COVID-19

Effectiveness of a vaccine recovery plan after the COVID-19 pandemic in the Siracusa Local Health Authority, Italy. Results of one year follow-up

FABIO CONTARINO[1], ERMINIO DI PIETRO[1], CONCETTA RANDAZZO[1], FRANCESCA BELLA[2], MARIA LIA CONTRINO[3]
[1] Department of Public Health, Epidemiology Unit, Provincial Health Authority of Siracusa, Italy;
[2] Siracusa Cancer Registry, Provincial Health Authority of Siracusa, Italy;
[3] Head of Department of Public Health, Provincial Health Authority of Siracusa, Italy

Keywords

COVID-19 pandemic • Childhood immunization • Vaccine coverage • Missed vaccinations • Recovery plan • Vaccine-preventable diseases • Catch-up programmes

Summary

Introduction. *The COVID-19 pandemic has strongly impacted on the immunization services around the world, threatening the gains made in the control of vaccine-preventable diseases.*
Methods. *A vaccination recovery plan of missed vaccinations has been put in place in the LHA of Siracusa after the pandemic. We compared 2021 and 2020 vaccination coverage by age group and vaccine type after one year of follow-up of the recovery plan. The Chi-square test was executed on proportions for the years 2021 vs 2020. Results were considered statistically significant at a two-tailed p-value ≤ 0.05.*
Results. *36-month coverage rates were 92.5% for polio and 93.7% for measles-containing-vaccine, representing -0.3% and -1.8% decreases, respectively, as compared to 2020. By 8 years of age (booster doses), immunisation coverage was 80.7% for polio and 80.1% for measles, representing a -5.7% and -3.7%, respectively, compared to 2020. 36-month coverage was 56.6% for Men B (-5.0% as compared to 2020), 73.2% for Men ACW135Y/C (+1.1% as compared to 2020) and 86.9% for PNC vaccine (-1.7%, as compared to 2020). Regarding HPV vaccination, in 2021, vaccine coverage was 44.2% (-4.4% compared to 2020). Compared to the previous report, the VC difference among the cohorts narrowed for all almost vaccinations, except for the anti-men B and the anti-HPV vaccination, for which we recorded an increase in VC difference, and for men ACW135Y/C, for which a significant increase has been recorded.*
Conclusions. *Despite the efforts to organize and realize an extensive and well-designed vaccination recovery, our data show that even after the 1-year follow-up, globally deficits in coverage for these routine vaccinations persist, although there has been a substantial and significant recovery of missed vaccinations, especially among younger children and for primary cycles.*

Introduction

A significant and deleterious effect of the COVID-19 pandemic was the decline in vaccination coverage (VC), especially in the first wave, when many vaccinations have been often delayed and/or cancelled, evidenced by epidemiological studies conducted in many countries all over the world and by WHO global immunisation surveillance and monitoring, threatening the gains made in the control of vaccine-preventable diseases (VPDs) for the past decades [1-8]. The causes of the drop of vaccinations are different: social distancing measures, reallocation of health care workers, de-prioritization of routine health care services, and concerns that patients and caregivers seeking routine preventive services, like vaccinations, may be exposed to COVID-19 [5, 9].
Previous research show that the most affected vaccinations by the pandemic have been the non-mandatory ones, particularly those addressing the adolescent and adult population, such as immunization against papillomavirus and that the reductions in vaccination rates were highest among older children (10-17 years) *vs* new-borns (0-2 years) and young children (3-9 years) [7, 10-12].
Left unaddressed, declines in VC will cause a resurgence in disease outbreaks leaving communities across the world at risk of disease and death from VPDs [13-16]. Interim guidelines warning about the risk of VPDs outbreaks have been published, which could cause further pressure on health services [17-19].
The drop of VC rate may represent a particular threat for low- and middle-income countries (LMIC's) for battling the pandemic alongside pre-existing challenges, including the threat of other VPDs [20-22]. Reduction in VC was also observed in industrialized countries [10, 22-27].
For vaccination coverage to recover to pre-pandemic levels, immediate and sustained catch-up efforts are necessary [28]. Efforts are needed to administer missed doses to adolescents nearing the end of the recommended vaccine age windows [29-31].
Improving routine immunization program capacity is essential for countries to adeptly prevent, manage, and recover from outbreak-prone VPDs, as well as VPD-attributable longer-term cancers and diseases [11].
In this study, we assessed the effects of a recovery vaccination program on routine childhood VC in the

