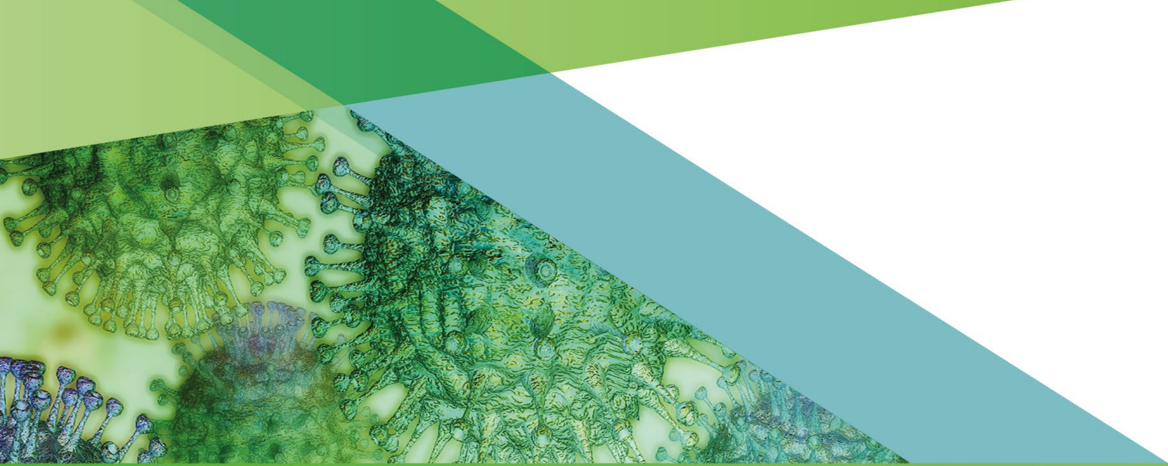

TECHNICAL REPORT

Interim public health considerations for COVID-19 vaccination of adolescents in the EU/EEA

1 June 2021

Key messages

- The vaccination of adolescents against COVID-19 should be considered in the broader context of the COVID-19 vaccination strategy for the whole population, including its overarching goals, the status of implementation, and its priorities.
- The vaccination of adolescents at high risk of severe COVID-19 should be considered a priority, as with other age groups.
- The overall direct benefits of vaccinating adolescents will mainly depend on the incidence of SARS-CoV-2 infection and on the prevalence of underlying conditions increasing the risk of severe COVID-19 in this age group.
- The individual direct benefits from COVID-19 vaccination in adolescents are expected to be limited in comparison to older age groups.
- The overall benefit for the general population of vaccinating adolescents will be proportional to the SARS-CoV-2 transmission within and from this age group.
- Given the anticipated reduced individual benefit-risk ratio from COVID-19 vaccination of adolescents compared to older age groups, careful consideration of the epidemiological situation and of vaccine uptake in older age groups should be given before targeting this age group.
- It is important to continue to monitor the spread of variants of concern among younger individuals and to continue to assess the actual burden of COVID-19 in younger age groups also in relation to COVID-19 sequelae (e.g. 'long COVID').
- Equity issues concerning vaccine availability and access need to be carefully considered when deciding on expansion of COVID-19 vaccination to groups with lower individual risk of severe disease.

Scope of the document

This technical report provides information on the following aspects related to COVID-19 vaccination of adolescents:

- the current status and national recommendations concerning the vaccination of adolescents in the European Union/European Economic Area (EU/EEA);
- the epidemiology of COVID-19 in adolescents;
- COVID-19 vaccines' effectiveness against transmission of SARS-CoV-2;
- the potential objectives of vaccinating adolescents; and
- considerations for implementing the vaccination of adolescents.

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This technical report provides a set of interim public health considerations to support EU/EEA public health authorities taking decisions on the administration of COVID-19 vaccines to adolescents (12- to 18-year-olds). As new evidence is continuously being generated and safety monitored on an ongoing basis, it is essential to consider the latest available information and recommendations issued by regulatory and public health authorities at national level.

The focus of this document is on the overall potential public health impact, rather than on the individual benefits and risks, of COVID-19 vaccination in adolescents.

Target audience

Target audiences for this document are the European Commission, the Health Security Committee (HSC), the EU/EEA National Immunisation Technical Advisory Groups (NITAGs), national public health institutes and ministries of health in the EU/EEA, and public health experts and decision-makers at national and subnational levels.

Background

As of 1 June 2021, four vaccines have received conditional marketing authorisation in the EU/EEA following evaluation by the European Medicines Agency (EMA). These vaccines are: COVID-19 vaccine Comirnaty; COVID-19 Vaccine Moderna; COVID-19 Vaccine Vaxzevria; and COVID-19 Vaccine Janssen. Comirnaty is authorised for use in people aged 12 years and older [1,2], while the other three vaccine products are currently for use in people aged 18 years and older [2-4].

On 28 May 2021, the EMA concluded its evaluation of an application to expand the use of Comirnaty to 12- to 15-year- olds, approving it for use in this age group [2].

The United States' (US) Food and Drug Administration (FDA) issued an Emergency Use Authorization for the use of Comirnaty in 12- to 15-year-olds on 10 May 2021 [6]. One randomised, double-blind, placebo-controlled Phase II/III clinical trial with 2 200 participants aged 12 to 15 years showed efficacy was 100% (95% confidence interval [CI] = 75.3-100%) in preventing symptomatic, laboratory-confirmed COVID-19. No specific safety concerns were identified among the vaccine recipients [7]. Following the CDC's Advisory Committee on Immunization Practices (ACIP) recommendations on the use of Comirnaty in 12- to 15-year-olds on 12 May 2021, the US has now expanded the vaccination campaign for this vaccine to include those aged 12 to 15 years [8]. As of 20 May 2021 [9], 0.9% of 12- to 15-year-olds in the US had been vaccinated with one dose of the vaccine.

In EU/EEA countries, the roll-out of COVID-19 vaccine campaigns started at the end of December 2020, when the first vaccine doses were delivered. On 19 January 2021, the European Commission set out actions to step up the response against the pandemic and accelerate the rollout of vaccination campaigns, with the targets of vaccinating at least 80% of people over the age of 80 years and 80% of health and social care professionals in every Member State by March 2021. In addition, a minimum of 70% of the adult population (i.e. above 18 years old) should be vaccinated by the summer of 2021 [10]. So far, countries have prioritised older adults (with various age thresholds), residents and personnel in long-term care facilities, and healthcare workers, and have gradually been progressing to younger age groups, social care personnel, and people with certain comorbidities [11]. As of 21 May 2021, the median cumulative uptake of at least one dose of the COVID-19 vaccine and full COVID-19 vaccination in individuals 80 years old or older was 80.6% and 61.1%, respectively (based on 25 reporting countries). While countries are slowly progressing to the target, some important efforts remain to be made in younger age groups (e.g. individuals below 60 years old).

