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Supplementary Material: Early COVID-19 Vaccine Impact on Confirmed Cases in Older Populations in the Americas

This supplementary material is presented as supporting information alongside the article **"Early COVID-19 Vaccine Impact on Confirmed Cases in Older Populations in the Americas"**, on behalf of the authors, who remain responsible for the accuracy and appropriateness of the content. The same standards for ethics, copyright, attributions, and permissions as for the article apply.

Appendix A

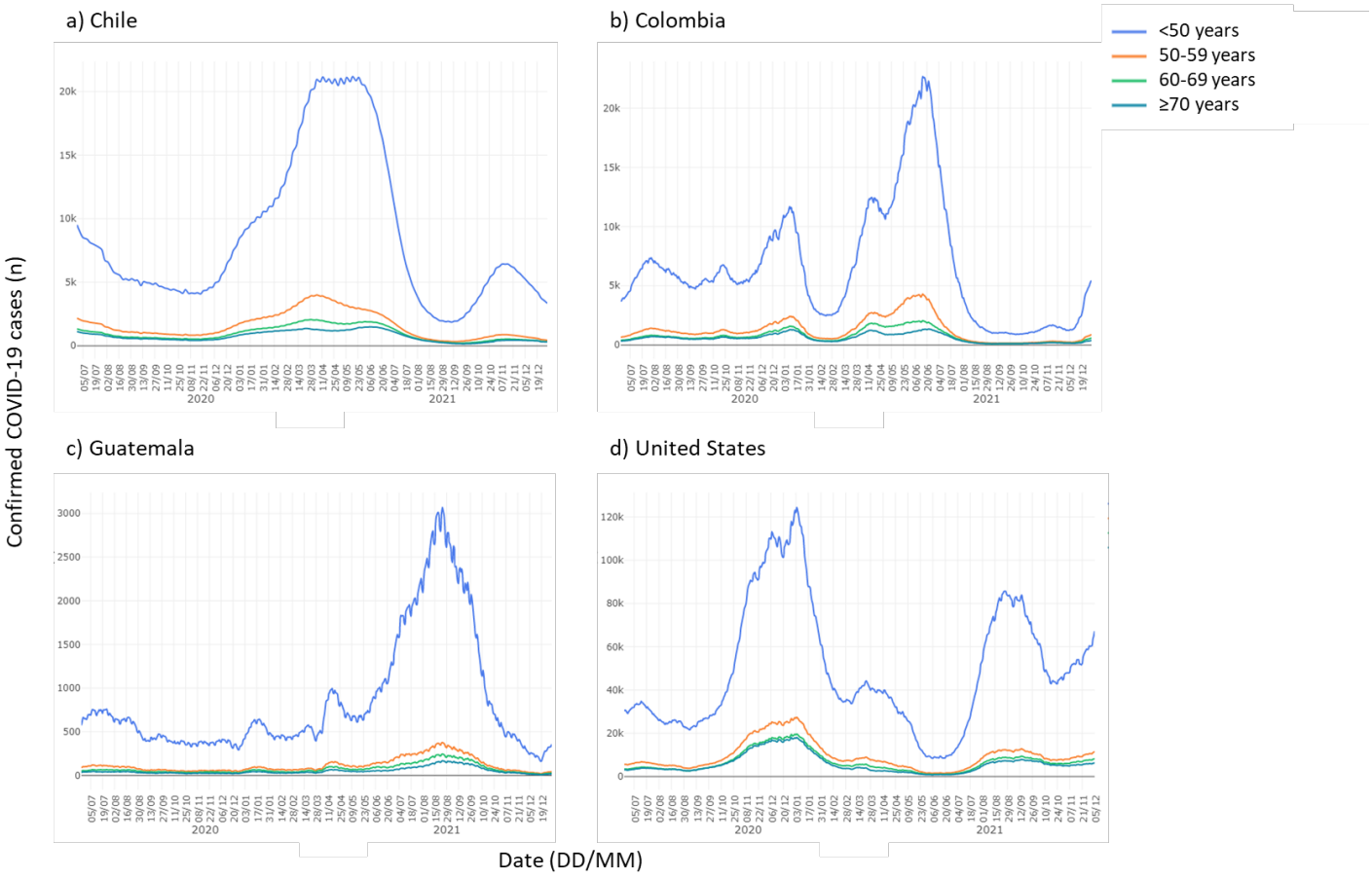
Epidemiological context, use of non-pharmaceutical interventions and COVID-19 vaccination roll-out by country: Chile, Colombia, Guatemala and the United States

