Transitioning from non-pharmaceutical interventions to vaccination to control COVID-19 transmission

Ellen Brooks-Pollock Lorenzo Pellis Emily Nixon Francesca Scarabel
Hannah Christensen Jon Read Angela McLean Julia Gog Leon Danon
JUNIPER consortium

Summary

Methods

We use social contact data collected in the Social Contact Survey (SCS) in combination with age-specific vaccination rates to construct a framework for estimating the effective COVID-19 reproduction number and attack rate as a function of social distancing restrictions, COVID-security, contact tracing and vaccination. We consider the effect of lifting of non-pharmacuetical interventions at snapshots in the vaccine rollout programme: at the end of May 2021, end of June 2021, once all adults have been offered a first vaccine dose and once all adults have been offered two vaccine doses. We capture the emergence of new variants by increasing the transmission potential, Infection Fatality Rate and the potential for vaccine escape.

Findings

- Lifting social distancing restrictions once all adults are eligible for at least 1 vaccine dose (with an average vaccine uptake of 96% for dose 1 and 65% for dose 2) leads to an estimated reproduction number of 2.1 (95% CI 1.8, 2.7), and 2.3×10^4 (95% CI 2.1×10^4, 2.4×10^4) COVID deaths.
- Lifting social distancing restrictions once all adults are eligible for two doses (with an average vaccine uptake of 96% for dose 1 and 90% for dose 2) leads to an estimated reproduction number of 1.8 (95% CI 1.4, 2.6), and 1.8×10^4 (95% CI 1.7×10^4, 2×10^4) COVID deaths.
- With high vaccine uptake in adults, approximately half of all deaths are estimated to be in vaccinated individuals.
- COVID-security and contact tracing and retaining some more limited social distancing restrictions, as implemented in the model, has the potential to make a meaningful contribution to reducing cases and deaths. With all adults eligible for two doses (with an average vaccine uptake of 96% for dose 1 and 90% for dose 2), retaining some social distancing could bring the reproduction number close to 1 and result in non-linear decreases in cases and deaths.
- We find that a 10% drop in vaccine uptake (with all adults having been offered at least 1 dose) increases the number of cases by 3 million cases and results in a three-fold increase in COVID deaths due to older individuals not being protected.
- When returning to pre-COVID contact patterns, there is a ever-present risk of a new variant transmitting as the reproduction number is still above 1.

Conclusions

- The vaccine/restriction lifting scenarios we considered result in lower numbers of deaths than those seen so far in England.

- This is a complementary approach to full dynamic modelling, and lends itself for comparison between strategies.

Limitations

- This framework is only able to estimate final sizes, and cannot capture the epidemic profile (including the peak burden of cases) or changes in epidemiology over time.

Introduction

In the absence of a vaccine to protect against SARS-CoV-2 infection, COVID-19 transmission has been largely controlled using non-pharmaceutical interventions, including limiting non-essential social contact, social distancing and mask wearing. While non-pharmaceutical interventions have proven effective, they come at a high social and economic cost, and are challenging to maintain over prolonged periods, often leading to spikes in COVID-19 cases.

Vaccination offers a viable and long term solution to COVID-19 management. Multiple vaccines are now available which provide good levels of protection against infection, morbidity and onward transmission.

The aim is to rely on vaccination to control COVID-19 transmission, rather than social distancing. As vaccination is rolled out, social distancing restrictions can be lifted, but the speed of lifting restrictions needs to be carefully managed to avoid a resurgence of cases.

Mathematical modelling is a key technique used to understand the required balance between vaccination and social distancing. The most common approach involves developing a dynamic transmission model to simulate a population of people and their infection and vaccination status over time. These approaches integrate complex evidence into a single framework and provide a fine level of control over the assumptions.

Here, we present a simple framework to evaluate the trade off between vaccination rollout and social distancing measures for COVID-19. Our approach is amenable to wide sweeps of parameter space, providing a visual tool for planning the exit from social distancing restrictions.

Methods

Estimating the reproduction number

We use an approach for mapping from individual-level social contact data to the population-level wide COVID-19 reproduction number, in this case using data from the Social Contact Survey (SCS) (Danon et al. 2012, 2013).

For each individual, we calculate their individual reproduction number R_j from their k_j social contacts.

$$R_j \propto \sum_{k=1}^{k_j} n_k d_k,$$

where n_k is the number of individuals who take part in contact k and d_k is the duration of that contact. If we assume proportionate mixing between individuals, then the probability that any individual contacts individual k is $R_k / \sum_k R_k$, therefore the individual Next Generation Matrix can be written as

$$NGM = \mathbf{G} = \begin{pmatrix} R_{11} & R_{12} & \cdots & R_{1k} \\ R_{21} & R_{22} & \cdots & R_{2k} \\ \vdots & \vdots & \ddots & \vdots \\ R_{k1} & R_{k2} & \cdots & R_{kk} \end{pmatrix} = \frac{1}{\sum_j R_j} \begin{pmatrix} R_1 R_1 & R_1 R_2 & \cdots & R_1 R_k \\ R_2 R_1 & R_2 R_2 & \cdots & R_2 R_k \\ \vdots & \vdots & \ddots & \vdots \\ R_k R_1 & R_k R_2 & \cdots & R_k R_k \end{pmatrix}.$$

The elements of the NGM, R_{ij}, are the average number of secondary j cases due to individual i, and the row sums equal the individual reproduction number $R_i = \sum_j R_{ij} = \tau \sum_j n_j d_j$, where τ is the transmission probability calibrated to a given baseline reproduction number.

The population-level reproduction number R_t is the maximum eigenvalue of the NGM. Now, because $R_{ij}R_{ji} = R_{ii}R_{jj}$, the off-diagonal elements of the matrix cancel in the formulation of the determinant, therefore

$$R_t = \frac{\sum_j (R_j)^2}{\sum_j R_j}.$$

In order to estimate the uncertainty associated with the sample, we bootstrap over the values:

$$R_t^* = \text{boot}((R_j)^2).$$

Calculating the final size

The final size of an epidemic is defined as the proportion of a population that get infected during an epidemic, and is calculated as 1 minus the proportion of that population that do not get infected, often denoted as $S(\infty)$ (Keeling and Rohani, 2008, equation 2.7).

In our individual-based formulation, we calculate the probability that an individual j gets infected during the outbreak. Following the method in Andreasen (2011), we denote the proportion of uninfected individuals who are remain uninfected at the end of the epidemic as σ_j. In our formulation,

$$\log \sigma_j = \sum_k R_{kj}(1 - \sigma_k). \tag{1}$$

The attack rate for individual j is $1 - \sigma_j$. Equation 1 links the attack rate for individual j to the attack rate of all other individuals.

Simulating social distancing restrictions

To simulate social distancing measures we "switch" contacts on and off and recalculate the reproduction number. To simulate COVID security, we reduce the transmission probability of contacts outside the home by x%. To simulate contact tracing, we reduce the number of secondary cases arising from symptomatic individuals, where the probability of an individual developing symptoms is age-dependent.

For all scenarios considered we assume that contact tracing remains in place, with 20% of close contacts effectively traced and isolated.

Including vaccination and seroprevalence

To model vaccination, we reduce the probability that an individual is infected (the susceptibility) and the probability that the individual will transmit to others (the transmissibility). Reduced transmission due to vaccination is incorporated into the individual reproduction number

$$R_j^{vac} = t_j \tau \sum_{k=1}^{k_j} n_k d_k,$$

where t_j is the expected value of the reduction in transmission due to vaccination given vaccine rollout.