Current status and national recommendations concerning vaccination of adolescents in the EU/EEA

The information provided below on COVID-19 vaccination policies in adolescents was collected through the Integrated Situational Awareness and Analysis (ISAA) report sent by the European Commission to EU/EEA countries. The ISAA report is prepared under the Integrated Political Crisis Response Mechanism (IPCR) of the Council of the European Union. Since 9 December 2020, a weekly set of questions has been sent via the ISAA report to representatives of countries, as validating authorities of the IPCR, to gather regular information on various topics around COVID-19. One section of these questions covers vaccination strategies and deployment. The representatives of countries gather the responses to the questions from different agencies and ministries in their countries.

According to the last published report [11] and as of 6 May 2021, 12 EU/EEA countries had initiated COVID-19 vaccination in individuals aged under 18 years of age (Table 1).

Table 1. COVID-19 vaccination of individuals aged <18 years (n=21) as of May 6, 2021

Vaccination of individuals <18 years	Countries
Yes	Austria, Belgium, Croatia, Czechia, Denmark, Estonia, Finland, Malta, the Netherlands, Portugal, Romania, Sweden
No	Germany, Iceland, Ireland, Latvia, Lithuania, Norway, Poland, Portugal, Spain

Denmark, Finland, and Portugal planned to target all individuals aged 16-17 years. Other countries, including Estonia, Malta, the Netherlands, Sweden, and Norway reported targeting young individuals with underlying conditions, those vulnerable or at risk of severe outcomes. Belgium decided to target 16- to 18-year-olds in healthcare facilities and young healthcare students. Spain plans on expanding vaccination to 12- to 18-year-olds when the vaccines are authorised for that age group, but initially only for adolescents with high risk factors. In Austria, due to a high circulation of variant B.1.351 in the Tyrolian district of Schwaz, all inhabitants aged 16 years and older were offered the vaccination, and almost 50 000 people of all ages have already been vaccinated with Comirnaty [11].

In addition to the published report described above, additional responses as of 19 May 2021 indicate that six EU/EEA countries plan to initiate vaccination of 12- to 18-year-olds, provided that available COVID-19 vaccines are authorised for this age span. One country is planning to vaccinate only 12- to 18-year-olds belonging to a risk group for severe COVID-19 disease. Four countries mentioned that the option of vaccinating adolescents is currently under discussion. One country reported no intention to vaccinate this age group, and no answer was provided for the remaining 18 countries.

1. Epidemiology of COVID-19 in adolescents

1.1 Age-specific rates and distribution of cases and hospitalisations according to surveillance data

Analysis of country-level and pooled case-based data reported to The European Surveillance System (TESSy) by 16 EU/EEA countries shows that case notification rates among adolescents in most countries are among the highest currently reported, and at similar levels to those of young adults. Adolescents, children, and young adults (19-24 years) have accounted for an increasing proportion of weekly cases since January 2021, although this is not unexpected given the clear falling and persistently lower case rates that have been observed in older adults (aged 60 years and above) in the same period, likely contributed to by vaccination in this population (Figures A1 and A2). Age-specific testing data, available for a subset of nine of these 16 countries, show weekly testing rates that have increased dramatically since February 2021 among the 10-19 years age group (the nearest proxy for adolescents available in the TESSy testing record type), at a similar speed to those aged 20-59 years (Figure A5). This increased testing likely partially explains the higher case rates observed among these groups, since trends in test positivity among the 10-19 years age group mirror those of most other age groups.

The recent declining trends in hospitalisation observed among older adults is reflected in a decreasing weekly proportion of people aged 60 years and older among those hospitalised. Adults aged 40-59 and 25-39 years make up a higher proportion of hospitalised cases. Hospitalisation remains a very rare outcome for adolescents, with no indication of increases in either hospitalisation rates or the proportion hospitalised among this group (Figures A3 and A4).

1.2 Risk factor analysis

Unpublished ECDC analysis of COVID-19 cases reported to TESSy estimated adjusted age-specific associations between 11 underlying health conditions and severe COVID-19 outcomes. After controlling for sex, reporting period, and reporting country, the odds of hospitalisation among cases aged below 20 years were higher if they had any of cardiac disorder, diabetes, HIV, hypertension, kidney disease, liver disease, lung disease, or neuromuscular/neurological disorders, compared to the reference group of cases of the same age with no underlying condition. Despite high estimates of relative risk, the absolute risk of hospitalisation is low for cases aged below 20 years. Overall models predicted that the probability of hospitalisation increased with age, but there was an additional probability of hospitalisation among people of the same age with an underlying condition compared to those without. The predicted probability of hospitalisation for cases in this age group with cancer, cardiac disorder, diabetes, hypertension, kidney disease, or neuromuscular/neurological disorders was at least as high as that for people without an underlying condition in some of the adult age groups.

1.3 Clinical manifestations

Unlike adults, most adolescents with COVID-19 have mild symptoms and very low risk of death [12]. However, some adolescents develop significant respiratory disease and need hospital admission. According to peer-reviewed studies, one -third of the hospitalised paediatric patients with COVID-19 experience severe disease, which is often associated with underlying chronic conditions [13]. The most common comorbidities in hospitalised adolescents are diabetes, gastrointestinal, neurological, cardiac, and pulmonary diseases, specifically asthma [14,15]. A significant proportion of hospitalised adolescents with SARS-CoV-2 infection are also obese [16]. However, some of these underlying conditions commonly observed among hospitalised adolescents may not necessarily be causally associated with COVID-19 severity. Notably, critical illness is associated with increasing age of adolescents. A recent analysis of 1733 patients with multiple inflammatory syndrome in children (MIS-C) found that older adolescents had the highest proportion of myocarditis, pneumonia and acute respiratory distress syndrome [17]. In a multicentre cohort study in the United Kingdom (UK) among children and young people aged below 19 years, critical care admission was associated with the age group 10-14 years [15]. A French study found that age above 10 years was independently associated with severity of COVID-19 [18]. However, mortality among adolescents remains low [15], and caution should be used when generalising data from hospital-based studies to the general adolescent population.