Epidemiological context

COVID-19 cases were first identified in December 2019. The epidemiological context has varied worldwide, characterized by waves of cases seen in all countries. North American countries first detected positive cases in January 2020, followed by Latin American countries in February and March 2020. Lockdowns or stay-at-home orders were employed by governments, with different degrees of restrictions. These restrictions to mobility contributed to a reduction in the number of cases. North America and Latin America saw increases in the number of cases in June-August 2020, November-February 2021 and July 2021. The highest number of notified COVID-19 cases were observed after the periods corresponding to end-of-year holiday seasons (December), likely coinciding with lifting mobility restrictions, increases in population movement, and family events (1) (Supplementary Figure 1). Daily testing rates have varied throughout the pandemic by country, but have increased in periods that correspond to peak transmission periods (1). Proportions of positive cases have ranged between 1.8-20.1% in North America, and 4.5-53.2% in Latin American countries (1). Constant test-seeking behavior has been reported for all four countries included in this analysis (1), although publicly age-specific data on testing behaviors is limited.

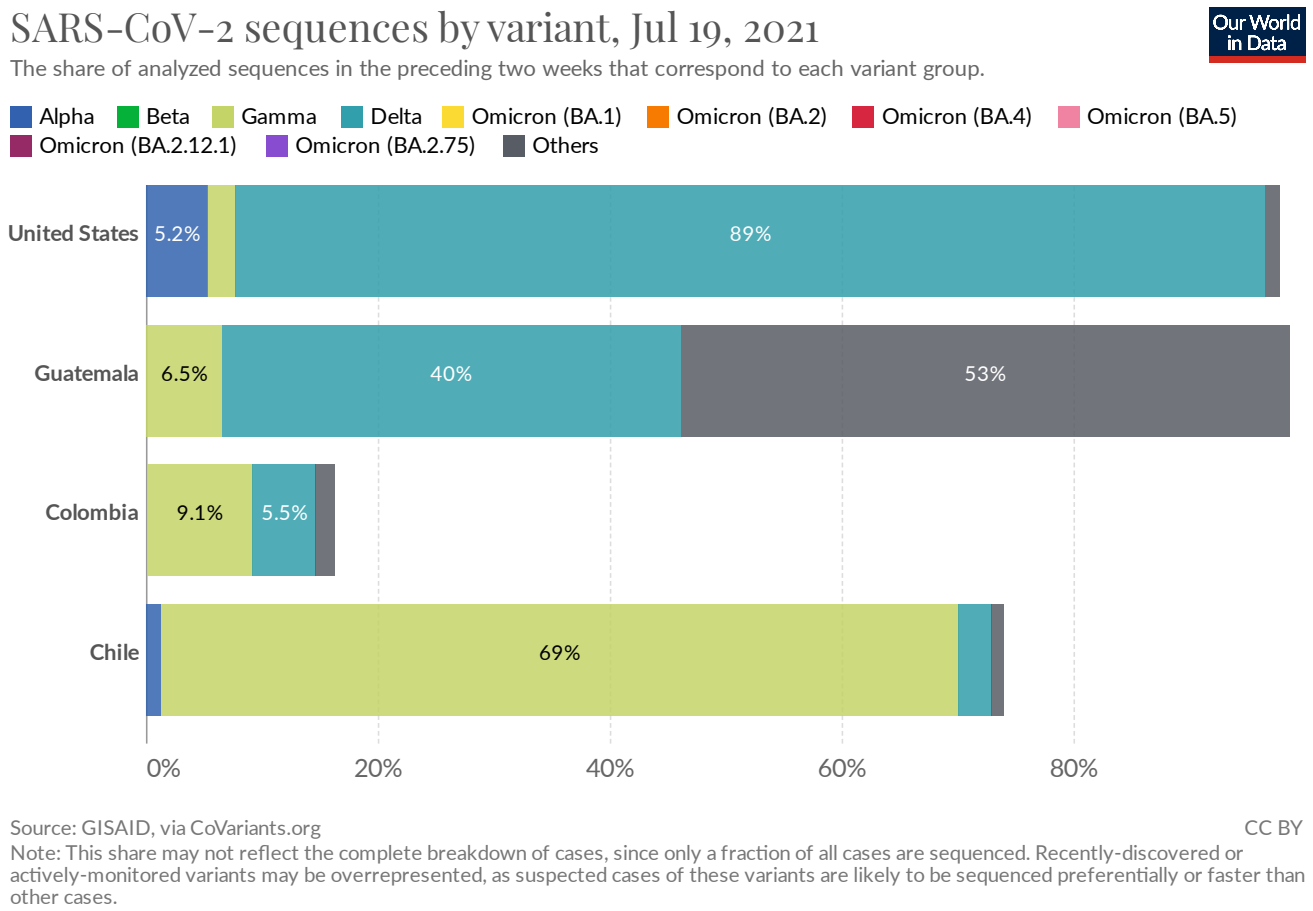
Supplementary Figure 1. Confirmed COVID-19 cases, by studied age groups in selected countries, 2020-2021.

