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COVID-19 pandemic: Practical considerations on the organization of an allergy clinic - an EAACI/ARIA Position Paper

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Abbreviations

AAAAI, American Academy of Allergy, Asthma and Immunology
ACT, Asthma Control Test
AD, Atopic Dermatitis
AIT, allergen immunotherapy
AR, Allergic Rhinitis
ARIA, Allergic Rhinitis and its Impact on Asthma
BAD, British Association of Dermatologists
BAL, bronchoalveloar lavages

BSL, Biosafety Level
CRF, case report form
CRS, Chronic Rhinosinusitis
CRSwNP, chronic rhinosinusitis with nasal polyps (
CRU, Clinical Research Unit
COVID-19, corona virus disease 2019
DMZ, demilitarized zones
EAACI, European Academy of Allergy and Clinical Immunology
ECDC, European Centre for Disease Control
EPIT, epicutaneous immunotherapy
ERS, European Respiratory Society
ETFAD,Task Force on Atopic Dermatitis
EHR, Electronic Health record
EMA, European Medicinces Agency
ENT, Ear, Nose and Throat
FDA, Food and Drug Administration
FFP, Filtering face-piece particles
GCP, good clinical practice
GDPR, General Data Protection Regulation
GINA, Global Inititiative on Asthma
HCP, health care providers
ICS, inhaled corticosteroids
ICU, intensive care unit
IEC, institutional ethic committee
INCS, Intranasal corticosteroids
IP, investigational product
IRB, institutional review board
ISOA, isolated onset of anosmia
IT, Information Technology
MDM, Multi-Disciplinary Meetings
OCS, Oral corticosteroids
OIT, oral immunotherapy
PBMC, peripheral blood mononuclear cells
pMDI, Pressurized metered dose inhaler
PAPRs, Powered Air Purifying Respirators
PEF, Peak Expiratory Flow
SCIT, subcutaneous AIT
SLIT, sublingual AIT

SCS, systemic corticosteroids
SP, Standard Precautions
WHO, World Health Organization

Abstract

Background: The Coronavirus disease 2019 (COVID-19) has evolved as a pandemic infectious disease transmitted by the severe acute respiratory syndrome coronavirus (SARS-CoV-)2. Allergists and other health care providers (HCPs) in the field of allergies and associated airway diseases are in the front line, taking care of patients potentially infected with SARS-CoV-2. Hence, strategies and practices to minimize risks of infection for both HCPs and treated patients have to be developed and followed by allergy clinics.

Method: The scientific information on COVID-19 was analyzed by a literature search in Medline, Pubmed, national and international guidelines from the European Academy of Allergy and Clinical Immunology (EAACI), the Cochrane Library and the Internet.

Results: Based on diagnostic and treatment standards developed by EAACI, on international information regarding COVID-19, on guidelines of the World Health Organization (WHO) and other international organizations as well as on previous experience, a panel of experts including clinicians, psychologists, IT experts and basic scientists along with EAACI and the "Allergic Rhinitis and its Impact on Asthma (ARIA)" inititiative have developed recommendations for the optimal management of allergy clinics during the current COVID-19 pandemic. These recommendations are grouped into nine sections on different relevant aspects for the care of patients with allergies.

Conclusions: This international Position Paper provides recommendations on operational plans and procedures to maintain high standards in the daily clinical care of allergic patients whilst ensuring necessary safety in the current COVID-19 pandemic.

Keywords: COVID-19, allergen immunotherapy (AIT), SARS-CoV-2, allergy clinic, asthma, anaphylaxis, clinical trials, psychological COVID, position paper

Introduction

On March 11, 2020, the World Health Organization (WHO) declared the "*corona virus disease 2019* (COVID-19)" as a pandemic viral disease. Since the first transmission dynamics reported in China [1], the number of infected patients and fatalities have been increasing worldwide [2]. Typical symptoms of COVID-19 include general malaise, fever, respiratory problems, and especially cough and shortness of breath. The clinical pattern differentiates somewhat from other airway diseases (Table 1).

INSERT: TABLE 1

Table 1: Differences and similarities in the clinical pattern of COVID-19, common cold, flu, allergic rhinitis, chronic rhinosinusitis and allergic asthma (modified from [3]).