Reduced susceptibility is incorporated by reducing the probability of being infected. s_j is the expected value of the reduction in susceptibility of individual j due to vaccination. Natural immunity is modelled as having received a single dose of the vaccine. The NGM with vaccination is

$$NGM^{vac} = \frac{1}{\sum_j R_j} \begin{pmatrix} t_1 R_1 s_1 R_1 & t_1 R_1 s_2 R_2 & \cdots & t_1 R_1 s_k R_k \\ t_2 R_2 s_1 R_1 & t_2 R_2 s_2 R_2 & \cdots & t_2 R_2 s_k R_k \\ \vdots & \vdots & \ddots & \vdots \\ t_k R_k s_1 R_1 & t_k R_k s_2 R_2 & \cdots & t_k R_k s_k R_k \end{pmatrix}.$$

We calculate a final size for each individual without vaccination, with one dose, and with two doses given a reduction in susceptibility after one dose of ξ_1 and after two doses of ξ_2, and a reduction in onward transmission after one dose of ε_1 and after two doses of ε_2. For unvaccinated individuals, the remaining proportion of susceptible individuals is:

$$\log(\sigma_j^{(U)}) = \sum_{k=1}^{k_j} n_k d_k \Lambda.$$

For individuals with one dose:

$$\log(\sigma_j^{(1)}) = (1-\xi_1) \sum_{k=1}^{k_j} n_k d_k \Lambda.$$

For individuals with two doses:

$$\log(\sigma_j^{(2)}) = (1-\xi_2) \sum_{k=1}^{k_j} n_k d_k \Lambda.$$

In each case, the incoming force of infection experienced by all individuals is:

$$\Lambda = \sum_k R_k [v_k^{(0)}(1-\sigma_k^{(U)}) + v_k^{(1)}(1-\varepsilon_1)(1-\sigma_k^{(1)}) + v_k^{(2)}(1-\varepsilon_2)(1-\sigma_k^{(2)})] / \sum_k n_k d_k, \tag{2}$$

where $v_k^{(0)}$ is the proportion of individuals in k's age group that are unvaccinated, $v_k^{(1)}$ is the proportion that have received one dose and $v_k^{(2)}$ is the proportion that have received two doses, as determined by the vaccine roll out schedule.

To estimate the total number of cases, we weight the attack rate by the number of people in England that are effectively represented by individual j, calculated as $w_j = N_{ENG}(age = age_j)/N_{SCS}(age = age_j)$. The number of cases represented by individual j is:

$$C_j = w_j [v_k^{(0)}(1-\sigma_j^{(U)}) + v_k^{(1)}(1-\varepsilon_1)(1-\sigma_j^{(1)}) + v_k^{(2)}(1-\varepsilon_2)(1-\sigma_j^{(2)})]$$

The number of deaths represented by individual j is

$$D_j = \mu_j w_j [v_k^{(0)}(1-\sigma_j^{(U)}) + v_k^{(1)}(1-\varepsilon_1)(1-\sigma_j^{(1)})(1-\delta_1) + v_k^{(2)}(1-\varepsilon_2)(1-\sigma_j^{(2)})(1-\delta_2)]$$

where δ_1 is the reduction in mortality from one dose and δ_2 is the reduction in mortality from two doses and μ_j is the age-specific mortality rate for individual j in the absence of vaccination. The total number of deaths is a sum of the individual j contributions

$$D_{total} = \sum_j D_j.$$

Variant-of-concern assumptions

We model variants as having increased transmission, modelled through an increased initial reproduction number R_0, using values of 3 (wild type), 5 (alpha), and 7 (delta). We assume an increased mortality rate for alpha and delta variants of a factor of two.

Vaccination scenarios

To estimate the uptake within each age group, we use the PHE vaccination data to calculate the number of vaccines given to individuals in each age group and the Office for National Statistics (ONS) 2021 population projections for England and Wales as the denominator for each age group. This provides the percentage of each age group vaccinated up until the latest data, relating to 23 June 2021. However, because our uptake estimates are lower than PHE's estimates, we increase our values by 10%.

For future scenarios, we assume A) (future scenario 1) that all adults over 18 years old have been offered a first dose with uptake as in table 1; B) (future scenario 2) that all adults over 18 years of age have been offered 2 doses with uptake as in table 1.

Demographic data, disease severity estimates and vaccine effectiveness

We divide the population into 20 age groups: 0-4, 5-9, 10-14,15-17, 18-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90+. The number of individuals in each age group is taken from ONS projections for England and Wales in 2021.

The baseline COVID-19 hospitalisation rate and Infection Fatality Rate (IFR) by age in the absence of vaccination is taken from Verity et al (2020) - see table 1. We consider the impact of an increase in IFR associated with new variants (Challen et al. 2021). We assume a seroprevalence of 30% for all age groups, which is modelled as equivalent to having received a single dose of the vaccine. We investigate the outputs using a low, medium and high vaccine effectiveness scenarios, detailed in table 2.

Table 1: Demography, baseline mortality rate and vaccine uptakes used in the model.

Age group	N	IFR	Dose 1 uptake 23-Jun-21 (%)	Dose 2 uptake 23-Jun-21 (%)	Dose 1 uptake projected (%)	Dose 2 uptake projected (%)
0-4	3359000	0.00000	0.0	0.0	0.0	0.0
5-9	3716000	0.00000	0.0	0.0	0.0	0.0
10-14	3695000	0.00000	0.0	0.0	0.0	0.0
15-17	2010000	0.00010	5.5	3.3	5.5	3.3
18-19	1340000	0.00015	33.0	12.0	94.0	88.0
20-24	3612000	0.00020	43.0	18.0	94.0	88.0
25-29	3947000	0.00040	57.0	22.0	94.0	88.0
30-34	4074000	0.00060	74.0	26.0	94.0	88.0
35-39	3951000	0.00100	81.0	31.0	94.0	88.0
40-44	3739000	0.00100	89.0	43.0	94.0	88.0
45-49	3724000	0.00200	95.0	58.0	95.0	88.0
50-54	4085000	0.00500	98.0	89.0	98.0	88.0
55-59	4048000	0.00800	98.0	91.0	98.0	88.0
60-64	3501000	0.01700	98.0	94.0	98.0	94.0
65-69	2997000	0.02700	98.0	96.0	98.0	96.0
70-74	3016000	0.04300	100.0	98.0	100.0	98.0
75-79	2255000	0.06200	97.0	97.0	97.0	97.0
80-84	1545000	0.09600	100.0	98.0	100.0	98.0
85-89	966000	0.09600	96.0	94.0	96.0	94.0
90+	566000	0.09600	92.0	89.0	92.0	89.0

Table 2: Model parameters for vaccine effectiveness (%).

	Dose 1 (low)	Dose 1 (medium)	Dose 1 (high)	Dose 2 (low)	Dose 2 (medium)	Dose 2 (high)
Mortality	70	85	85	90	96	97
Infection	30	34	50	60	73	80
Transmission	25	45	45	40	45	60

Results

Impact of vaccination on the effective reproduction number

If R_0 is above 5, the effective reproduction number is above 1; as in all scenarios, we assume that 20% of contacts are effectively traced and isolated (fig 1a-h).

With all adults eligible for at least one dose and an average vaccine uptake of 96% for dose 1 and 65% for dose 2, we estimate that 24% of the population is unvaccinated. We estimate the reproduction number of the delta variant would be 2.1 (95% CI 1.8, 2.7) in the absence of any social distancing or COVID security (fig 1e). Increasing vaccination so that all adults are eligible for two doses (with an average vaccine uptake of 96% for dose 1 and 90% for dose 2), we estimate the reproduction number of the delta variant would be 1.8 (95% CI 1.4, 2.6) in the absence of any social distancing or COVID security (fig 1g).