Graphs show weekly number of confirmed COVID-19 cases by age group and country. Data sources: (2–5)



The changes in circulating variants of concern (VOC) have added a level of complexity to the pandemic. Between January and May 2021, Alpha, Beta and Gamma SARS-CoV-2 variants were reported in all countries. By July 2021, variants of concern (VOCs) had been reported in all four countries under study: Alpha, Beta and Gamma were predominant variants detected primarily in early 2021 in the United States and Latin America. Beginning in mid-2021, the Delta variant was reported first in North America; and subsequently in Guatemala and Colombia (Supplementary Figure 2). Case sequencing, however, varied between countries and ranged from 16.2% of confirmed cases in the United States to 0.1% in Colombia (1) . The circulation of variants is assumed based on reporting date by country (first detection) and percentage of circulation.

Supplementary Figure 2. SARS-CoV-2 sequences by variants by country, July 2021 (1).
Source: Our World in Data.



Use of non-pharmaceutical interventions as a tool to control COVID-19 transmission

Non-pharmaceutical interventions (NPI) continued as a tool to reduce COVID-19 cases as vaccination efforts increased world-wide. Within each country, the implementation of these NPIs has been nation-wide affecting all age groups in each setting, though they have begun at different moments during the pandemic. NPIs have been, for the most part, aimed at reducing contacts and have thus been implemented in different ways given population social mixing dynamics vary in each of these countries. The United States implemented public health interventions aimed at social distancing in low social mixing settings (6), where a higher prevalence of elderly adults live in closed settings with similarly-aged adults (approximately 6.5% of adults aged ≥65 years living in nursing homes and assisted care) (7,8). In the United States, non-pharmaceutical interventions have varied by state and have changed throughout the study period (after vaccination, specific recommendations on mask use were modified) (6). In Latin America non-pharmaceutical interventions have varied between countries, but were characterized by strict initial lockdowns and mobility restrictions. Latin American countries, on the other hand have high social mixing patterns (9), and low prevalence of elderly living in closed settings (estimates range from <0.1% to 1.9% of adults aged ≥60 who live outside a family home (10,11). In the context of COVID-19, these conditions must be considered when evaluating the impact of measures that affect transmission dynamics at the population level. Settings in which individuals of all ages interact continuously allow for a stable incidence ratio, since population mixing dynamics do not differ by age groups. In setting where population dynamics differ between age groups because of separate housing conditions (such as France (12,13) or the United States (8), to a lesser extent), the infection risk also differs; therefore the ratio of confirmed COVID-19 cases is not stable and does not favor proper comparisons following this approach.

COVID-19 Vaccination roll-out

COVID-19 vaccination deployment in the United States began in late December 2020 and prioritized health care workers, long-term care facilities, and older age groups. In the United States, criteria for prioritization differed by state. In Latin America, vaccination deployment occurred between late December 2020 and mid-February 2021, prioritizing health care workers and older age groups. The roll-out of COVID-19 vaccines in the Americas coincided with a period of virological change due to the emergence of the Delta variant, as mentioned in Appendix A, a variant characterized by higher transmissibility (14,15).