Other symptoms include muscle and joint pain, sore throat, headache, nausea or vomiting, diarrhoea, nasal symptoms, and especially dysfunction in smell and loss of taste. In about 80% of the registered cases, the disease shows a milder and transient course. However, in about 5% of patients, admission to the intensive care unit (ICU) is necessary due to hypoxaemia and extensive pneumonia, often resulting in respiratory failure due to severe acute respiratory syndrome, often accompanied by coagulopathy and pulmonary embolism and the involvement of other organs including kidney, heart, and the central nervous system [4] [5] [2]. Preventive measures have been implemented worldwide to adjust ambulatory health services and decrease direct patient contacts to a minimum. However, until now, there is no clear advice on how to manage allergic patients with co-morbid COVID-19 or non-SARS-CoV-2 infected allergic patients during the ongoing pandemic [6]. The European Academy of Allergy and Clinical Immunology (EAACI) in alliance with the global initiative "Allergic Rhinitis and Its Impact on Asthma" (ARIA) has published several recommendations and assessments in the field of allergic diseases such as allergic rhinoconjunctivitis (ARC), allergic

asthma and others [7] regarding pharmacotherapy, Allergen Immunotherapy (AIT), biological treatment and others [5] [8] [9] [10] [11] [12] [13] [14] [15] [16] [17] [18].

As allergists and other healthcare providers (HCPs) with a focus on allergic diseases are frequently treating patients with manifestations of atopic disease in the upper and lower airways, they are on the front line in caring for patients potentially infected with SARS-CoV-2. As such, the clinical setting in an allergy outpatient clinic or hospital must ensure optimal care for the patients as well as sufficient prophylactic measures to minimize risks of infection for both the medical personnel and the patients requiring treatment as reported in an academic Allergy Centre initiative [19]. Therefore, clinical procedures in allergy clinics and outpatient practices must be optimized and standardized, within the contextual considerations regarding national regulations [20].

The aim of this Position Paper - prepared by EAACI in collaboration with ARIA - is to provide allergy clinics, specialized centres and practices with practical recommendations on measures for daily practice and optimal care for allergic patients during the current COVID-19 pandemic. These recommendations are grouped into nine sections (key-conclusions in table 2) as elaborated by experts including clinicians, psychologists, information technology (IT) experts and basic scientists in the field of allergy. These recommendations are conditional and should be adapted regularly on the basis of evolving clinical evidence.

Section	Key-conclusions
I. COVID-19: General considerations for HCPs	Protective measures should be taken following the general recommendations from the European Centre for Disease Control and the World Health Organization and current rules must comply with the national responsible government agencies.

II. COVID-19: clinical course in allergic patients	Viral infections, including infections with Coronaviruses, are associated with aggravation of allergies such as asthma exacerbations. Limited knowledge is available on the differences in the course of COVID-19 infection in allergic compared to non-allergic patients and further clinical evidence is needed.
III. Care of allergic patients: preclinical setting and triage of patients	Many clinics and medical offices already use remote health care tools to triage and manage patients after hours and as part of usual practices. These measures can ideally be used to prioritize and triage allergic patients on the basis of the severity of the allergic disease, the need for in-person consultation and the differentiation of allergic symptoms from clinical symptoms of COVID-19.
IV. Challenges and Chances of Information Technology (IT)	Digital health solutions, especially the use of telemedicine, has been previously proposed as a useful tool to provide medical advice remotely when physical presence is impossible or should be limited to a strict minimum such as in the current COVID-19 pandemic. However, certain limitations of this technology need to be considered and special emphasis should be placed on data-security and –protection.
V. Clinical Setting	General hygiene rules should be followed, especially in the preclinical and clinical setting. The entrance, which is the first point of contact, further patient traffic organization as well as the triage of allergic patients should be organized to minimize the risks of viral infection. Moreover, the organization of staff should be optimized and regular training of procedures should be provided. Any physical contact with the patient should be minimized, and effective preventive measures should be carried out for any further examination and