COVID security and social distancing continue to contribute meaningfully to controlling transmission across all vaccine scenarios. With 96% of adults covered by 1 dose and 90% covered by two doses, and 25% COVID security and 30% of work and leisure contacts prevented, we estimate the effective reproduction number to be 0.94 (95% CI 0.77, 1.4) (fig 1h).

Future cases and deaths

For the delta-like variant, with 96% of adults covered by 1 dose and 65% covered by two doses, and the vaccine having had time to reach its maximum effectiveness, we estimate that without COVID-security or social distancing (retaining 20% effective contact tracing) there would be 20 (95% CI 19, 21) million cases (fig 2e). This would result in a total of 2.3×10^4 (95% CI 2.1×10^4, 2.4×10^4) COVID deaths (fig 3e), of which an average of 45% are unvaccinated, 14% have received 1 dose and 41% have received two doses (fig 4e).

With 96% of adults covered by 1 vaccine dose and 90% covered by two doses, without COVID-security or social distancing, we estimate 1.4×10^7 (95% CI 1.3×10^7, 1.5×10^7) cases (fig 2g) and 1.8×10^4 (95% CI 1.7×10^4, 2×10^4) COVID deaths. Retaining 25% COVID security and a 30% reduction in social contacts could reduce this to 2.7×10^5 (95% CI 2.5×10^5, 3×10^5) cases (fig 2h). This large reduction is due to COVID-security and social distancing reducing the effective reproduction number from 1.8 to under one. Under this last scenario, we estimate a low number of additional COVID deaths.

Table 3: Summary results for a baseline reproduction number equal to 7.

	Rt	Million cases	Deaths
96% dose1 / 65% dose 2	2.11 (1.81-2.66)	20.3 (19.4-21.3)	22800 (20500-24400)
96% dose 1 / 90% dose 2	1.79 (1.44-2.59)	14.1 (13.2-14.9)	18100 (16900-19600)
All adults 1+ dose 25%CS	1.48 (1.27-1.84)	10.9 (10.3-11.7)	12000 (11100-13100)
All adults 2 doses 25%CS	1.21 (1-1.73)	4.55 (4.13-4.84)	5950 (5540-6630)

Table 4: Summary results for a baseline reproduction number equal to 7 with high vaccine effectiveness assumptions. *Projecting numbers of cases and deaths when $R_t < 1$ is beyond the capacity of the model.

	Rt	Million cases	Deaths
All adults 1+ dose	1.65 (1.3-2.18)	11.4 (10.8-12)	12400 (11500-13400)
All adults 2 doses	1.32 (0.996-1.91)	4.7 (4.44-5.06)	6020 (5500-6830)
All adults 1+ dose 25%CS	1.12 (0.919-1.41)	3.07 (2.9-3.33)	3320 (3030-3630)
All adults 2 doses 25%CS	0.869 (0.676-1.34)	*	*

Table 5: Summary results for a baseline reproduction number equal to 7 with low vaccine effectiveness assumptions.

	Rt	Million cases	Deaths
All adults 1+ dose	2.88 (2.45-3.7)	29.5 (28.1-31.2)	65800 (59500-69900)
All adults 2 doses	2.44 (2.01-3.41)	25 (23.9-25.9)	57300 (53300-61500)
All adults 1+ dose 25%CS	1.96 (1.74-2.33)	21.4 (20.6-22.3)	45200 (42200-49800)
All adults 2 doses 25%CS	1.63 (1.4-2)	15.4 (14.5-16.2)	34200 (32100-36800)

Extinction probability

The extinction probability considers the probability that a newly introduced case would not result in onward transmission (fig 5). An extinction probability close to 1 would indicate that newly introduced cases would be highly likely to die out and not generate a secondary case. Logically, reducing social distancing restrictions reduces the probability that a lineage will die out, and this can be seen across all vaccination strategies considered. With all adults eligible for double dose vaccination, the extinction probability for the delta variant ($R_0 = 7$) is estimated to lie between 0.58 and 1.

Impact of vaccine uptake

Re-running all scenarios with a 10% lower vaccine uptake results in more cases and deaths (figs 6-10). With 87% of adults protected by a first vaccine dose and 59% protected by a second dose, we estimate that the number of cases would increase to 23 (95% 23, 25) million cases (fig 7e). This translates to a total of 6.9×10^4 (95% 6.2×10^4, 7.4×10^4) COVID deaths (fig 8f).

With 87% of adults protected by a first vaccine dose and 82% protected by a second dose, without COVID-security or social distancing, the number of cases is estimated at 1.8×10^7 (95% 1.7×10^7, 2×10^7) cases (fig 7g) and the number of deaths increases to 6.1×10^4 (95% 5.6×10^4, 6.6×10^4) (fig 8g).

Discussion

We believe that our framework provides a useful complementary approach to fully dynamic transmission models. The simplicity of our approach allows for rapid comparison of multiple scenarios and model dependencies. The approach can be readily translated to other settings as it relies only on social contact data, which is now available for many different settings, either from contact surveys directly or as synthetic social data generated from census and demographic variables.

While our analytically-tractable approach has advantages, it also has disadvantages in that it is not able to capture some key epidemiological details. This framework is not time dependent, therefore we cannot model

the time course over which hospitalisations and deaths occur, which means, for example, that we cannot estimate peak hospitalisation and death numbers. We do not capture the on-going impact of vaccine rollout. We also do not capture the age distribution of cases and deaths, which are necessary when considering the individual-level loss of life years. The relationship between NPIs, vaccination and deaths presented here are dependent on variable mortality by age and should the distribution of mortality shift towards younger age groups then lifting restrictions before younger adults have been vaccinated will result in more deaths. Furthermore, the results are dependent on future infections not being caused by variants that evade vaccine derived or natural immunity. As the restrictions on social contacts are relaxed the chance of a new variant spreading rapidly in the population is likely to increase, so this assumption may need revisiting.