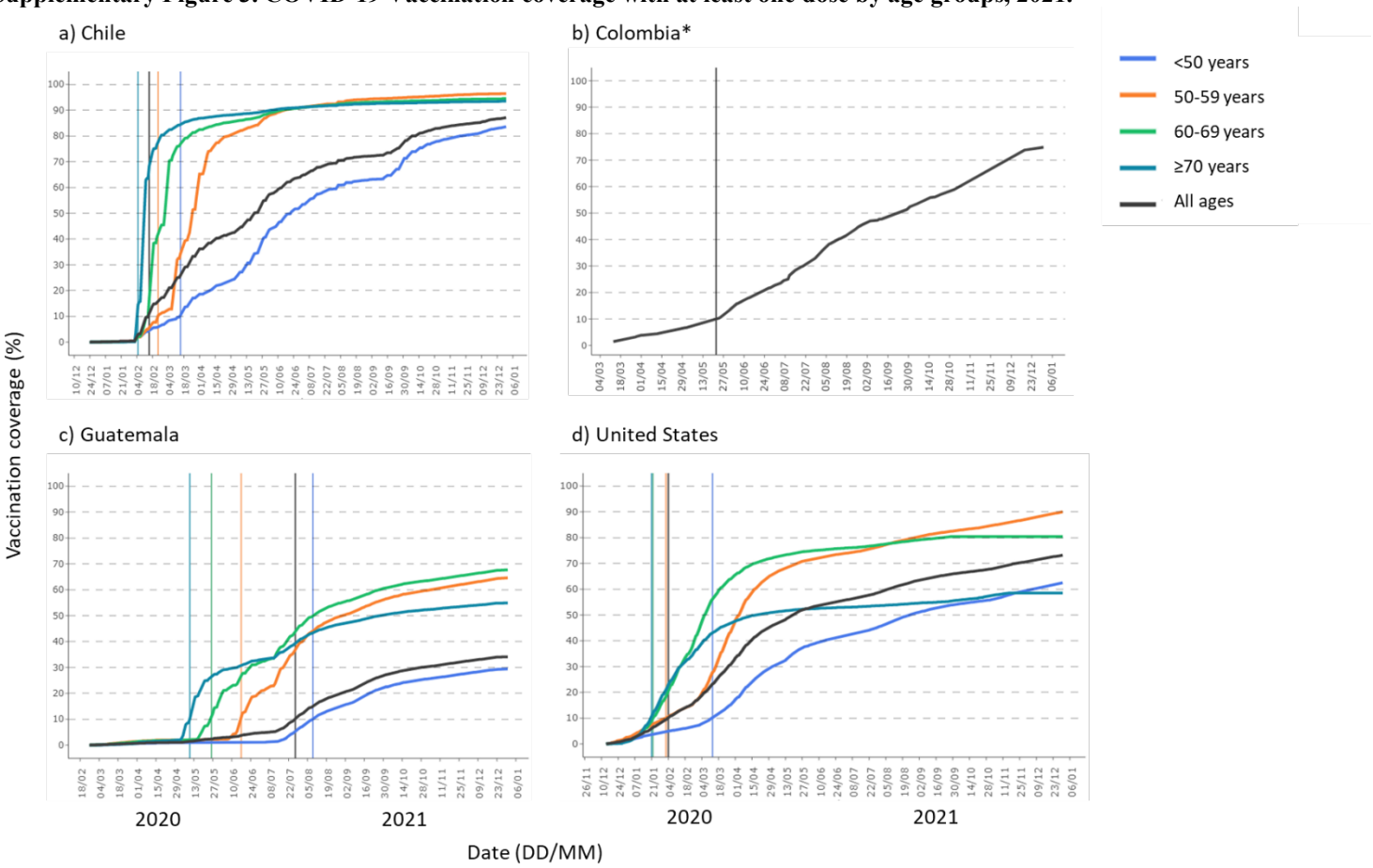
Countries included in this analysis employed either mRNA, viral vector, or inactivated vaccines concurrently during 2021, all of which have high efficacy/effectiveness against severe disease, hospitalization and death (16,17) (Supplementary Table 1). Nevertheless, specific vaccines administered in each country varied and were implemented at different moments based on availability (18).

Supplementary Table 1. Vaccines administered by country, 2020-2021.

COVID-19 Vaccine	Vaccine Type	Chile	Colombia	Guatemala	United States
Pfizer BioNTech (Comirnaty)	mRNA	X	X	X	X
Moderna (mRNA-1273)	mRNA		X	X	X
AD26.COV 2.5 (Janssen)	Viral vector		X		X
AstraZeneca (Vaxzevria)	Viral vector	X	X	X	
Gamaleya (Sputnik V)	Viral vector			X	
SII- Covishield	Viral vector			X	
Sinovac (CoronaVac)	Inactivated virus	X	X		

Up to July 16, 2021 vaccination coverage with at least one dose of any COVID-19 vaccine among all ages was 56% in the Unites States, 5.5% in Guatemala, 29% in Colombia, and 70% in Chile (1,19). Cumulative vaccination coverage data by day show that vaccination in the age group of those over 70 years was quick, increasing markedly once vaccination was implemented in each country (Supplementary figure 3). Vaccination in the 50-59 and 60-69 year age groups increased subsequently, reaching coverage rates well above 30% in all four analyzed countries by July 16, 2021. Specific dates by which 10% vaccination coverage had been achieved in each analyzed age group are presented in Supplementary table 2.

