

Safe ART services during the third phase of the COVID-19 pandemic



Guidance from the ESHRE COVID-19 Working Group

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By early June most European ART centres had resumed their routine treatments. However, new local outbreaks and second waves of infection are now reported from several countries, particularly among people of reproductive age. Many of them are asymptomatic. In addition, there is still uncertainty about the effect of SARS-CoV-2 infection during pregnancy. Thus, while fertility clinics have adopted routine triage and testing protocols, caution is still required.

This updated guidance firstly reaffirms ESHRE's initial guidance published in April and secondly advises additional measures based on a two-step principle for the provision of safe services during a second wave of coronavirus infection. With winter approaching, COVID-19 case numbers are likely to increase even further, prompting a need to adopt new measures and adjust patient access.

Guidance on resuming fertility treatments

ESHRE's guidance on the resumption of routine ART was published on 23 April 2020 (<https://www.eshre.eu/Home/COVID19WG>). Its recommendations were made in response to a decreasing risk of COVID-19 infection – though were still subject to local regulations. The guidance was based on six pillars of good medical practice : *i. Discussion, agreement and consent to the start of treatment; ii. Staff and patient triage; iii. Access to advice and treatment; iv. Adaptation of ART services; v. Treatment cycle planning; and vi. Code of Conduct for staff and patients.*

Updated information

Now, in the face of a new wave of infections, that initial guidance may be complemented by the following interventions:

- **More testing** This may be feasible with greater access to accurate testing and a quicker turnaround of results. The triage questionnaire of the initial guidance is still relevant to identify high-risk and symptomatic individuals, but in high-risk areas triage should be combined with asymptomatic patient testing.
- **Increased counselling and information to patients planning a pregnancy or already pregnant** This should cover the knowledge we have on COVID-19 during pregnancy and how to reduce the risk of infection before and during pregnancy (see Code of Conduct from the April guidance).

Both interventions are especially important in regions with an increasing or high COVID-19 prevalence.

Guidance on maintaining safe ART services

There are large variations in regional and national case numbers and in testing protocols in Europe. As a result the mitigation measures for safe ART services should be guided by local circumstances. All possible factors which might affect ART services should be assessed to ensure that plans of action are in place to maintain services.

Epidemiological information

Several epidemiological parameters for COVID-19 are available and should be used to guide decision-making for mitigation measures. These parameters include the reproduction number (R_0 and R_t), prevalence and incidence, and growth rate (*see Annex 1*).

The European Centre for Disease Control (ECDC) collects COVID-19 data according to region (<https://www.ecdc.europa.eu/en/cases-2019-ncov-eueea>). Incidence figures are reported as newly confirmed cases per 100,000 persons. The ECDC additionally reports the 14-day COVID-19 case notification rate per 100,000 in five categories: no cases reported, <20 cases; 20.0-59.9 cases; 60.0-119.9 cases; and ≥ 120.0 cases. We used this measurable and regularly reported rate as the reference for this guidance.

Internal and external factors

Clinics should also consider the impact which COVID-19 may have on staff availability (resulting from illness or quarantine) and on healthcare supplies.

Mitigation measures

The following mitigation measures could be considered for maintaining safe ART services depending on the incidence of infection:

- Decrease the number of patients treated
- Limit access to treated patient only (no partners)
- Increase patient and staff triage and testing
- Limit staff exposure and allow more time between patient appointments
- Enhance sanitation measures
- Use personal protective equipment (PPE) intensively
- Increase the use of telemedicine
- Avoid embryo transfer and advise a freeze-all strategy to all patients, particularly in high COVID-19 incidence areas
- Reaffirm the Code of Conduct

Emergency measures

Clinics may need to temporarily reduce or even suspend their activity as a result of staff shortages. In such circumstances, all ART centres should have agreements with other centres to guarantee continuity of treatment.

Summary recommendations

There are two core steps in this guidance for maintaining services in the next phases of the pandemic. The **first step** is to assess the impact of the pandemic's

current status based on epidemiological factors and internal and external risk factors (for example related to staff and supplies availability). Depending on this assessment, the **second step** would include mitigation measures as outlined in *Figure 1* below.

- Centres should monitor epidemiological data via national health systems and/or from the ECDC.
- Centres should monitor internal and external risk factors which may have an impact on ART services, including but not limited to staff number and availability of supplies.
- Centres should consider mitigation measures to reduce these risks.
- Clinicians should inform their patients about the risk of infection before and during pregnancy.
- Routine testing of asymptomatic staff and patients (based on service-specific protocols) should be considered, especially in areas of high COVID-19 prevalence.