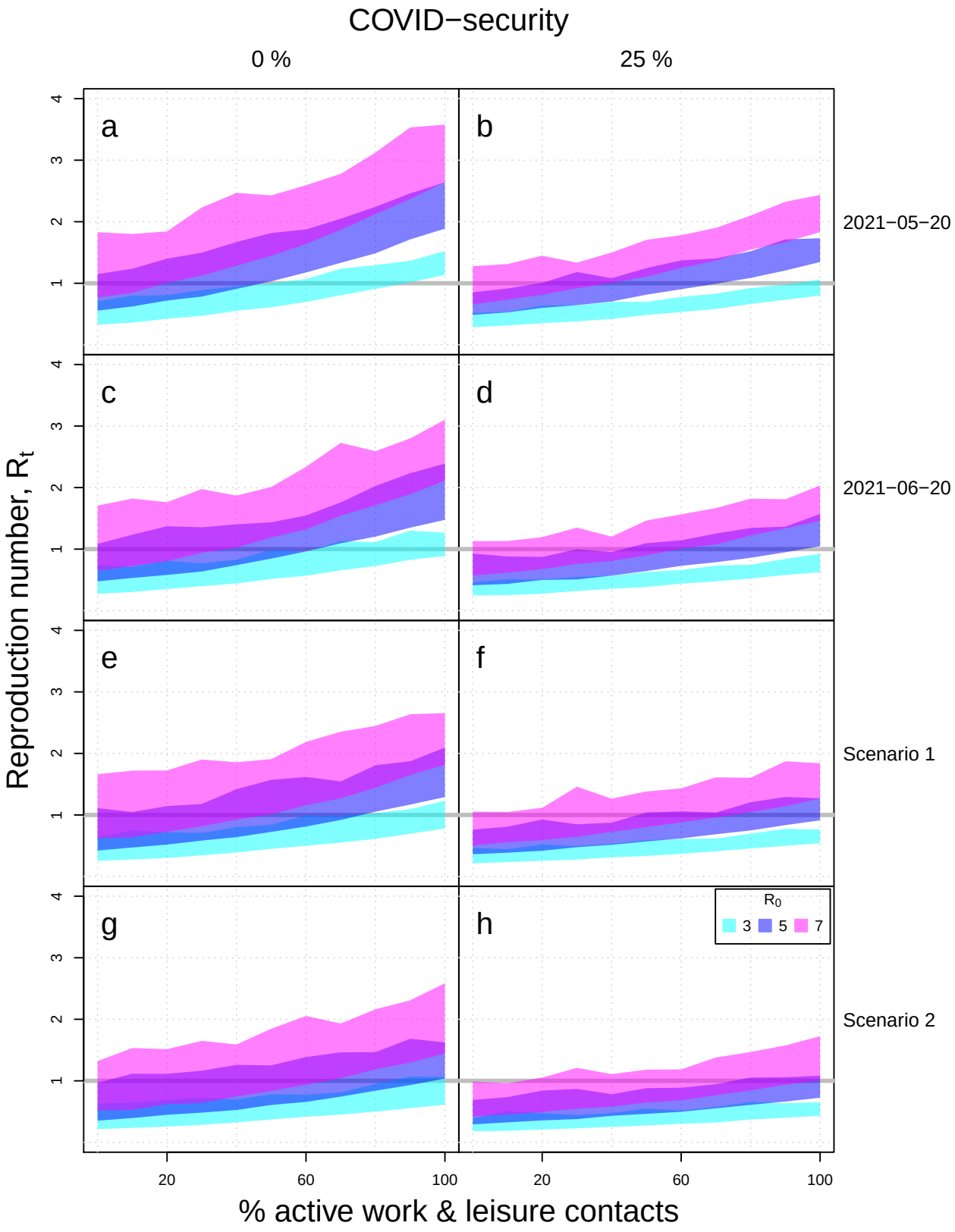

Figure 1: The projected reproduction number as a function of active contacts for different initial reproduction numbers.

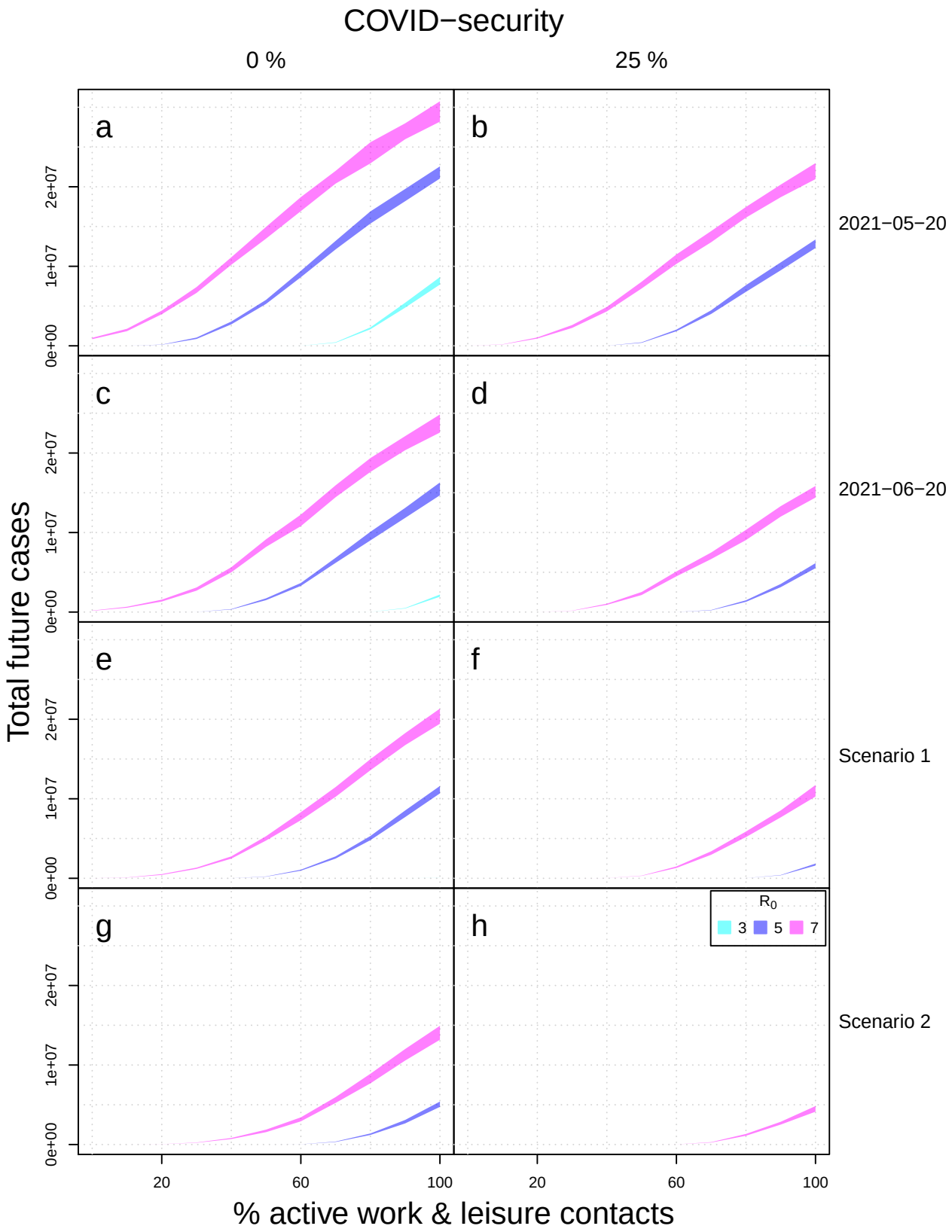

Figure 2: The projected number of cases as a function of active contacts for different initial R_0 values.