Supplementary Figure 3. COVID-19 Vaccination coverage with at least one dose by age groups, 2021.



*Note: Solid vertical lines indicate date by which 10% vaccination was achieved by age group. *Granular data by age group not available for Colombia, vaccination coverage reference dates obtained from Colombian Ministry of Health COVID-19 vaccination dashboard* (20).

Supplementary Table 2. Date by which 10% vaccination coverage was achieved, by country and age groups, 2021.

Age group (years)	Chile	Colombia	Guatemala	United States
<50	15 March	20 July	9 August	13 March
50 to 59	23 February	28 May	17 June	2 February
60 to 69	15 February	24 April	26 May	22 January
≥70	5 February	12 March	10 May	21 January
All ages	15 February	22 May	27 July	4 February

Data sources: (1,5,21)

Appendix B. Sensitivity Analyses

Methods
Following the same approach to calculate vaccination impact as used in the main analysis, we conducted a sensitivity analysis using different reference age-group populations (18-49 years and 40-49 years). Additional sensitivity analyses were also conducted incorporating a 14-day lag in defining pre-vaccination period, using the <50 years group as reference. This was defined as the period between 1 July 2020 and 14 days after 10% one-dose-vaccination coverage was reached in a given eligible age group, to account for the time it takes to mount a protective immune response after COVID-19 vaccination. We defined post-vaccination period as 14 days after 10% one-dose vaccination coverage was reached in a given eligible age group, and when 10% vaccination coverage was achieved in the reference group.

For data on COVID-19 deaths in Chile and Guatemala, sensitivity analyses were also conducted using 18-49 years and 40-49 years as reference groups.

Results
Using 18-49 and 40-49 years as reference groups in this analysis resulted in smaller percent changes in the ratio of COVID-19 cases between compared groups after, compared to before, vaccine implementation in all countries (Supplementary Tables 3 and 4, respectively). Analyses in Chile using other reference age groups were not possible for 50+ and 50-59 year groups, because the 10% vaccination coverage endpoint of both groups was met at the same time, leaving no margin of available data for calculating post-vaccination ratios (hence limiting calculation of percent changes).

The ratio of COVID-19 cases among those aged ≥50 years vs. 18-49 years decreased by 21.0% (95%CI 20.4; 21.6) in Colombia, and 19.1% (95%CI 18.9; 19.4) in Guatemala after vaccine implementation. In the United States, the percent change observed was -1.0% (95%CI -1.0; -1.1) (Supplementary Table 3). Specific reductions in the ratio of COVID-19 cases by age group (50-59, 60-69, and ≥70 vs. those aged <18-49 years) ranged from 3.1% to 6.1% in Chile, 10.5% to 28.5% in Colombia, 13.8% to 20.8% in Guatemala, and -5.4% to 0.5% in the USA. The reduction in the ratio of confirmed cases between pre- and post-vaccination periods was highest in the earliest vaccination-eligible group (≥70 years) (range: 0.5% (95% CI 0.5; 0.6) in the USA – 28.5% (95% CI 27.0; 29.9) in Colombia), and lowest in the latest eligible group (50-59 years) (range: -2.8% (95% CI -2.8; -2.8) in the USA – 13.8% (95% CI 13.6; 14.0) in Guatemala (Supplementary Table 3).

The ratio of COVID-19 cases among those aged ≥50 years vs. 40-49 years decreased by 24.3% (95%CI 23.7; 24.9) in Colombia, and 19.3% (95%CI 18.9; 19.7) in Guatemala after vaccine implementation. In the United States, the percent change observed was -1.6% (95%CI -1.6; -1.6) (Supplementary Table 4). Specific reductions in the ratio of COVID-19 cases by age group (50-59, 60-69, and ≥70 vs. those aged <40-49 years) ranged from 2.9% to 6.2% in Chile, 13.3% to 34.0% in Colombia, 12.9% to 22.1% in Guatemala, and -4.6% to -0.5% in the USA. The reduction in the ratio of confirmed cases between pre- and post-vaccination periods was highest in the earliest vaccination-eligible group (≥70 years) (range: -0.5% (95% CI -0.5; -0.5) in the USA – 34.0% (95% CI 32.2; 35.8) in Colombia), and lowest in the latest eligible group (50-59 years) (range: -2.6% (95% CI -2.0; -2.1) in the USA – 13.3% (95% CI 12.8; 13.8) in Colombia (Supplementary Table 4).