Recently, cohorts of children and adolescents with post-acute sequelae of SARS-CoV-2 (PASC) or 'long COVID' have been described in Italy, Sweden, and Russia [19-21]. Post-acute sequelae of SARS-CoV-2 are characterised by persistent symptoms such as fatigue, dyspnoea, chest pain, cognitive impairment, and sleeping disturbances that last up to several months after infection. Allergic diseases and age above six years have been associated with higher risk of developing PASC. In the small case series of children with persistent symptoms in the above countries, the median age was 11.4, 10.4, and 12 years, respectively. Data from the UK's National Statistics Office also show a significant number of children report symptoms several weeks after SARS-CoV-2 infection [22].

1.4 Role of adolescents in COVID-19 transmission

It is well established that children and adolescents can be infected by, and transmit, SARS-CoV-2 [23]. While there is some heterogeneity in the literature, and although case ascertainment in children and adolescents may be lower than for other age groups [23,24], multiple studies indicate an age gradient: children in the range of 10-14 years old and younger appear to be less susceptible to SARS-CoV-2 infection than older adolescents and adults [25,26]. While data on adolescents' susceptibility remain scarce, older adolescents are thought to be comparable to adults in susceptibility to SARS-CoV-2 infection [26].

It has been reported that children shed viral RNA (whether this means viable virus or not) in a similar manner to adults [27-29]. However, this does not indicate whether they transmit the infection to an equal extent, given that the exact load of viable virus is unknown [23]. A more recent study concluded that SARS-CoV-2 culture positivity rates were lower from paediatric samples than adult samples, and when the virus was successfully cultured, significantly less viable virus was present in children under 18 years [30]. The study did, however report higher culture positivity rates among 11- to 17-year-olds than individuals under 10 years [30].

Several studies have not identified children and adolescents as index cases or identified them as index cases less often than adults [23,31], but the balance of the evidence points towards the possibility for onward transmission by children and adolescents, with mixed results about whether adolescents are more likely to transmit SARS-CoV-2 than younger children. One study from South Korea reported that for index cases 10-19 years, the secondary attack rate (SAR) was 18.6%, the highest rate across age groups in the study, but a follow-up study concluded that transmission was more common from adults to children than from children to adults [32]. A household study from the Netherlands estimated that secondary attack rates were lowest in 1-11-year-olds (35%), higher in 12-17-year-olds (41%), and highest in adults 18 years of age and older (51%) [33]. A household seroprevalence study from Germany identified significantly higher secondary attack rates for index cases over 18 years than for index cases under 18 years (SAR 0.38 vs 0.15) [34]. A household study from the USA found high secondary attack rates overall, but in contrast to the aforementioned studies, secondary transmission was found to be higher from index cases under 12 years (53%) than from index cases aged 12-17 years (38%), although this finding was based upon a very low number of index cases in the younger than 12 years age group [35]. Similarly, a national registry-based study from Norway has indicated that, while parents are more likely than children or adolescents to be index cases, SARs were comparable between children <6 years of age (24%) and parents (24%), which were higher rates than they were for 7-12-year-olds (14%), 13-16-year-olds (14%), or 17-20-year-olds (11%) [31]. The authors of this study speculated that it may be because very young children cannot reduce contacts with other family members, even if a positive case is detected.

It has generally been concluded that SARS-CoV-2 transmission in school settings is reflective of, and not a driver of, community transmission [23,36]. While outbreaks have been documented in preschools, primary schools and secondary schools, it has also been generally observed that there are low secondary attack rates in these settings when appropriate mitigation measures are in place [23,37,38]. Consistent with the general hypothesis that SARS-CoV-2 transmission is more likely by older than younger children and adolescents, it has been assessed that there is likely to be a greater effectiveness in reducing community SARS-CoV-2 rates by temporarily closing secondary schools than primary schools [39-41].

While variants of concern show increased transmissibility across all age groups [42], younger adults currently account for a high proportion of cases in many European countries, and this could be related to more social interactions and to lower adherence to non-pharmaceutical interventions (NPIs) [43]. The second wave in the UK, for example, is thought to have started in young adults due to higher social contacts [24]. Clusters of more transmissible variants of concern have been observed among university students in, for example, Sweden [44]. Modelling in the UK has estimated that university students would need to be tested every three days in order to prevent outbreaks of variant viruses [45]. In response to outbreaks and clusters, targeting older adolescents and younger adults may be effective, particularly when there is increased clustering of variants in these age groups.

Ultimately, the role of adolescents in SARS-CoV-2 transmission as compared to adults will depend upon their overall levels of susceptibility to infection, likelihood of leading to secondary transmission, and overall levels of social mixing [46]. Adolescents likely have increased susceptibility to infection compared to children [26] and higher culture positivity rates than children [30], and it may be expected as a result that the role of transmission by adolescents approximately 15-17 years will differ than those 12-14 years of age. By autumn 2021, a greater proportion of adults than adolescents will have been vaccinated in the EU/EEA, and as adolescents also appear to generally have higher number of social contacts than adults [47], it is reasonable to assume that the relative role of adolescents in SARS-CoV-2 transmission, as well as the places where they congregate, including but not limited to schools, will become a greater focus of attention in the COVID-19 pandemic.

2. COVID-19 vaccine effectiveness against transmission

There is emerging evidence from post-licensure studies on COVID-19 vaccine effectiveness against transmission, but information is still limited and there are no available data about COVID-19 vaccine effectiveness against SARS-CoV-2 transmission in adolescents [48]. Observed reductions in infection rates, viral load, and duration of viral shedding are, however likely to translate into a reduction of transmission from vaccinated individuals. Since long-term follow-up on duration of immunity following vaccination has not yet occurred given the recent introduction of COVID-19 vaccines and the amount of time that has passed since vaccinations have been received, it is currently not possible to draw conclusions on the duration of protection against SARS-CoV-2 infection beyond six months.

A study from Scotland has shown that household members of healthcare workers vaccinated with a single dose of either Vaxzevria or Comirnaty (results based on pooled analysis) were at a significantly reduced risk (HR=0.70; 95% CI: 0.63–0.78) of PCR-confirmed SARS-CoV-2 infection, and non-statistically significant reduced risk of hospitalisation (0.77; 95% CI: 0.53-1.10), compared to household members of unvaccinated healthcare workers, 14 days after vaccination [49]. A pre-print report of a study from England included results from over 57 000 contacts from 24 000 households in which there was a laboratory-confirmed SARS-CoV-2 case that had received a vaccination with either Vaxzevria or Comirnaty, compared with nearly 1 million contacts of unvaccinated cases. Results show that the likelihood of household transmission is 40-50% lower for households in which the index cases are vaccinated 21 days or more prior to testing positive (compared to no vaccination), with similar effects for both Vaxzevria and Comirnaty [50].