Siracusa Local Health Authority (LHA), just over 380,000 inhabitants, in south Italy after the impact of the COVID-19 pandemic of some different cohorts. In more details, we evaluated the vaccination coverage of the same subjects reported in a previous publication, after one year of follow-up [32].
The goals of this analysis are to estimate the level of routine vaccination coverage and above all to evaluate the results of catch-up vaccination strategy have had on curtailing vaccination deficits in this area.

Material and methods

An extensive and well-designed vaccination recovery plan has been put in place in the LHA of Siracusa after the pandemic. The plan included several phases: active calls for children who had missed vaccinations during the pandemic; extraordinary openings of vaccination centres; prioritizing vulnerable people, children and adult, according to their health status and their priorities; and finally, prioritizing the younger children and the completion of primary courses, regardless of the vaccinations, with a special attention for those of the first two years of life.
The birth cohorts, population, target age group, number of doses and year of administration are showed in Table I. Vaccine coverage was calculated using the number of vaccinated in the numerator (extracted from the official records of Epidemiology Unit of the local Health Department) and the eligible population in the denominator (according to Istat data, Italian National Statistical Institute).
We used polio and measles-containing-vaccine as the usual proxy for the hexavalent vaccine (polio, diphtheria, tetanus, hepatitis B, pertussis, *Haemophilus influenzae* type b) and quadrivalent vaccine (measles, rubella, mumps and chicken pox) or trivalent vaccine (measles, rubella, mumps) respectively, since these vaccines are administered in six-in-one and four-in-one (or three-in-one) vaccine formulations in Italy. As for polio, measles-containing-vaccine, men B, men ACW135Y/C and PNC vaccination, we used the available data at 36 months of age, even though these vaccines are usually administered in the first two years of life according to Italian and regional immunization schedule [33, 34], comparing VC rates for the years 2020 (administered till December 2020 to the 2017 cohort) and 2021 (administered till December 2021 to the 2018 cohort).
Polio with diphtheria, tetanus, pertussis and measles with rubella, mumps and chicken pox (the latter being mandatory only for children born after the 2017) vaccinations are boosted at 6 years of age, mandatorily. We used data on polio and measles vaccinations in 2021 (VC 2021) to the 2013 cohort (8 years old), as well as data on vaccinations administered through the year 2020 (VC 2020) to the 2012 cohorts (8 years old).
Regarding anti-HPV vaccination, we used the full-cycle coverage for 15-year-old (2005 cohort in 2020, 2006 cohort in 2021) since it is offered during the 12th year of life, according to national and regional immunization schedule [33, 34].
The vaccination against rotavirus were not impacted by the recovery plan, being this vaccine administered in the first weeks of life, so the related data are the same reported in the previous report [32].
For all vaccinations, data are reported for birth cohort and a complete vaccination cycle, regardless of the schedule adopted and the vaccine type administered.
We performed a statistical analysis at 36 months (polio, measles, men B, men ACW135Y/men C vaccinations; cohort 2017 and 2018), 8 years (polio and measles booster doses; cohort 2012 and 2013) and 15 years (HPV; cohort 2005 and 2006) for mandatory and recommended vaccinations.
The Chi-square test was executed on proportions for the years 2021 vs 2020. Analysis findings were considered statistically significant at a two-tailed p-value ≤ 0.05.

Results

The 2020 and 2021 VC rates for all vaccinations are reported in Table II.
With reference to the mandatory childhood immunisations,

Tab. I. VDP, birth cohort, population, target group, number of doses and year of administration of vaccinations to assess the vaccine coverage.