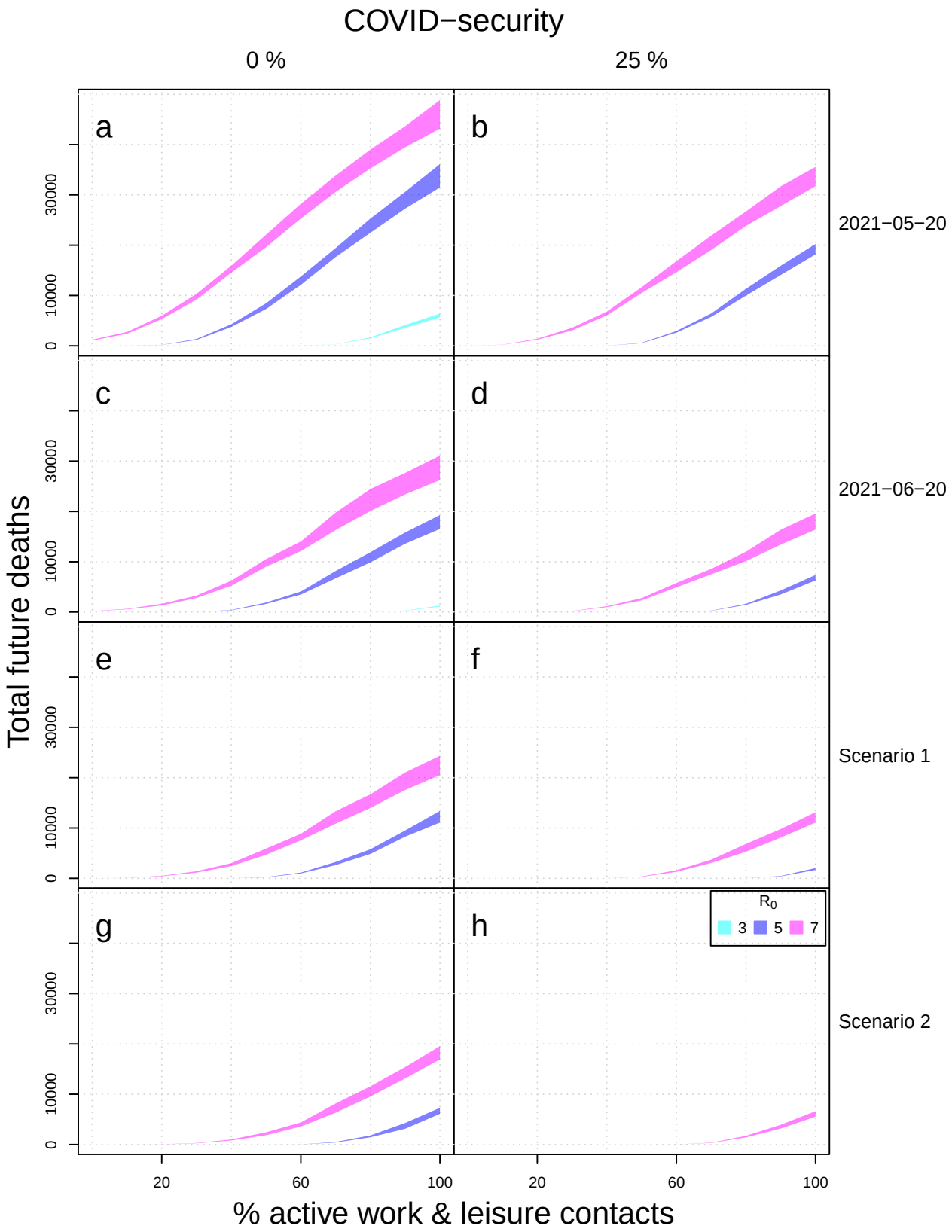

Figure 3: The projected number of deaths as a function of active contacts for different initial R_0 values.

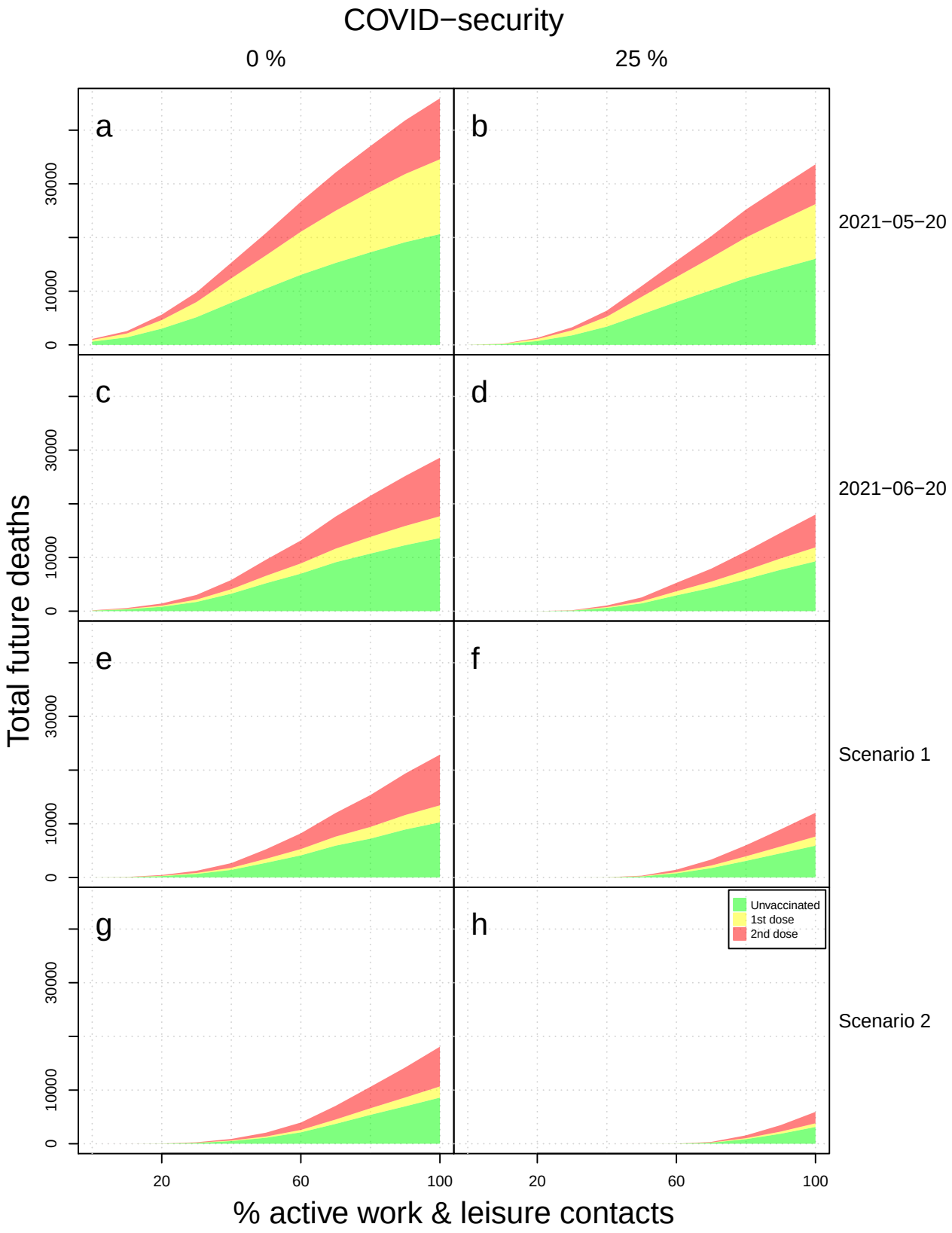

Figure 4: The number of deaths broken down by vaccine status as a function of active social contacts, for a delta-like variant with $R_0 = 7$.