A modelling study using data from the Moderna COVID-19 vaccine trial estimated a reduced potential for transmission of SARS-CoV-2 of at least 61% in vaccinated individuals compared to unvaccinated individuals [51]. Reductions of viral load and duration of viral shedding have been observed in the Vaxzevria trial (with no difference between B.1.1.7 and non-B.1.1.7 infections) in symptomatic and asymptomatic PCR positive vaccinated individuals compared to PCR-positive unvaccinated controls [52]. Data from Israel showed a four-fold reduction of viral load in infections occurring 12-28 days after the first dose of Comirnaty [53]. A registry-based cohort study in long-term care facility residents in Spain estimated that indirect protection to other unvaccinated residents conferred by vaccination at >29 day following a first dose of Comirnaty was 81.4% (95% CI 73.3-90.3%) and 12.8 infections were prevented per 10 000 unvaccinated per day [54].

Variants of concern (VOC), which are currently circulating in EU/EEA, are estimated to be more transmissible than previously circulating SARS-CoV-2 variants, with evidence that B.1.1.7 is at least 50% more transmissible [55-57], B.1.351 is about 1.2-2.3 times more transmissible [58], and P.1 is 1.7-2.4 times more transmissible [59] than previously circulating variants. In the UK, the B.1.617.2 variant has recently shown higher attack rates compared to the B.1.1.7 variant [60]. There are not yet any estimates of transmissibility of VOCs specifically in fully vaccinated individuals or in populations with high coverage of COVID-19 vaccines. Immune escape could possibly also be associated with increased transmission risk from a fully vaccinated individual to an unvaccinated contact. There is evidence of reduced vaccine efficacy against mild and moderate COVID-19 for B.1.351, and possibly also for P.1 and B.1.617.2 [60-64]. However, there are also emerging data indicating vaccine efficacy is maintained for B.1.1.7 [63,65,66].

3. Potential objectives for vaccinating adolescents

When implementing a new vaccination programme, or refining an existing one, it is important to define the objectives. Vaccination offers direct protection to the person vaccinated, but it may also confer indirect protection on others in the community, due to reduced circulation of a virus. The degree of indirect protection depends on the efficacy of a vaccine in preventing onward transmission, and also on the connectedness of the people being vaccinated. As vaccine efficacy against transmission is difficult to measure, efficacy against infection is often used as a proxy. At the outset of the COVID-19 vaccination programme, it was unclear whether the vaccines would be efficacious against infection. This uncertainty, together with the disproportionate burden of severe disease and mortality in older people, meant that the prioritisation of older generations was a strong and rational choice [67]. This has been the approach throughout Europe. As vaccination coverage increases in older age groups, a re-assessment of the overall vaccination objectives will be relevant. The potential objectives of vaccinating adolescents against COVID-19 may span both direct benefits to their own health and well-being and the indirect benefit of reducing onwards transmission of SARS-CoV-2 in the wider population.

3.1 Protecting adolescent health from COVID-19

It is well established that adolescents as a group are at low risk of severe disease, hospitalisation, and death as a direct result of infection, although severe COVID-19 may occur particularly in individuals with underlying conditions, while rare cases of 'multisystem inflammatory syndrome in children' (MIS-C) have been observed among previously healthy children and adolescents [68]. The health impact of COVID-19 may be due to an acute period of severe disease or more chronic effects, including both 'long COVID' (sustained symptoms following an episode of disease that may have been mild in nature) and the long-term sequelae of an episode of severe disease. Severe COVID-19 is rare among 12-18-year-olds (see Section 1.1), and may be concentrated in risk groups who would benefit from prioritised vaccination, as described in Sections 1.2 and 1.3. However, the longer-term impacts of the disease are not well understood, and as yet it is not possible to assess whether a heavy burden of disease may accumulate over time in this population. Further studies should be conducted to establish the chronic effects of the disease, including among younger people. It is conceivable, although not observed, that emerging SARS-CoV-2 variants could cause an increase in rates of severe outcome in adolescents. In this case, the direct benefit of vaccinating 12- to 18-year-olds will increase and the risk-benefit should be re-evaluated.

3.2 Normalising life for adolescents

The COVID-19 pandemic has had a significant negative impact on the mental health and well-being of adolescents, including increased incidence of anxiety, eating and sleeping disorders, depression, and post-traumatic stress disorder [69]. One study showed that adolescents' greatest concerns during the COVID-19 crisis were around the disruption to their social interactions and activities, rather than becoming infected by the virus or developing disease [70-72]. Vaccinating 12- to 18-year-olds may mean that they can more rapidly resume sports and other activities and socialise more fully, including strengthening inter-generational relationships within their extended family and communities. This is particularly important since social isolation, interpersonal stress, and mental health problems during adolescence are likely to continue throughout life [70].

Due to the negative public health and educational impacts of school closures, a key objective is to keep schools open while preventing COVID-19 transmission [73]. Prolonged school closures are very disruptive for children and their families, and cause high social, health, and economic impacts [23,74-76]. The effectiveness and quality of remote learning is lower than in school learning, causing negative educational effects such as reduced educational performance, decreased motivation in school- and homework and increased risk of school drop-out and learning losses [77]. A study based on the eight-week school closure in 2020 due to the pandemic in the Netherlands revealed a learning loss equivalent to one fifth of a school year, the same period that schools remained closed. Losses were up to 60% larger among students from households with lower levels of education, confirming the uneven toll of the pandemic across groups [76]. Prolonged school closures have also considerably affected the health of children and adolescents, as between 18-60% of young people were found to be at risk for psychological distress, particularly anxiety and depressive symptoms. Screen time and social media use increased, physical activity decreased, while sedentary behaviour and unhealthy dietary habits increased. Vaccination roll-out to adolescents could significantly prevent prolonged school closures and learning disruptions, and slowly allow for the relaxation of in-school protection measures and non-pharmaceutical interventions such as the use of masks and physical distancing, which can be disruptive to normal school life. Vaccination of adolescents in situations of clinical vulnerability or special educational need may help ensure their safe and timely access to school and education.