VDP	Mandatory/ Recommended	Birth cohort	Eligible population§	Target age group	Number of doses	Year of vaccine administration (1st January-31st December)
Polio, Measles, Men B, Men ACW135Y/Men C	Mandatory	2017	3,155	36 months	3 for polio and 3 (or 4) for Men B; 1 for measles and Men ACW135Y/C	2020
	Recommended	2018	3,090			2021
Polio, Measles	Mandatory	2012	3,605	8 years	4 for polio; 2 for measles	2020
		2013	3,408			2021
HPV	Recommended	2005	3,909	15 years	2 or 3	2020
		2006	3,890			2021

§ Data from www.demoistat.it.
VPD: vaccine-preventable disease; Men B, ACW135Y and C: Neisseria meningitidis serogroups B; ACW135Y and C; PNC: *Streptococcus pneumoniae*; HPV: human papillomavirus.

Tab. II. Vaccine coverage rates (%) registered for mandatory and recommended vaccinations at 36 months. 8 years and 15 years of age, stratified by vaccine type and year of administration, along with the percentage differences between the 2020 and 2021 rates in Siracusa Local Health Authority.

Target age group	VDP	VC Rates (%) by Year of Vaccine Administration		% Difference (2021 *vs* 2020)	p-value*
		2020	2021		
		Cohort 2017	Cohort 2018		
36 months	Polio	92.8	92.5	-0.2	0.7
	Measles	95.5	93.7	-1.8	< 0.01
	PNC	88.6	86.9	-1.7	< 0.05
	Men B	61.6	56.6	-5.0	< 0.001
	Men ACW135Y	72.7	73.2	+1.1	0.3
		cohort 2012	cohort 2013		
8 years	Polio	86.4	80.7	-5.7	< 0.001
	Measles	83.9	80.1	-3.7	< 0.001
		cohort 2005	cohort 2006		
15 years	HPV	48.6	44.2	-4.4	< 0.001
	HPV females	57.8	52.9	-4.9	< 0.01
	HPV males	39.9	36.3	-3.6	< 0.05

* Chi-square test (2021 vs. 2020); VC: vaccination coverage; VPD: vaccine-preventable disease.
Men B, ACW135Y and C: Neisseria meningitidis serogroups B, ACW135Y and C; PNC: *Streptococcus pneumoniae*; HPV: human papillomavirus

in 2021, 36-month coverage rates were 92.5% for polio (hexavalent vaccine) and 93.7% for measles-containing-vaccine, representing -0.3% (not statistically significant) and -1.8% decreases, respectively, as compared to 2020. By 8 years of age (booster doses), immunisation coverage was 80.7% for polio and 80.1% for measles, representing a -5.7% and -3.7%, respectively, compared to 2020.

With reference to the recommended childhood immunisations, in 2021, 36-month coverage was 56.6% for Men B (-5.0% as compared to 2020), 73.2% for Men ACW135Y/C (+1.1% as compared to 2020; not statistically significant) and 86.9% for PNC vaccine (-1.7%, as compared to 2020). Regarding HPV vaccination, in 2021, vaccine coverage was 44.2% (-4.4% compared to 2020; -4.9% in females and -3.6% in males).

Compared to the previous report (Tab. III), the VC difference among the cohorts was -0.2% for polio (hexavalent vaccine); -1.8% for measles-containing-vaccine (primary vaccination course doses) and -5.7% and -3.7% for booster doses (8 years of age) (Tab. III, column B).

Discussion

Similar to what has been noted nationally and in other countries, the vaccine coverage of routine childhood immunisations was negatively affected during the COVID-19 pandemic also in the LHA of Siracusa.

We showed reductions in VC for all vaccines and age groups investigated in 2021 compared with the previous year (range from -0.3% to -5.7%), except for the men ACW135Y vaccination (+1.1%).

