 2023). While manufacturers still assumed in their marketing authorization applications that the vaccine administered intramuscularly would remain at the injection site, it has now been shown that the nanoparticles of the vaccine, consisting of mRNA and a lipid molecule coating, can be transported with blood and lymph. In some cases, mRNA and spike protein can still be detected weeks or months after vaccination in organs far away from the infection site. Healthy cells that take up the nanoparticles produce the spike protein and, as it is a membrane protein, can incorporate it into the cell membrane, where it then presents its immunogenic epitopes to the immune system. The immune system then regards the cell as an enemy and destroys it, which can lead to blood clots and tissue damage. The myocarditis that is frequently observed, especially in younger vaccinated people, can be explained in this way (Bellavite P. et al., 2023).

Reverse transcriptase (revertase) is an RNA-dependent DNA polymerase that uses RNA molecules as a template, synthesizes a complementary DNA strand and completes it to form a DNA double strand. The enzyme is found in retroviruses, some bacteria, fungi and also in higher organisms. Thermostable bacterial revertases form the core of the RT-PCR reaction. The telomerase of eukaryotes also has revertase activity. The enzyme restores the end pieces (telomeres) of the chromosomes, which become shorter during DNA replication, to their original length and thus delays cell ageing. The LINE elements (long interspersed nuclear elements) of humans are 6 - 8 kbp (kilobase pairs) long DNA sequences that appear to be randomly distributed in the genome and make up more than 20% of the human genome. The most frequent is LINE-1 with a genome share of 17%. LINES carry 2 genes, one of which encodes a revertase. LINEs belong to a group of transposable DNA elements ("jumping genes") that can leave their location in the genome and reintegrate elsewhere via an intermediate RNA stage, thus creating insertion mutations. The activity of LINES is quite high. It is estimated that there are around 8,000 retrocopies in the human genome, which originally came from around 2,500 human genes. LINES can transport exogenous RNA and probably also the spike mRNA in the cytoplasm of cells that have taken up the nanoparticles of the mRNA vaccines into the cell nucleus, where they are transcribed into DNA and then incorporated into the chromosomes at random positions. Spike mRNA, which thus comes to lie behind a constitutive promoter, is then permanently expressed. This makes a variety of transposon-induced vaccination damage conceivable (Kyriakopoulos A. et al., 2022).

If germline cells take up the nanoparticles of the vaccine, transcribe the mRNA of the spike protein into DNA and integrate it into the genome or incorporate it into extrachromosomal replication-capable elements such as plasmids, it will be inherited and can be expressed in the offspring. If this occurs in a child's body while its immune system is maturing and developing self-tolerance, the spike protein will not be recognized as foreign to the body and the child may produce few or no antibodies against the spike protein. In the worst case scenario, the child is then almost defenceless against the virus for the rest of its life (Seneff S. & Nigh G., 2021).

The now almost forgotten *Thalidomide* tragedy has demonstrated the consequences of the widespread use of drugs containing substances whose spectrum of action is not completely known. The long-term consequences of mRNA vaccines mentioned here, some of which span generations, are hypothetical and may be unlikely, but they are conceivable and should no longer be ruled out a priori, at least in the future (Domazet-Lošo T., 2022). However, it is now too late for a systematic evidence-based preliminary clarification of these risks, now that more than 13 billion doses of COVID-19 vaccine have already been administered worldwide (as of February 2023; Statista, 2023).

11 Conclusion

The SIRTM model can reproduce the time series of morbidity (R^2 = 0.98) and mortality (R^2 = 0.91) with a high degree of accuracy and thus confirms the assumptions on which its development is based. Overall, the following picture emerges for the spread mechanism of the SARS-CoV-2 pandemic in Germany: The pandemic began several months before the pathogen was first detected in Germany, with the immigration of an infected person into the population or the mutation of an endemic, previously inconspicuous coronavirus strain in a previously healthy individual. Since then, the infected population has been mutating at an average mutation rate of 5.9 - 10^{-4} per calendar week, continuously generating escape mutants that can evade the immune system and multiply independently of each other. This results in multiple infections with different SARS-CoV-2 mutants. Infections that have been overcome generate lasting pathogen-specific resistance. There are no signs that this will slowly decay during the pandemic, but this does not mean that Covid-19 will disappear on its own sooner or later. As long as the virus can produce escape mutants to which there is little or no resistance in the host population, it is potentially immortal.