3.3 Reduction of viral circulation in the overall population

Since the burden of severe COVID-19 disease in adolescents is low, the primary benefit, in terms of reducing the levels and the impact of COVID-19 disease, of vaccinating this age group is likely to be the indirect effect of reduced viral transmission within the population. Throughout the pandemic, the number of people that adolescents meet on average has remained higher than that of adults [78], particularly where secondary schools have remained open. This means that even if the rate of SARS-CoV-2 infection or transmission were lower in this age group, as it appears to be for younger adolescents and children, they may still contribute disproportionately to the circulation of the virus when larger shares of the adult population are already vaccinated. As significant progress is made towards the objective of reducing severe disease and mortality, through the prioritised vaccination of older people and risk groups, focus may shift to reducing transmission. In this case, the inclusion of adolescents may be effective. The tipping point, although difficult to observe, is when more severe disease is averted by stopping the downstream cascade of infections attributable to one adolescent than by vaccinating an individual who was at high risk. Vaccine effectiveness studies should continue to monitor the consequences of these policy choices [79].

4. Considerations around implementation

4.1 Programmatic considerations

The COVID-19 pandemic has been a challenging period for maintaining high coverage of routine immunisation programmes in children and adolescents. Social distancing measures, stay-at-home orders, healthcare systems under strain, and school closures may all have impacted the performance of national vaccination programmes [80]. Recommendations to vaccinate adolescents against COVID-19 could become an opportunity to also reinforce communication regarding the benefits of other vaccinations for the prevention of infectious diseases in young people. It may also be an important opportunity to address any gap in the immunisation course of young individuals. There are currently no data on the co-administration of COVID-19 vaccines, although no differences in safety and immunogenicity profile have been observed with other vaccines when administered alone or simultaneously [81]. While COVID-19 vaccination may not be comparable with routine adolescent immunisation programmes, previous experience and lessons learned from HPV vaccination could be considered when targeting adolescents.

In general, two options to target adolescents with COVID-19 vaccines could be contemplated [82]:

- a structured vaccination programme in which target groups are systematically offered vaccination (this approach seems to be associated with higher rates of vaccination coverage);
- an opportunistic vaccination programme in which vaccination is mainly offered individually at the discretion of the general practitioner during visits motivated by reasons other than vaccination (this approach is seemingly associated with lower rates of vaccination coverage).

Other aspects related to implementation need to be taken into consideration when targeting adolescents. These include the possible necessity to involve the parents in the decision-making and the option of offering vaccination against COVID-19 to the whole family at a single appointment to avoid logistical constraints associated with individual appointments. A single family appointment may also ease the obtaining of parental approval at the same time, if such approval is required.

In younger age groups, the roll-out has started in those at higher risk of severe COVID-19 and could now be extended to all young individuals. While adolescents represent a lower proportion of the general population, integration of this age group into the national COVID-19 vaccination programme should be done in such a way as to ensure within-country equity, so that it does not impair the deployment among adults. The objective of having 70% of adults vaccinated as early as possible should remain a target. Further, when considering initiating COVID-19 vaccination programmes for low-risk young people in the EU/EEA aged 12-18 years, the wider context of a global vaccine supply shortage should also be taken into account. Many individuals in resource-constrained settings who are at high risk of COVID-19 infection, such as health workers and those with pre-existing conditions, who are high risk of severe disease and death, have yet to be vaccinated [79].

4.2 Risk communication

Promoting the uptake of COVID-19 vaccines for 12- to 18-year-olds will require a risk communication strategy that takes into account the needs and concerns of both the young people themselves as well as those of their parents/caregivers. Any such strategy should follow the standard principles of risk communication [83], including: (i) consistency in messaging; (ii) use of appropriate channels to reach these audiences (i.e. both traditional and social media); (iii) using trusted messengers (e.g. the voices of young people who have been vaccinated [84]; and (iv) using accessible language, thereby ensuring that the message is simple to grasp.

Behavioural insights research can facilitate strategy development by shedding light on vaccination intentions and potential barriers to uptake. For example, the results of surveys conducted in the US with parents and adolescents, prior to the use of COVID-19 vaccines in adolescents, were systematically assessed as part of the criteria used in the evidence-to-recommendations framework that led to the vaccine recommendations [85].

A behavioural insights study conducted in Germany found that the key reasons for young people wanting to be vaccinated (as reported by their parents) were the wish to be protected, the wish for a return to 'normal life', and the need to protect others [86]. For many young people, socialising with friends may be a more important driver of behaviour than the desire to avoid COVID-19 (which, for most of them, is unlikely to lead to a serious outcome). As a result, it may be important to promote COVID-19 vaccination for them as a means of freeing themselves from the need to adhere to some of the restrictive non-pharmaceutical interventions, such as self-quarantine after exposure to an infected individual [87]. Further, since some young people have a strong aversion to needles [88], sensitive approaches to addressing this issue could be useful in promoting uptake.

Experience with HPV vaccination programmes suggests that there can be disagreements between parents/caregivers and young people about whether or not to vaccinate [89]. In such cases, it would be important for healthcare professionals to provide appropriate support to the decision-making process.

Since any side effects following vaccination, even if mild, may lead to concern, early communication about possible side effects, as well as rapid investigation of any safety signals and the transparent communication of results, will be key to ensuring community trust in the vaccination programme [90]. In some national and regional contexts, previous safety events related to other vaccination programmes for adolescents, which may affect trust, will also need to be taken into account when developing risk communication strategies [90].

Studies on vaccine acceptance emphasise the importance of making vaccines available in safe, familiar, and convenient settings in order to facilitate uptake [91]. Such settings can include primary care providers' offices [92], vaccination centres, and schools [86]. Utilising the principles of community engagement [93], the school community may be viewed as a partner and resource in these efforts, providing a platform for Q&A sessions, webinars, and live sessions on social media channels organised by educational authorities and/or public health experts [94].

Limitations and knowledge gaps

- Prevalence among adolescents of each underlying condition associated with an increased risk of severe COVID-19 is difficult to estimate and may vary according to context.
- Evidence around long COVID is scarce and subject to reporting bias, making quantifying the actual burden of COVID-19 in adolescents challenging.
- There are currently no data on vaccine effectiveness against SARS-CoV-2 transmission in adolescents and younger adults.
- Data on adolescents' mixing patterns across age groups are currently limited, and may vary significantly according to country and context.
- Very scarce data on post-marketing safety of COVID-19 vaccines among adolescents and younger adults are currently available.
- There is limited information about the circulation of variants of concern among adolescents and their implications.
- Studies on the risk of hospitalisation among adolescents could be subject to bias concerning admission rates and intensive care admissions in the absence of representative community data on infection in this age group.