The observed reduction of VC was greater for children aged > 36 months compared to the younger (-4.6% vs -1.5%) and for booster doses compared to the primary vaccinations (-4.7% *vs* -1.0%).

VC rates for mandatory vaccinations decreased in 2021 compared with 2020 (-2.9%; range from -0.3% to

Tab. III.% Differences among the cohorts in each survey (column A and B) and among the two different surveys (see the text).

Target age group	VDP	% Difference 2020 *vs* 2019 (%)	% Difference 2021 *vs* 2020 (%)	% VC recovery from survey (A) to survey (B) (%) (*)
36 months	Polio	-1.4	-0.2	+82
	Measles	-3.8	-1.8	+52
	PNC	-2.4	-1.7	+30
	Men B	-4.6	-5.0	-9
	Men ACW135Y/Men C	-5.6	+1.1	+120
8 years	Polio	-7.8	-5.7	+26
	Measles	-5.0	-3.7	+27
15 years	HPV	-4.3	-4.4	-2
	HPV females	-4.8	-4.9	-1
	HPV males	-3.4	-3.6	-4

Men B, ACW135Y and C: Neisseria meningitidis serogroups B, ACW135Y and C; PNC: *Streptococcus pneumoniae*; HPV: human papillomavirus
(*) Comparison of the two surveys: positive values indicate a narrowing of the vaccination coverage gap between the two surveys, negative values an increase in the gap.

-5.7%), while recommended vaccinations ranged from +1.1% to -5.0% (-2.5%).
Compared to the previous report [32], we observed a positive and significant percentage reduction of the difference in VC between the two surveys for all compulsory vaccinations, with a greater recovery for primary vaccination courses: 82% for polio and 52% for measles-containing-vaccine (primary cycle), 27% and 26% for polio and measles-containing-vaccine of booster doses, respectively. A positive and significant reduction was also observed for PNC vaccination (-30%) (Tab. III, column C).
As mentioned above, a little increased difference between the two surveys was observed for Men B (-9%) and for HPV vaccination, (-2% overall, -1% and -4% for females and males, respectively).
Finally, a significant increase in VC for men ACW135Y/C vaccination in 2021 vs 2020 has been recorded (+120%) (Tab. III, column C).
Our findings show that the infants were less likely to miss their vaccination than older toddlers during the COVID-19 pandemic in the LHA of Siracusa, as a result of a correct attempt to give priority to the infants and to primary cycles, but also it may suggest that parents put the vaccination of their infants at priority. This is consistent with other findings [35, 36].
During the pandemic, a significant drop in vaccinations coverage was observed in Italy [37, 38]. According to a survey of the Italian Ministry of Health, vaccination activity has slowed down, even if with regional differences [39, 40]. The most affected vaccinations by the pandemic have been the non-mandatory ones, particularly those addressing the adolescent and adult population, such as immunization against papillomavirus [40]. Even prior to the COVID-19 pandemic, vaccine coverage for the adolescent vaccine was suboptimal particularly for HPV [41, 42]. For example, lower HPV vaccination coverage may have long term health implications, resulting in excess cases of genital warts, CIN1/2/3 and cervical cancer as well as other HPV-related diseases and cancers, with potential to slow progress made in recent years toward the goal of eliminating cervical cancer [43]. Catch-up programs are essential to try to reach the optimal level of coverage targeted by the Italian National Immunization Plan, that is 95% for both males and females of 11-year-old [44].
Our findings are consistent with national data (Tab. IV), except for men B vaccination (Siracusa -5.5; Italy +7.7) and men ACW135Y vaccination (Siracusa +1.1; Italy -6.3) [45, 46]. Regarding the HPV vaccination, the observed difference largely depends on the different HPV vaccination strategies in the Italian regions for the 2005 and 2006 cohorts. Indeed, the HPV-vaccination campaign started irregularly in Italy in 2007, with pre-adolescent girls as the primary target; later, other cohorts were introduced such as 12-year-old boys. Moreover, the start of the vaccination campaign was not uniform in Italy [47].
A decline in immunizations could endanger the vaccination coverage target that is necessary for herd immunity against diseases [21, 48, 49]. In such circumstances, an increased risk of resurgence of VPDs that were controlled or eliminated in children who missed vaccinations during the pandemic is expected, thereby posing a twofold challenge to public health systems [50, 51], especially in the low-income countries [52, 53].
Despite the reductions in vaccination coverage, we did not register an increase in VPD outbreaks in the LHA of Siracusa in the last years (Tab. V). At least in the short-term, the impact of the pandemic on possible VPD outbreaks has been balanced by public health measures (personal protective equipment, hand hygiene, quarantine/isolation, physical distancing), which likely prevented the spread of other respiratory diseases as well. Similar data have registered in the rest of Italy, where no increase in outbreaks due to VPDs has been recorded [38, 54, 55]. Other countries reported different data in VPDs rates [56-58].