Supplementary Table 3. Number and ratio of confirmed COVID-19 deaths pre-and post-vaccination by specific prioritized age groups vs. reference group (18-49 years) by country, 2020-2021.

	Age group (years)	Chile	Colombia	Guatemala	USA
	18-49	367 502	2 117 786	178 895	9 883 062
Pre-Vaccination	≥50	202 348	1 017 682	61 765	6 700 737
	Ratio	0.55	0.48	0.35	0.68
	18-49	0	767 016	62 172	612 446
Post-vaccination	≥50	0	291 613	17 362	419 531
	Ratio	NA	0.38	0.28	0.69
Percent change (95% CI)		NA	21.00 (20.44; 21.56)*	19.13 (18.85; 19.41)*	-1.03 (-1.01; -1.05)*
	18-49	367 502	2 117 786	178 895	9 883 062
Pre-Vaccination	50-59	95 160	484 364	29 788	2 824 012
	Ratio	0.26	0.23	0.17	0.29
	18-49	0	767 016	62 172	612 446
Post-Vaccination	50-59	0	157 206	8 968	180 249
	Ratio	NA	0.21	0.14	0.29
Percent change (95%CI)		NA	10.48 (10.01; 10.95)*	13.77 (13.57; 13.97)*	-2.80 (-2.76; -2.83)*
	18-49	338 571	1 727 434	161 389	9 327 376
Pre-Vaccination	60-69	54 493	245 248	17 253	1 890 559
	Ratio	0.16	0.14	0.11	0.20
	18-49	28 931	1 157 368	79 678	1 168 132
Post-Vaccination	60-69	4 512	136 323	7 139	250 375
	Ratio	0.16	0.12	0.09	0.21
Percent change (95%CI)		3.11 (3.07; 3.14)*	16.90 (16.04; 17.76)*	15.89 (15.22; 16.56)*	-5.42 (5.31; 5.53)*
	18-49	312 152	1 402 607	151 910	9 267 882
Pre-Vaccination	≥70	41 307	163 304	10 935	1 745 391
	Ratio	0.13	0.12	0.07	0.19
	18-49	55 350	1 482 195	89 157	1 227 626
Post-Vaccination	≥70	6 873	122 852	5 043	229 668
	Ratio	0.12	0.08	0.06	0.19
Percent change (95%CI)		6.06 (5.90; 6.22)*	28.45 (26.99; 29.90)*	20.83 (19.93; 21.73)*	0.53 (0.52; 0.55)*

* Statistically significant results, p<0.05. Pre-vaccination defined as the period between 1 July 2020 and when 10% one-dose-vaccination coverage was reached in a given eligible age group. Post-vaccination was defined as the period between 10% one-dose-vaccination coverage in a given eligible age group and when 10% vaccination coverage in the reference group was achieved. Reference group: 18-49 years. For data sources, see references (2,4,5,20).

Supplementary Table 4. Number and ratio of confirmed COVID-19 cases pre- and post-vaccination for prioritized age groups vs. reference group (40 - 49 years) by country, 2020-2021.

	Age group (years)	Chile	Colombia	Guatemala	USA
	40-49	101 604	565 042	43 259	2 911 443
Pre-Vaccination	≥50	202 348	1 017 682	61 765	6 700 737
	Ratio	1.99	1.80	1.43	2.30
	40-49	0	201 011	12 054	47 092
Post-vaccination	≥50	0	274 005	13 886	110 140
	Ratio	NA	1.36	1.15	2.34
Percent change (95% CI)		NA	24.32 (23.71; 24.93)*	19.33 (18.94; 19.71)*	-1.61 (-1.60; -1.62)*
	40-49	101 604	565 042	43 259	2 911 443
Pre-Vaccination	50-59	95 160	484 364	29 788	2 824 012
	Ratio	0.94	0.86	0.69	0.97
	40-49	0	201 011	12 054	47 092
Post-Vaccination	50-59	0	149 342	7 227	46 606
	Ratio	NA	0.74	0.60	0.99
Percent change (95%CI)		NA	13.30 (12.79; 13.82)*	12.92 (12.69; 13.15)*	-2.06 (-2.05; -2.07)*
	40-49	93 617	454,350	38,921	2,744,010
Pre-Vaccination	60-69	54 493	245,248	17,253	1,890,559
	Ratio	0.58	0.54	0.44	0.69
	40-49	7 987	311,703	16,392	214,525
Post-Vaccination	60-69	4 512	131,015	6,079	154,720
	Ratio	0.57	0.42	0.37	0.72
Percent change (95%CI)		2.92 (2.89; 2.95)*	22.22 (21.16; 23.23)*	16.25 (15.57; 16.94)*	-4.64 (-4.60; -4.69)*
	40-49	86 294	365 146	36 532	2 725 999
Pre-Vaccination	≥70	41 307	163 304	10 935	1 745 391
	Ratio	0.48	0.45	0.30	0.64
	40-49	15 310	400 907	18 781	232 536
Post-Vaccination	≥70	6 873	118 414	4 369	149 576
	Ratio	0.45	0.30	0.23	0.64