Conclusions

The vaccination of adolescents against COVID-19 should be considered in the broader context of the COVID-19 vaccination strategy for the whole population, including its overarching goals, the status of implementation, and its priorities.

The vaccination of adolescents at high risk of severe COVID-19 should be considered a priority in any case, as in other age groups.

The overall direct benefits of vaccinating adolescents as a group will mainly depend on the incidence of SARS-CoV-2 infection and on the prevalence of underlying conditions increasing the risk of severe COVID-19 in this age group.

The individual direct benefits from COVID-19 vaccination in adolescents are expected to be limited compared to older age groups.

The overall benefit for the general population of vaccinating adolescents will be proportional to the SARS-CoV-2 transmission within and from this age group.

Given the anticipated reduced individual benefit-risk ratio from COVID-19 vaccination of adolescents compared to older age groups, careful consideration of the epidemiological situation and of vaccine uptake in older age groups should be given before targeting this age group.

It is important to continue to monitor the spread of variants of concern among younger individuals, and to continue to assess the actual burden of COVID-19 in younger age groups, including in relation to COVID-19 sequelae (e.g. long COVID).

Equity issues concerning vaccine availability and access need to be carefully considered when deciding on the expansion of COVID-19 vaccination to groups with lower individual risk of severe disease.

Contributing experts

ECDC experts (in alphabetical order): Kim Brolin, Nick Bundle, Christiana Carstairs, Orlando Cenciarelli, Edoardo Colzani, Charlotte Deogan, Tarik Derrough, Helen Johnson, John Kinsman, Aikaterini Mougkou, Nathalie Nicolay, Anastasia Pharris, Jonathan Suk, Andrea Würz

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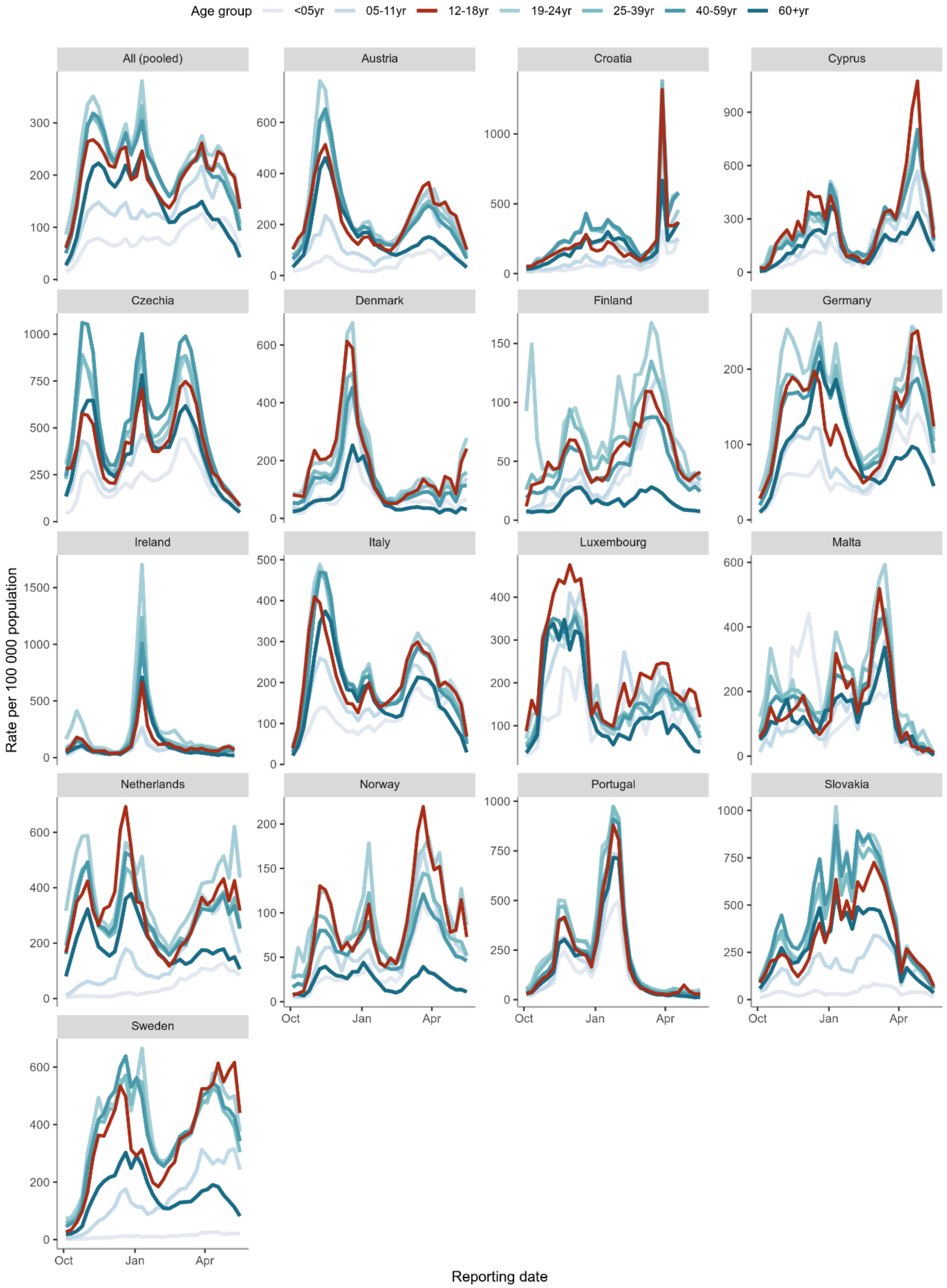
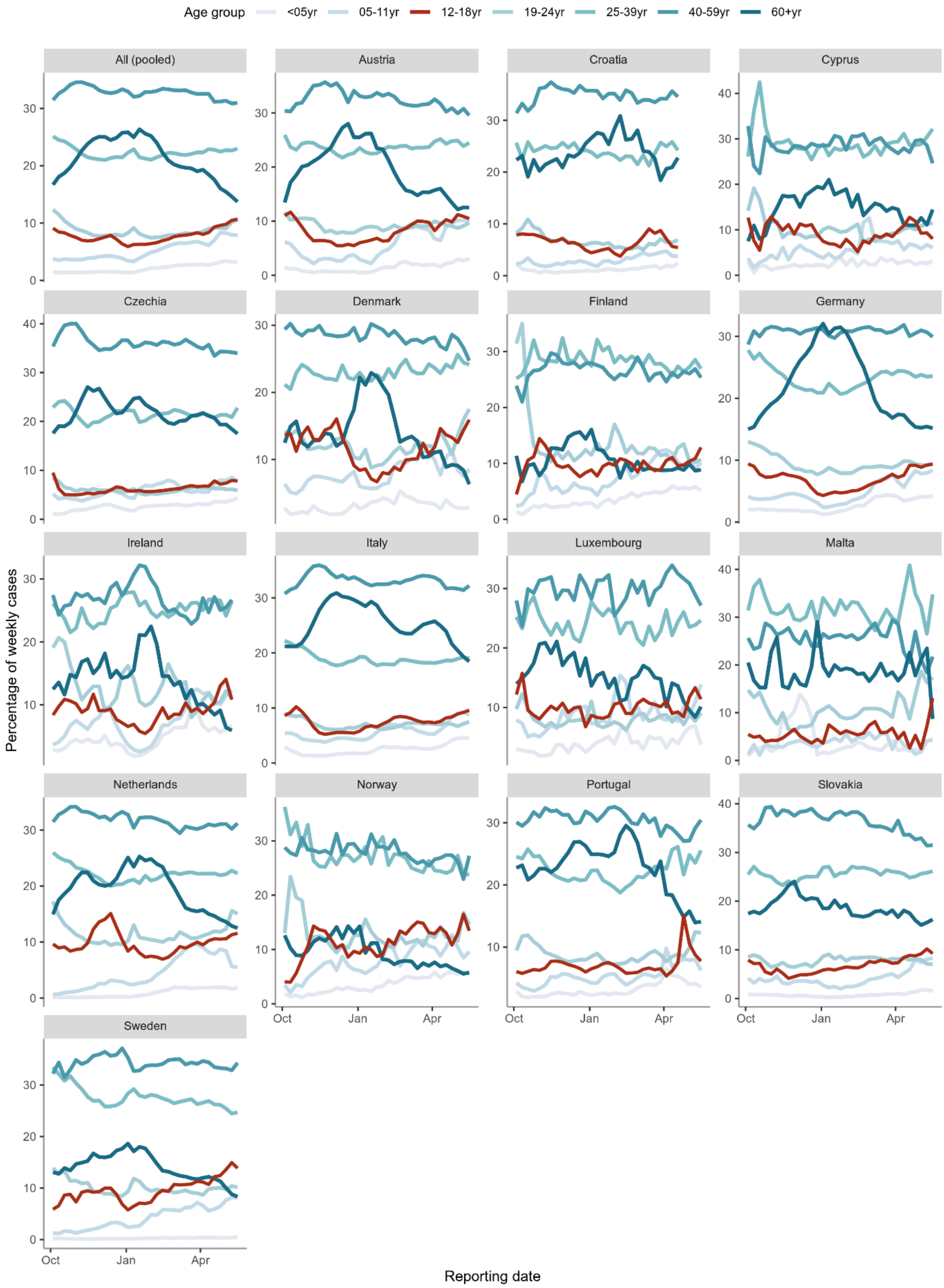
Annex