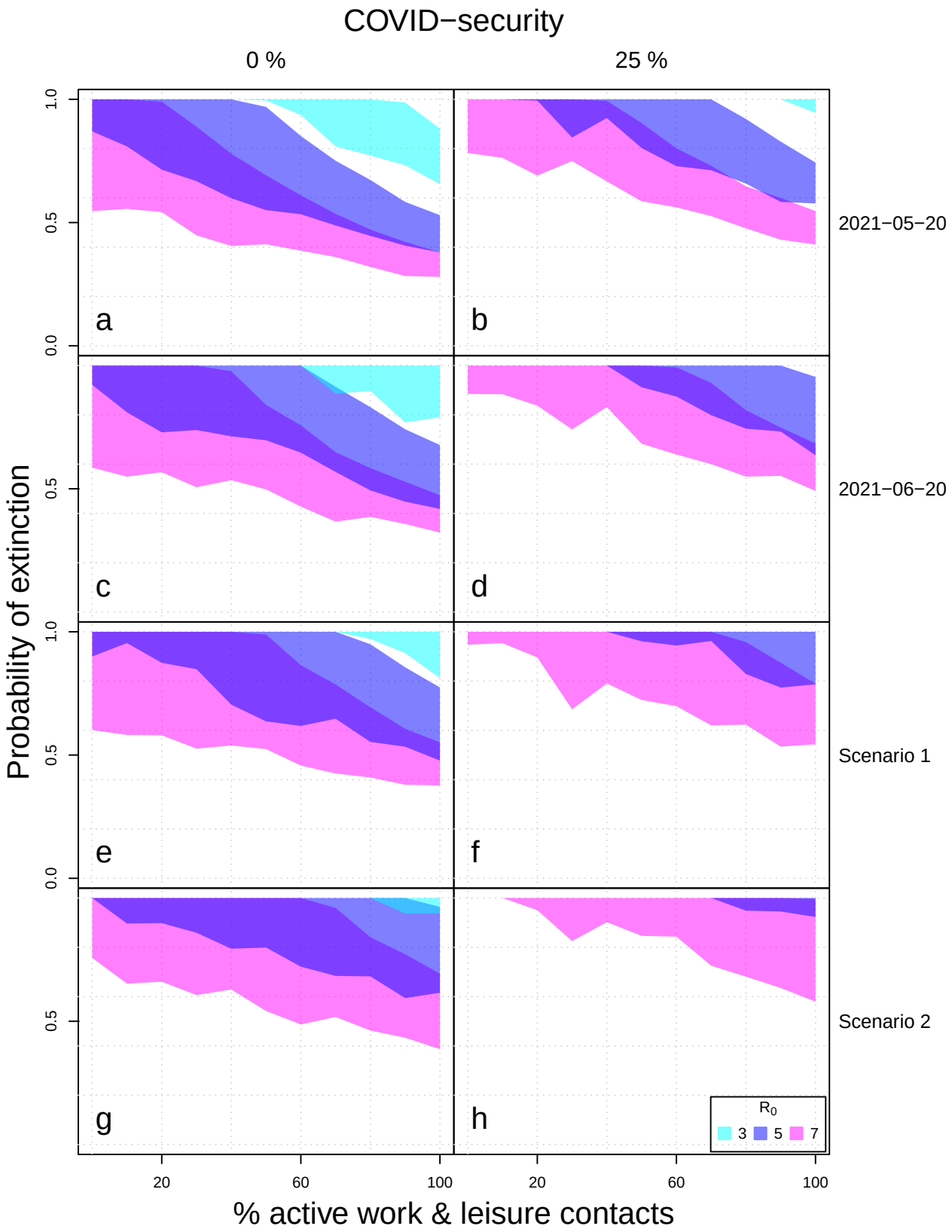

Figure 5: The probability of extinction as a function of active contacts for different initial R_0 values.

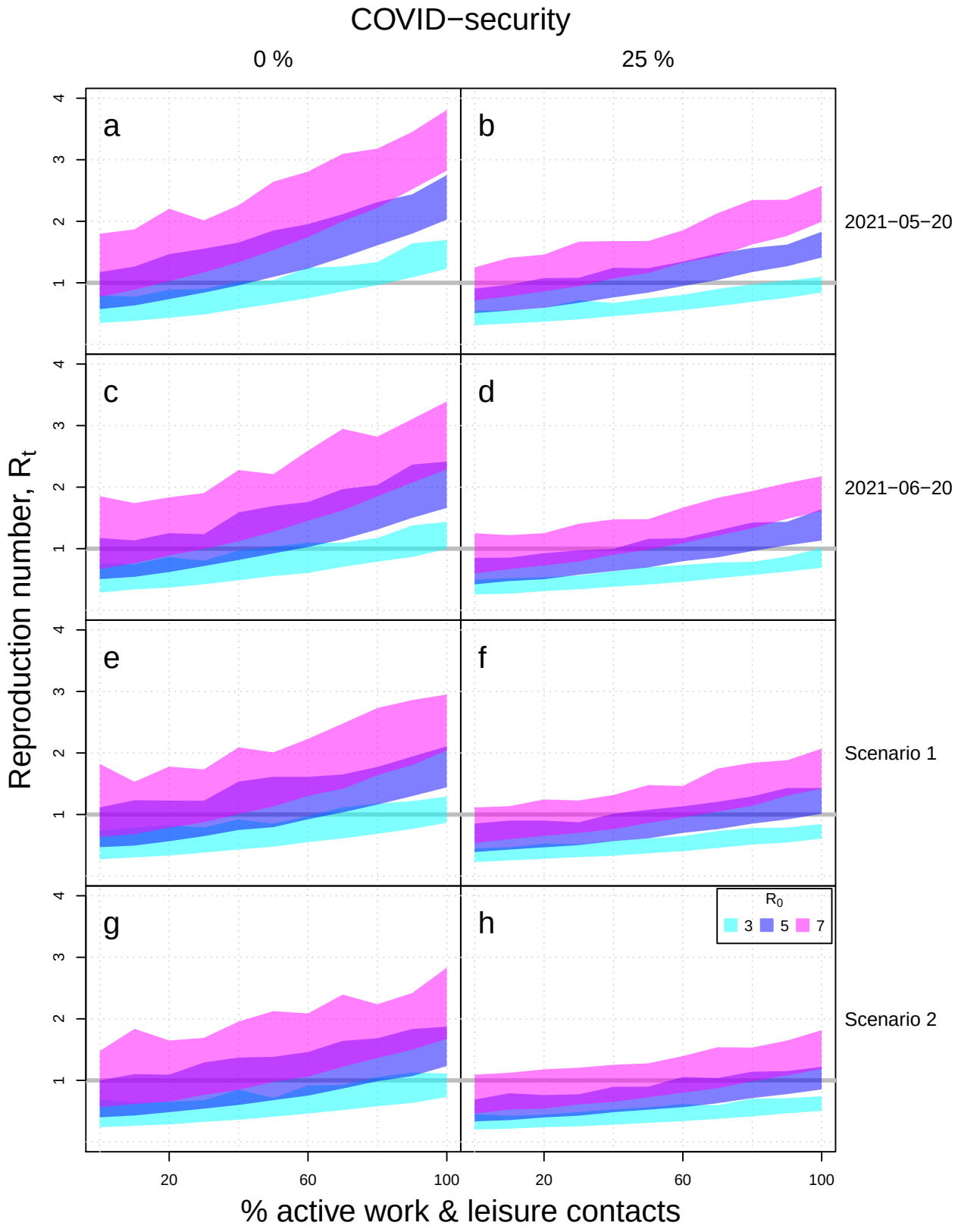

Figure 6: The projected reproduction number as a function of active contacts for different initial reproduction numbers with lower vaccine uptake.