The spread of the disease is high. Even the first wave of infection was able to infect 70%, later almost 100% of the population. Overall, 0.25% of the population died from/with corona during the 3 corona years, which corresponds to an average annual mortality of 0.082%. Since the general annual mortality during this period averaged 1.25%, corona deaths accounted for 6.5% of all deaths. Considering that Covid-19 was not the primary cause of death in an unknown but presumably high proportion of corona deaths, the true mortality of the disease is likely to be much lower. The lethality of Covid-19 is also low. As the spread of the disease increases, it approaches mortality more and more, and both variables converge towards the same limit of 0.25%. The 10 SARS-CoV-2 types assumed by the model differ only slightly from each other in terms of lethality, with the exception of the second wave, which caused significantly more deaths than the following waves. On average, it is 0.030%.

A protective effect of the government-imposed pandemic control measures is not recognizable. It should have been evident in the infection kinetics and its modeling requires that individual parameters of the model are changed in the course of the pandemic. As can be seen from the example of the hypothetical introduction of an effective mask requirement during the first wave of infections, this contradicts the data. In individual cases or under controlled conditions, protective measures may be successful, e.g. if it is ensured for a selected test group that masks are put on under sterile conditions, worn correctly and changed frequently, or if a pathogen-specific vaccine adapted to the virus subtype is used to vaccinate a susceptible test group. They are ineffective at the population level. If you consider this, there can only be one answer to the question of the value of all the coercive measures and campaigns such as lockdowns, compulsory masks, social distancing rules and mass vaccinations to get Covid-19 under control. The quote at the beginning of the last chapter sums it up perfectly.

12 Variables and their use

The following list shows the names and meanings of the variables used in alphabetical order. In the text, variables, constants and indices are in italics. Variables are capitalized with the exception of time *t*.

Cw Calendar week

D Cumulative deaths since the beginning of the pandemic, model variable

Dz Dark figure of the 7-day incidence

Em Sensitivity of an RT-PCR test

ε Observation error, residual (regression analysis)

Fn False negatives, PCR test negative infected persons in a sample

Fp False positives, PCR test positive non-infected persons in a sample

G Population, total population of Germany in the corona years

H Healthy people in a sample

I Infected persons in *G*, model variable

In 7-day incidence of *G*

J Infected persons in a sample

L Lethality of Covid-19 or a virus variant of Covid-19, model variable

Mb Morbidity of *G* determined as prevalence of a representative sample

$\hat{M}b$ Regression estimate of the morbidity

Mw Weekly mortality of *G*, number of weekly registered corona deaths

$\hat{M}w$ Regression estimate of weekly mortality

N Test negatives in a sample, sum of true and false negatives

P Test positives in a sample, sum of true and false positives

Pr Positive rate of a sample

Pv Prevalence of a sample, calculated from its positive rate

R Resistants in *G*, model variable

R^2 Coefficient of determination of the linear regression

Rn True negatives, PCR test negative non-infected persons in a sample

Rp True positives, PCR test positive infected persons in a sample

S Susceptibles in *G*, model variable

S Size of a sample

T Weekly mortality, model variable

Tr Selectivity of an RT-PCR test

V Pervasiveness (degree of spread) of Covid-19 or a single virus type of Covid-19, model variable

Vn negative predictive value of a PCR test

Vp	positive predictive value of a PCR test
$W(x)$	Probability of the event x
X	non-stochastic independent integer variable of the regression analysis of the SIRTM model
Y	linearly dependent discrete random variable (regression analysis)
$\hat{Y}$	Estimated value of Y (regression analysis)

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