Figure A1. Weekly COVID-19 age-specific cases notification rates, 2020-W40 to 2021-W19, country-specific and pooled across all countries included (adolescents shown in red)



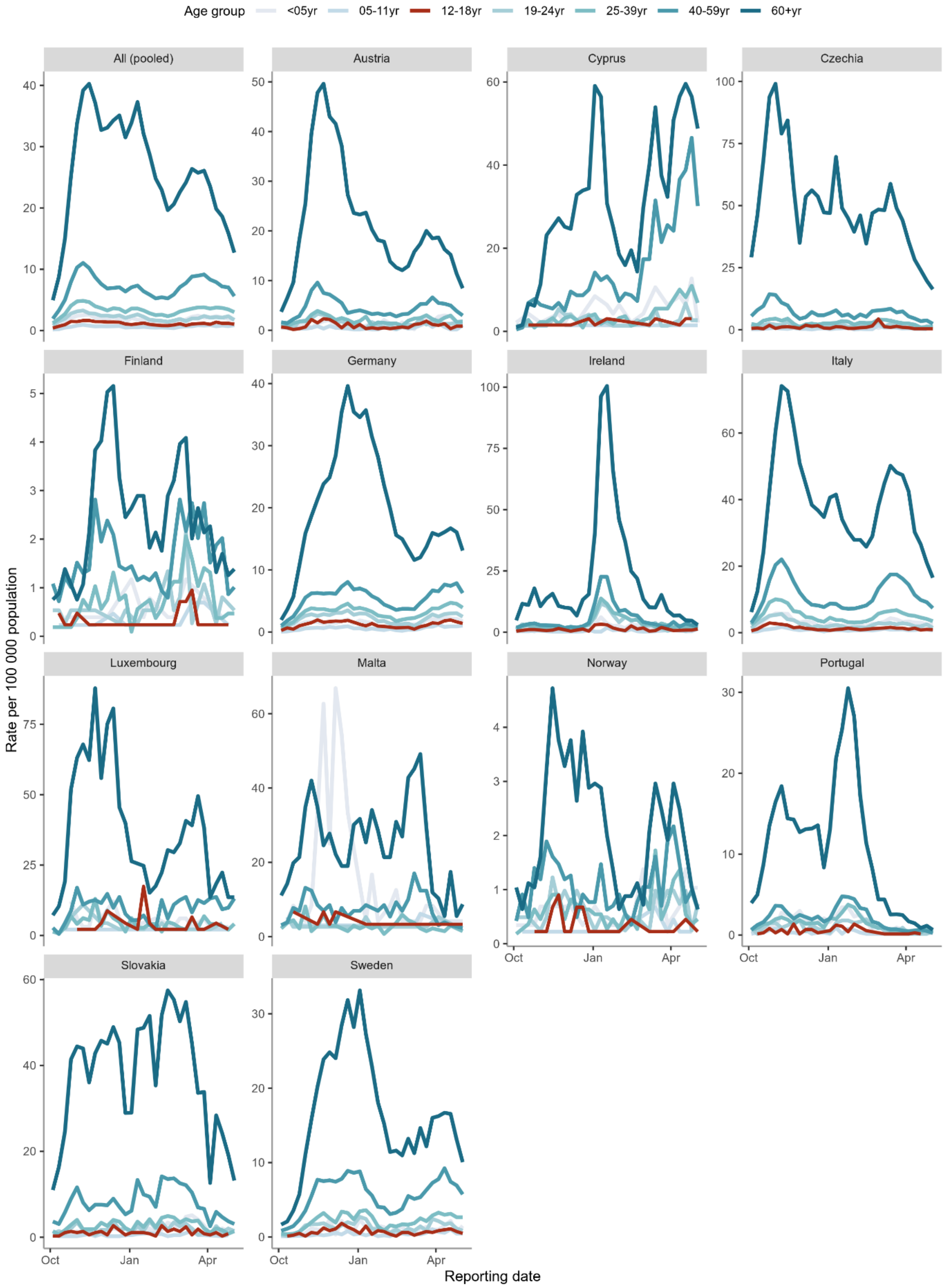
Note: y-axis scales may differ for each panel to more clearly show individual country trends.
Source: TESSy case-based data, limited to countries consistently reporting to this record type