Figure 1. The two-step approach to ART service maintenance

The risk mitigation measures recommended below are considered minimal actions. ART centres can take more stringent measures, regardless of case notification rate, based on internal and external factors or regulatory guidance.

STEP 1		STEP 2
14-day COVID-19 case notification rate per 100,000	Impact on ART services	Recommended mitigation measures
No cases reported	Insignificant	<ul style="list-style-type: none"> Continue as per routine Follow regional and country-specific guidance
<20	Minor	<ul style="list-style-type: none"> Triage recommended for all patients SARS-CoV-2 testing for triage-positive patients Follow regional and country-specific guidance
20.0-59.9	Moderate	<ul style="list-style-type: none"> Routine triage for patients and staff, and SARS-CoV-2 testing for triage-positive patients/staff Routine implementation of the Code of Conduct for staff and patients Follow regional and country-specific guidance
60.0-119.9	Major	<ul style="list-style-type: none"> Routine triage for patients and staff, and SARS-CoV-2 testing for triage-positive patients/staff Routine implementation of the Code of Conduct for staff and patients Remote consultation and counselling (tele-medicine) Reduction of visits to the ART clinic Routine use of PPE for staff Face mask recommended for patients No accompanying persons allowed Follow regional and country-specific guidance
≥120.0	Critical	<ul style="list-style-type: none"> Routine implementation of the Code of Conduct for staff and patients SARS-CoV-2 testing of all patients and staff Remote medical advice and counselling (tele-medicine) Reduced clinic visits Staff: routine use of PPE Patients: face masks recommended No accompanying persons allowed Laboratory: freeze-all policy to be considered Follow regional and country-specific guidance

References

Daily COVID-19 update for the EU/EEA and UK is available from the European Centre for Disease Prevention and Control (ECDC) via <https://www.ecdc.europa.eu/en/cases-2019-ncov-eueea>

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Annex 1: Epidemiological parameters for COVID-19

Basic reproduction number (R_0)

The reproduction number is an epidemiological parameter used to measure the transmissibility of a virus. The reproduction number reflects the expected number of secondary cases produced by a single infection in a population where everybody is susceptible. For example, if one individual develops the disease and passes it to three other individuals, the R_0 is 3. The R_0 measurement does not include new cases produced by the secondary cases.

This basic reproduction number is an estimated value linked to a certain virus and depends on three factors:

1. Rate of contact between infected and susceptible individuals
2. Probability of infection being transmitted during contact
3. Duration of infectiousness after the individual is infected

In denser populations, more people are susceptible; if the virus is highly infectious, the R_0 will be larger. R_0 reduces with the increased rate of removal of infected individuals, recovery or death.

If the average R_0 in the population is greater than 1, the infection will spread exponentially. If R_0 is less than 1, the infection will spread slowly, and it will eventually die out. The higher the value of R_0 , the faster an epidemic will progress.

Effective reproduction number (R_e or R_t)

Varying proportions of the population are immune to any given disease at any given time and not all contacts with an infected individual will become infected. To account for this, the effective reproduction number R_t is used, representing the average number of secondary infections caused by a single infected individual at a given time "t" in the partially susceptible population. The effective reproduction number R_t allows for better understanding of the transmissibility of COVID-19 as well as effectiveness of interventions. The effective reproduction number is recommended to be monitored per country/region and should be available from local governmental health agencies.

To summarise, the basic reproductive number R_0 describes the spread of a disease at the beginning of an outbreak, and R_t , an "effective" version of the metric, describes disease spread later on.

Prevalence and incidence

The prevalence of COVID-19 is defined as the proportion of infected individuals in the population, reported per 100,000 persons. The incidence is the number of new confirmed cases per 100,000 persons. The ECDC reports the 14-day COVID-19 case notification rate per 100,000 in five categories: no cases reported, <20 cases; 20.0-59.9 cases; 60.0-119.9 cases; \geq 120.0 cases.

The incidence (14-day cumulative number of *newly confirmed* cases per 100,000 persons) per region is available from the European Centre for Disease Control (ECDC) website (<https://www.ecdc.europa.eu/en/cases-2019-ncov-eueea>)

Growth rate

The growth rate which reflects how quickly the number of infections is changing day by day is an approximation of the percentage change in the number of infections each day, with rates above 0 indicating the epidemic is growing, while values below 0 reflect a shrinking epidemic.

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