Percent change (95%CI)	6.26 (6.12; 6.41)*	34.00 (32.18; 35.83)*	22.07 (21.14; 23.01)*	-0.47 (-0.46; -0.48)*

* Statistically significant results, p<0.05. Pre-vaccination defined as the period between 1 July 2020 and when 10% one-dose-vaccination coverage was reached in a given eligible age group. Post-vaccination was defined as the period between 10% one-dose-vaccination coverage in a given eligible age group and when 10% vaccination coverage in the reference group was achieved. Reference group: 40-49 years. For data sources, see references (2,4,5,22). NA: Not applicable, due to very short time window between one-dose vaccination coverage reached between comparison groups.

After incorporating a 14-day lag in the pre-vaccination period, the ratio of COVID-19 cases among those aged ≥50 years vs. <50 years decreased by 14.6% (95%CI 14.2; 15.0) in Chile, 24.8% (95%CI 24.4; 25.3) in Colombia, 20.1% (95%CI 20.0; 20.3) in Guatemala, and 13.0% (95%CI 12.7; 13.3) in the USA after vaccine implementation (Supplementary Table 5).

Specific reductions in the ratio of COVID-19 cases by age group (50-59, 60-69, and ≥70 vs. those aged <50 years) ranged from 5.7% to 24.3% in Chile, 21.7% to 30.8% in Colombia, 17.5% to 24.6% in Guatemala, and 4.6% to 23.1% in the USA. The reduction in the ratio of confirmed cases between pre- and post-vaccination periods was highest in the earliest vaccination-eligible group (≥70 years) (range: 23.1% (95% CI 22.1; 24.0) in the USA - 30.8% (95% CI 29.5; 32.0) in Colombia), and lowest in the latest eligible group (50-59 years) (range: 4.6% (95% CI 4.6; 4.7) in the USA – 21.7% (95% CI 20.8; 22.6) in Colombia (Supplementary Table 5).

Supplementary Table 5. Number and ratio of confirmed COVID-19 cases pre- and post-vaccination for prioritized age groups vs. reference (<50 years) by country, including 14-day lag, 2020-2021.

	Age group (years)	Chile	Colombia	Guatemala	USA
	<50	506 560	2 666 836	215 347	13 655 445
Pre-Vaccination	≥50	225 331	1 117 554	66 298	7 029 367
	Ratio	0.45	0.42	0.31	0.52
	<50	108 380	739 095	119 986	1 524 713
Post-vaccination	≥50	41 181	232 999	29 531	682 571
	Ratio	0.38	0.32	0.25	0.45
Percent change (95% CI)		14.61 (14.22; 14.99)*	24.82 (24.39; 25.26)*	20.13 (19.96; 20.30)*	13.01 (12.73; 13.29)*
	<50	506 560	2 666 836	215 347	13 655 445
Pre-Vaccination	50-59	106 522	541 439	32 142	2 964 444
	Ratio	0.21	0.20	0.15	0.22
	<50	108 380	739 095	119 986	1 524 713
Post-Vaccination	50-59	21 506	117 734	14 751	315 800
	Ratio	0.20	0.16	0.12	0.21
Percent change (95%CI)		5.71 (5.64; 5.79)*	21.68 (20.79; 22.56)*	17.45 (17.24; 17.66)*	4.61 (4.55; 4.67)*
	<50	463 566	2 097 654	190 070	13 160 311
Pre-Vaccination	60-69	60 579	267 467	18 443	2 037 310
	Ratio	0.13	0.13	0.10	0.16
	<50	151 374	1 308 277	145 263	2 019 847
Post-Vaccination	60-69	16 922	126 916	11 171	286 407
	Ratio	0.11	0.10	0.08	0.14
Percent change (95%CI)		14.50 (13.98; 15.03)*	24.22 (23.47; 24.97)*	20.62 (20.20; 21.03)*	8.39 (8.18; 8.60)*
	<50	426 788	1 639 541	177 080	13 106 827
Pre-Vaccination	≥70	45 815	170 501	11 561	1 880 800
	Ratio	0.11	0.10	0.07	0.14
	<50	188 152	1 766 390	158 253	2 073 331
Post-Vaccination	≥70	15 166	126 496	7 764	227 167
	Ratio	0.08	0.07	0.05	0.11
Percent change (95%CI)		24.29 (22.43; 26.17)*	30.77 (29.52;32.02)*	24.62 (23.97;25.26)*	23.08 (22.12; 24.03)*