Tab. IV. Vaccine coverage rates (%) registered for mandatory and recommended vaccinations at 36 months. 8 years and 15 years of age, stratified by vaccine type and year of administration, along with the percentage differences between the 2020 and 2021 rates in Italy.

Target age group	VDP	VC Rates (%) by Year of Vaccine Administration		% Difference (2021 *vs* 2020)
		2020	2021	
		Cohort 2017	Cohort 2018	
36 months	Polio	95.6	95.0	-0.6
	Measles	93.8	94.9	+1.1
	PNC	91.7	91.1	-0.6
	Men B	71.0	78.7	+7.7
	Men ACW135Y	50.3	44.0	-6.3
		Cohort 2012	Cohort 2013	
8 years	Polio	88.9	86.9	-2.0
	Measles	89.0	87.0	-2.0
		Cohort 2005	Cohort 2006	
15 years	HPV	41.3	60.7	+19.5
	HPV females	63.3	69.5	+6.2
	HPV males	20.3	54.2	+33.6

Men B, ACW135Y and C: Neisseria meningitidis serogroups B, ACW135Y and C; PNC: *Streptococcus pneumoniae*; HPV: human papillomavirus.

Tab. V. Number of Vaccine-Preventable-Diseases (VPDs) in Siracusa Local Health Authority, 2019-2022.

VDP	2019	2020	2021	2022
Measles	3	1	0	0
Chicken pox	17	6	8	6
Invasive bacterial diseases (IBDs)	2	0	2	2

IBDs: *Neisseriae meningitides, Streptococcus pneumoniae, Haemophilus influenzae*