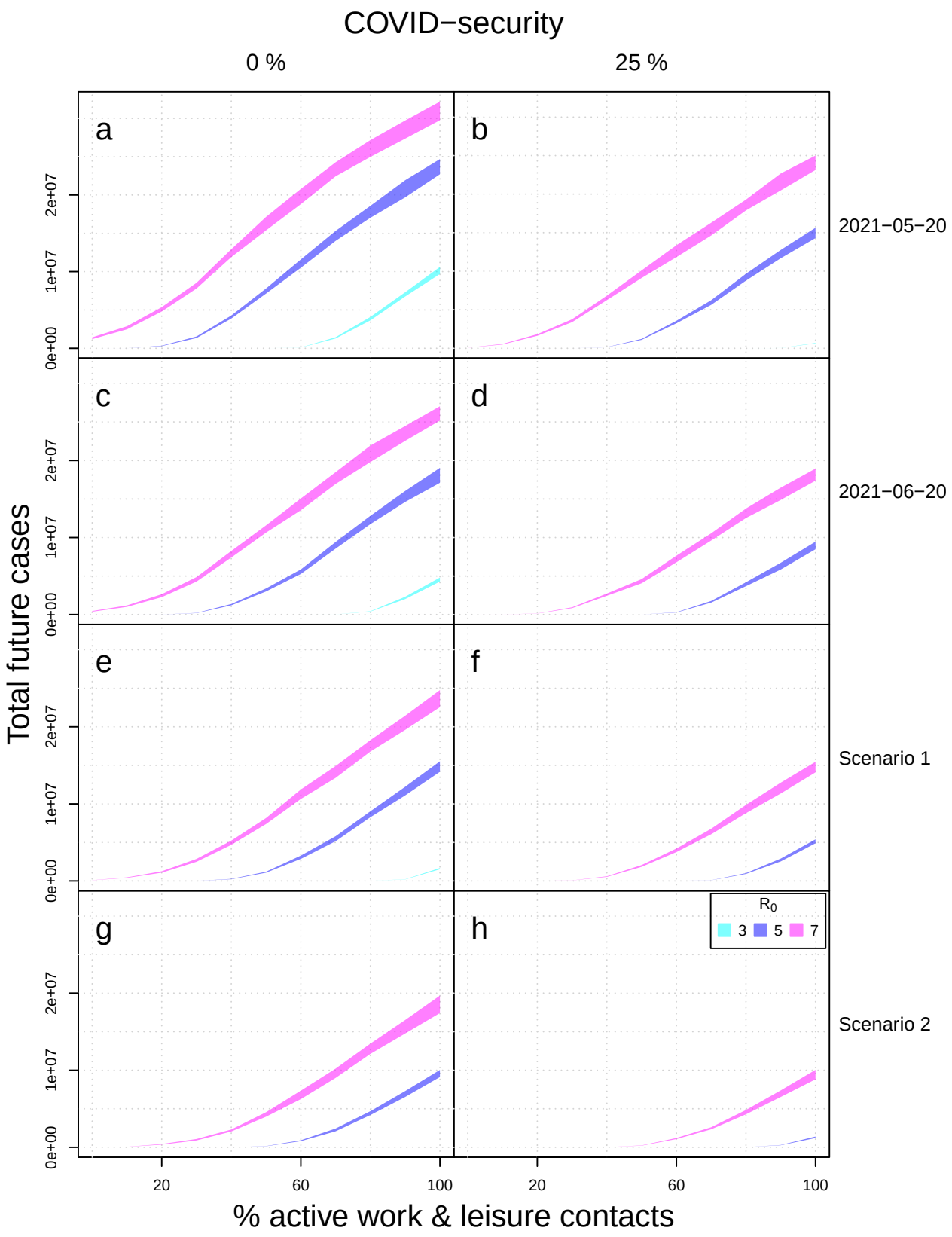

Figure 7: The projected number of cases as a function of active contacts for different initial R_0 values with lower vaccine uptake.

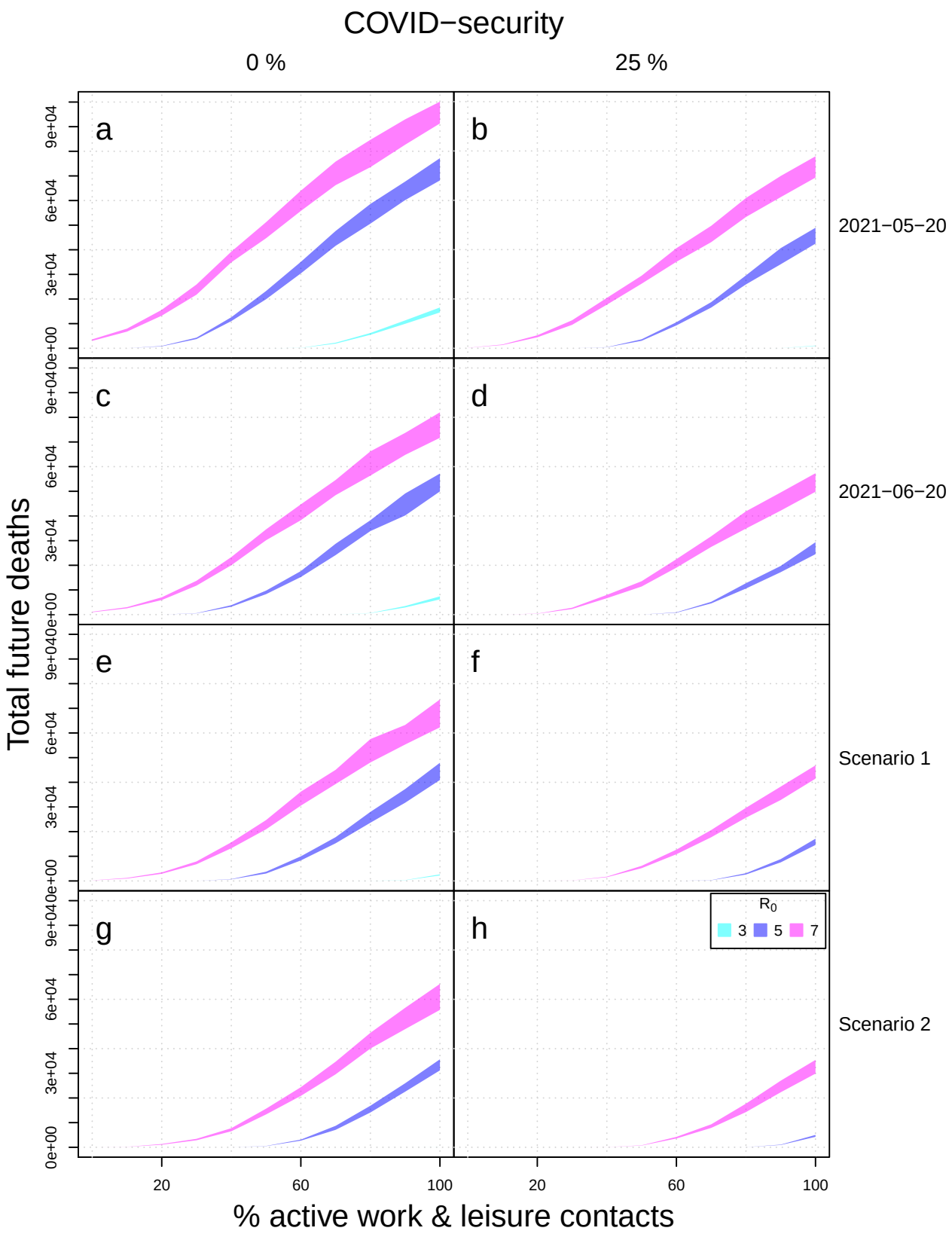

Figure 8: The projected number of deaths as a function of active contacts for different initial R_0 values with lower vaccine uptake.