Figure A2. Weekly distribution of COVID-19 cases, 2020-W40 to 2021-W19, country-specific and pooled across all countries included (adolescents shown in red)



Note: y-axis scales may differ for each panel to more clearly show individual country trends.
Source: TESSy case-based data, limited to countries consistently reporting to this record type

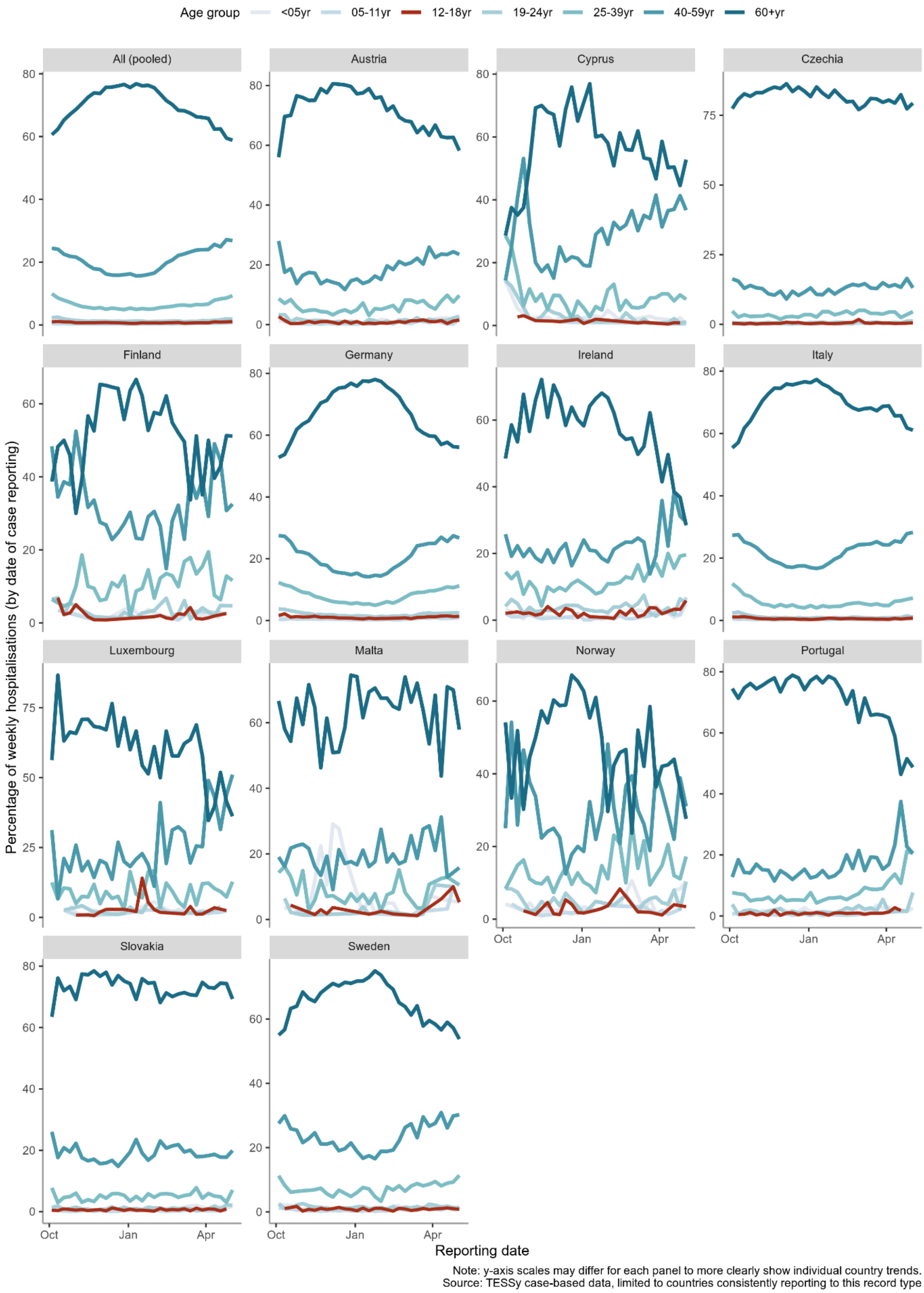
Figure A3. Weekly COVID-19 age-specific hospitalisation rate (by date of case reporting), 2020-W40 to 2021-W17* country-specific and pooled across all countries included (adolescents shown in red)



Note: y-axis scales may differ for each panel to more clearly show individual country trends.
Source: TESSy case-based data, limited to countries consistently reporting to this record type

** The last two weeks have been taken away to remove potential bias due to unknown outcome in more recent cases*

Figure A4. **Weekly age distribution of COVID-19 hospitalisations (by date of case reporting), 2020-W40 to 2021-W17*, country-specific and pooled across all countries included (adolescents shown in red)**



** The last two weeks have been taken away to remove potential bias due to unknown outcome in more recent cases*

Figure A5. Weekly age-specific testing rate, 2020-W40 to 2021-W19, country-specific and pooled across all countries included (people aged 10-19 years* shown in red)

Note: y-axis scales may differ for each panel to more clearly show individual country trends.
Source: TESSy, limited to countries reporting age-specific testing data

Figure A6. Weekly age-specific test positivity, 2020-W40 to 2021-W19, country-specific and pooled across all countries included (people aged 10-19 years* shown in red)

Note: y-axis scales may differ for each panel to more clearly show individual country trends.
Source: TESSy, limited to countries reporting age-specific testing data

** Due to five-year age bands in this aggregated testing record type it is not possible to recreate the adolescent 12-18 years group used in figures A1-A4.*