* Statistically significant results, $p<0.05$. Pre-vaccination defined as the period between 1 July 2020 and 14 days after 10% one-dose-vaccination coverage was reached in a given eligible age group. Post-vaccination was defined as the period between 14 days after 10% one-dose-vaccination coverage in a given eligible age group and when 10% vaccination coverage in the reference group was achieved. Reference group: <50 years. For data sources, see references (2,4,5,22).

Using 18-49 and 40-49 years as reference groups in this analysis resulted in similar percent changes in the ratio of COVID-19 deaths between compared groups after, compared to before, vaccine implementation in Guatemala (Supplementary Table 6). The percentage change in the ratio of confirmed deaths between pre- and post-vaccination periods in Guatemala was highest in the earliest vaccination-eligible group (≥70: 32.2% (95% CI 25.0; 39.4). The percentage change was lowest in the 60-69 year group, 22.1% (95%CI 17.1; 27.1). Results were similar when 40-49 years was used as reference group. In Chile, analyses were not possible using 18-49 year old group as reference as available data were not disaggregated by specific ages. Calculating impact measures for the 50-59 year old group using 40-49 years as reference was not possible due to a short observation period between the comparison and reference groups.

Supplementary Table 6. Number and ratio of confirmed COVID-19 deaths pre- and post-vaccination by specific prioritized age groups vs. reference group (18-49 and 40-49 years) in Chile and Guatemala, July 2020-August 2021.

	Age group (years)	COVID-19 confirmed deaths			
		Chile		Guatemala	
		Reference: 18-49 years	Reference: 40-49 years	Reference: 18-49 years	Reference: 40-49 years
Pre-Vaccination	Reference**	NP	NA	1 620	944
	50-59	NP	NA	1 400	1 403
	Ratio	NP	NA	0.86	1.49
Post-Vaccination	Reference**	NP	NA	470	213
	50-59	NP	NA	315	258
	Ratio	NP	NA	0.67	1.21
Percent change (95%CI)		NP	NA	22.09 (17.13; 27.05)*	18.79 (11.91; 25.67)*
Pre-Vaccination	Reference**	NP	659	1 502	872
	60-69	NP	3 625	1 850	1 824
	Ratio	NP	5.5	1.23	2.09
Post-Vaccination	Reference**	NP	21	596	287
	60-69	NP	121	524	448
	Ratio	NP	5.76	0.88	1.56
Percent change (95%CI)		NP	-4.73 (-2.91; -6.55)	28.46 (22.50; 34.42)*	25.36 (16.35; 34.37)*
Pre-Vaccination	Reference**	NP	633	1 414	820
	≥70	NP	10 816	2 060	2 027
	Ratio	NP	17.09	1.46	2.47
Post-Vaccination	Reference**	NP	48	685	338
	≥70	NP	827	678	577
	Ratio	NP	17.23	0.99	1.71
Percent change (95%CI)		NP	-0.82 (-0.57; -1.07)	32.19 (25.02; 39.36)*	30.77 (22.53; 39.01)*

* Statistically significant results, p<0.05. Pre-vaccination defined as the period between 1 July 2020 and when vaccination began in a given eligible age group. Post-vaccination was defined as the period between 1 July 2020 and when 10% vaccination coverage was achieved in reference group. **Reference groups: 18-49 and 40-49 years. Data source: see references (2,5). NP: Not possible to obtain results using 18-49 years as reference due to data aggregation limitations. NA: Not applicable, due to very short time window between one-dose vaccination coverage reached between comparison groups.

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