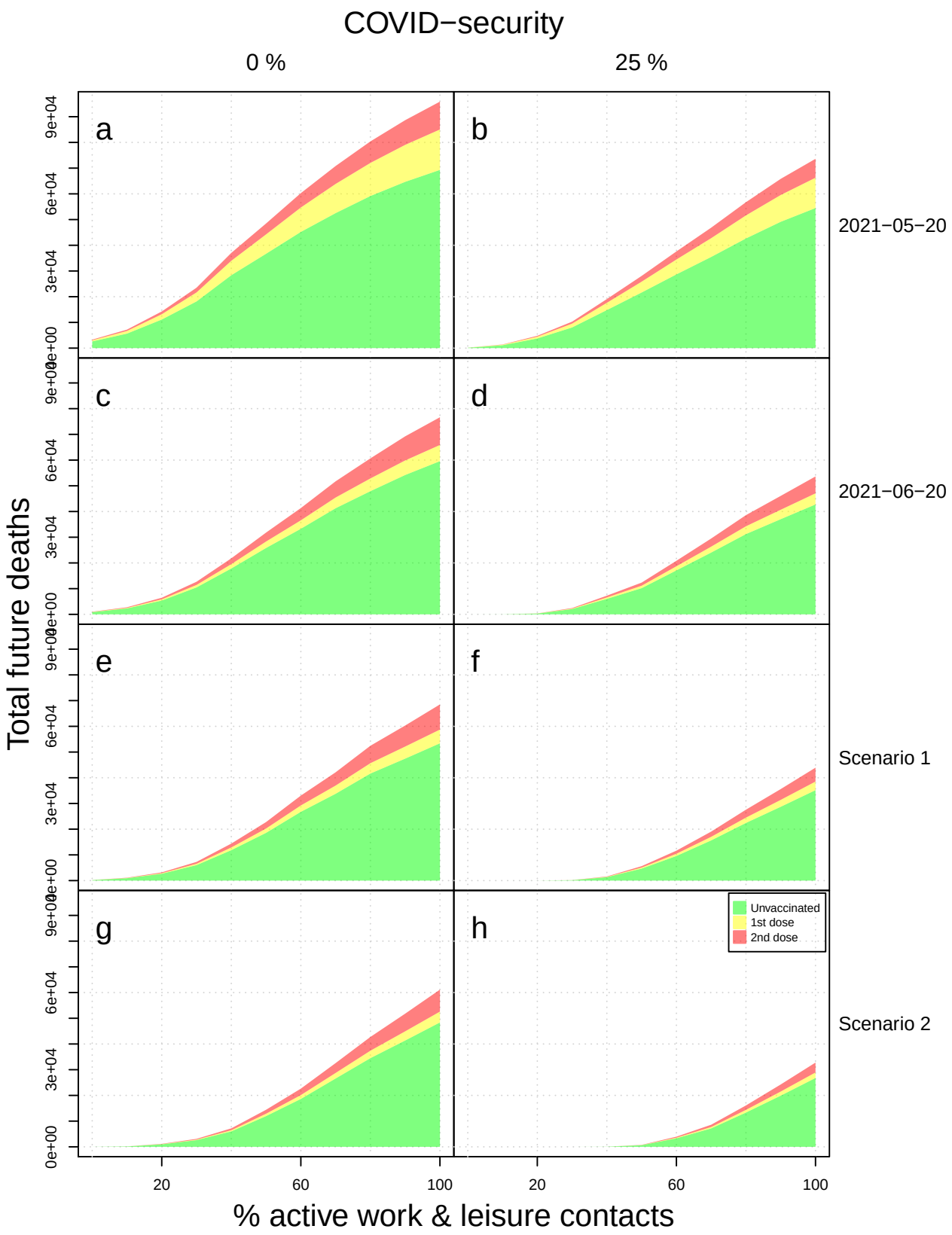

Figure 9: The number of deaths broken down by vaccine status as a function of active contacts with lower vaccine uptake for a delta-like variant of $R_0 = 7$.

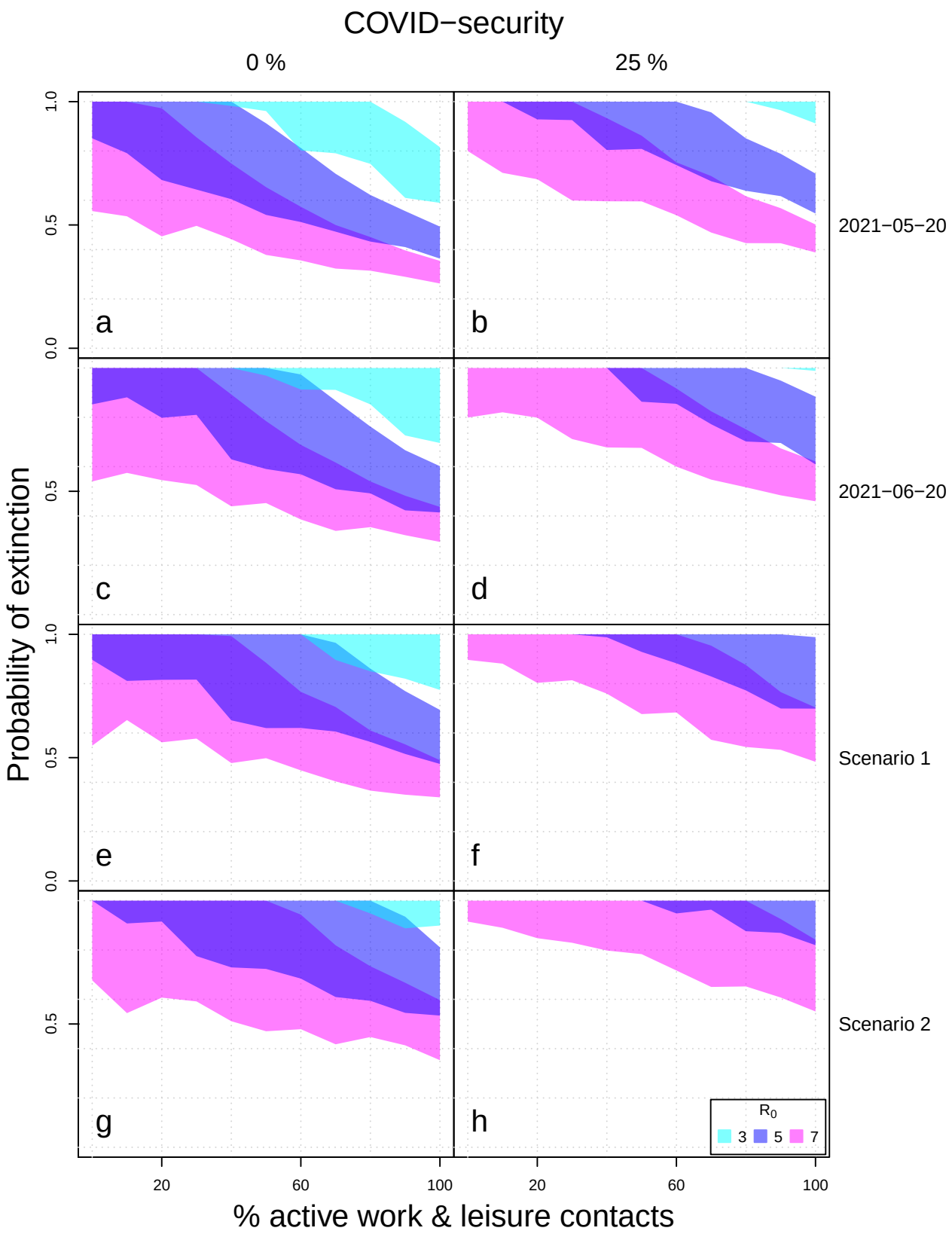

Figure 10: The probability of extinction as a function of active contacts for different initial R_0 values with lower vaccine uptake.