To avert the reported vaccination disruptions, World Health Organization released guiding principles suggesting compensation strategies for the disrupted immunization plan [17-19]. Any interrupted immunization services should be resumed, and catch-up vaccinations offered as quickly as possible [59, 60].
The urgency for efficient catch-up immunisation approaches needs emphasis again. For VC to recover to pre-pandemic levels, immediate and sustained catch-up efforts are necessary. These strategies may need to be tailored to specific age groups and other priorities. For example, identifying vulnerable people, children and adult, who have been missed during these disruptions and providing targeted catch-up services for these people, will be crucial for full recovery [61, 62].
Vaccinations services will still need innovative and impactful strategies to ensure that people who missed vaccines catch up and to return vaccination coverage to levels attained before the COVID-19 pandemic, and even higher levels [58, 61]. Specific strategies for recovery and expansion of routine immunisation services will vary by context.
There are potential barriers to achieving the necessary catch-up rates required to reverse the deficit resulting from the pandemic. For instance, it may not be feasible for providers to sustain catch-up efforts of this magnitude for the remainder of the catch-up period, as health care personnel and resources are already constrained. The staff of the vaccination services were not rarely understaffed, even before the pandemic, and lacking in some skills, such a strong ability of an effective communication to a wider public [63]. In addition, parents and providers may have vaccine hesitancy and adolescents may surpass the recommended age to receive these vaccines [64].
In addition to the last challenge, vaccine fatigue is becoming a growing concern for Public Health, after nearly three years of non-stop discussion about viruses and vaccines - some of it extremely contentious [65-67]. Vaccine fatigue is understood as people's inertia or inaction towards vaccine information or instruction due to perceived burden and burnout [66]. It is of crucial importance to avoid vaccine fatigue from progressing into worse forms on vaccine non-adoption, *e.g.*, vaccine hostility and vaccine hesitancy.
To the best of our knowledge, it is the first study that assess the effects of an extensive and well-defined recovery program of missed vaccinations due to the pandemic in a specific area in Italy.
We think that local level analysis is very useful to plan tailored and efficient catch-up strategies, and to verify the effectiveness of the recovery plan of missing vaccinations. In addition, is important for efficient catch-up strategies and future vaccinations campaigns also considering the characteristics of the local context or the different target groups based on their vaccination status and others group-specific characteristics (tailored approach), rather than one-size fits-all approach (uniform approach) [65].
Moreover, any recovery strategy must be measured with the effective availability of properly trained personnel, to cope with new challenges for vaccines, including vaccine hesitancy and vaccine fatigue, misinformation regarding safety and effectiveness of vaccinations in the mainstream media and social media. Nowadays, vaccine hesitancy and the 'infodemic' it fuels are key drivers of under-vaccination across the globe [64, 67-72].
Regarding limitations, we did not consider the possible temporal delay in the administration of vaccines, such as hexavalent, quadrivalent, men B and men ACW135Y vaccinations, which should be administered within the first year of life or at the beginning of the second year of life, according to the immunization calendar. Second, social determinants such level of the education, family income, social isolation, geographic location, or ethnic minorities, are important drivers of vaccination uptake behaviours and it is known that the COVID-19 pandemic has exacerbated the effects of those determinants [73-74]. Despite this, social determinants were not evaluated due to insufficient data availability. For the same reason, vaccine hesitancy has not been investigated, even though it is one of the top threats to public health and the nature of its challenge continues to shift with the social landscape [75].

Conclusions

Despite the efforts to organize and realize an extensive and well-designed vaccination recovery, our data show that even after the 1-year follow-up, globally deficits in coverage for these routine vaccinations persist, although there has been a substantial and significant recovery of missed vaccinations, especially among younger children and for primary cycles. For the 0-3 age group, VC uptake rebounded to near pre-pandemic levels for hexavalent vaccine, measles-rubella-mumps-chicken pox vaccine and PNC vaccine, exceeding the pre-pandemic level for Men ACW135Y/C vaccine.
The COVID-19 pandemic has reversed years of progress to expand vaccination programs around the world, reach target vaccination coverage rates, and achieve vaccine equity [30, 31].
Catch-up strategies in the next years are required for vaccination coverage to reach pre-pandemic levels, especially among adolescents.
It is therefore essential to try to implement even more

expanded catch-up interventions and to continue with vaccination programs involving more and more professionals close to children, adolescents and to their families such as general practitioners, paediatricians, gynecologists, midwives, and teachers.
Understanding the magnitude of these vaccination deficits is critical to reducing the risk of future outbreaks and potential increases in diseases prevalence.

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Informed consent statement

Ethical review and approval were waived for this study due to the use of anonymised and aggregated data on vaccination status.

Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

FC: Conceptualization; FC: methodology; FC, EDP, FB, CR: acquisition of data; FC, FB, EDP, MLC: formal analysis and interpretation of data; FC: writing - original draft preparation; FC, FB: writing - review and editing;FC statistical analysis; FC, EDP, MLC: supervision and project administration.
All authors have read and agreed to the submitted version of the manuscript.

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Correspondence: Fabio Contarino, Department of Public Health, Epidemiology Unit, Siracusa Local Health Authority. Traversa la Pizzuta, 96100 Siracusa SR, Italy. Tel.: 00393288772055 - E-mail: fabiocontarino@hotmail.it

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