	diagnostic.
VI. Specific considerations in diagnostic procedures in allergic patients	Specific considerations in a clinical setting are necessary for the diagnostic procedures of different allergic diseases during the current pandemic. As SARS-CoV-2 spreads primarily through respiratory aerosols, airways but also other allergy-related organs are affected and preventive measures should be ensured. These comprise ENT exams (including endoscopy), bronchoscopy, nasal or bronchial allergen provocation tests, tissue-sampling, lung function tests, skin testing and blood-sample collection, drug provocation tests, oral food challenges and esophageal exams.
VII. Specific considerations in the management of different allergic diseases	Though avoidance measures during the COVID-19 pandemic are similar in different allergic diseases, specific aspects should also be followed in optimal care for allergic rhinoconjunctivitis, asthma, atopic dermatitis, chronic rhinosinusitis, drug allergy, food allergy, urticaria and venom allergy. Different recommendations can be provided for patients with suspected SARS-CoV-2 infection or diagnosed COVID-19 disease versus noninfected individuals or patients having recovered from COVID-19 infection. After recovery from COVID-19, allergy care has to be resumed, but an interdisciplinary consultation is recommended before any further diagnostic or therapeutic procedure.
VIII. Socio-psychological considerations for allergic patients and optimal care during and after the pandemic	Socio-psychological mechanisms play a major role in terms of symptom development, symptom exacerbation and perception in allergic patients. Besides, the general

	population is highly sensitive to the perception of people showing respiratory symptoms during the COVID-19 pandemic. This increases the risk of stigmatization of patients with allergies, further increasing the psychosocial stress of patients. Therefore, optimal medical and psychological care for patients with allergies during the COVID-19 pandemic is essential.
IX. Considerations for performing non-COVID-19-related clinical trials	Clinical trials to combat the COVID-19 pandemic currently have top priority. However, a number of non-COVID-19 trials are also essential and should be continued if they can be conducted in a safe manner. Safety measures and new guidelines need to be established for participants, and research/laboratory staff dealing with non-COVID-19 related clinical trials to ensure the continuation of essential and critical non-COVID-19 trials.

Table 2: Key conclusions on the practical considerations on the organization of an allergy clinic during the current COVID-19 pandemic.

I. COVID-19: General considerations for HCPs

Viral respiratory infections like COVID-19 are most often transmitted by direct contact with the virus from the nose, mouth, or coughed / sneezed in droplets from an infected individual [2, 21]. Hand-to-hand contact, inhaling particles from the air after an infected person has coughed or sneezed or touching an infected surface are also common transmission mechanisms. Recommendations for allergic patients - just as for all subjects - include thorough hand washing with soap and water, frequent use of hand sanitizers, avoidance of people with cold-like symptoms, and taking prescribed medications to optimally control upper and/or lower airway disease.

Patients with a suspected or confirmed diagnosis of COVID-19 should wear a face mask [22] and be treated and examined in an individual room with the door closed. Ideally an isolation room should be used and equipped with technical measures to protect

against airborne infectious agents [2, 21].

HCPs are at risk of contracting COVID-19, primarily through droplet spread, with the droplets containing a high reservoir of viral load [23]. If any procedures involving the airway are strictly necessary for COVID-19 positive patients, it must be ensured that staff are supplied with the necessary personal protective equipment in order to avoid infection and possible fatalities. Filtering face-piece (FFP2/FFP3) masks, full eye protection or PAPRs (Powered, Air Purifying Respirators) and further measures are recommended [24].

In accordance with WHO [25] and the European Centre for Disease Control (ECDC [26]), preventive measures are recommended:

- keep a distance of at least 1.5-2 meters from other people (social distancing)

- promote compliance with general hygiene measures such as regular hand disinfection (using an effective disinfectant) / hand washing for at least 30 seconds, avoid touching face and mucous membranes with your hands

- minimize social contacts (social distancing)

- limit direct patient contacts to a strict minimum

- wear personal protective clothing

- encourage regular surface disinfection, especially door handles etc.

Conclusions: Protective measures should be taken following the general recommendations from the European Centre for Disease Control and the World Health Organization and current rules must comply with the national responsible government agencies.

II. COVID-19: clinical course in allergic patients

Coronaviruses, just like the common cold viruses, may be associated with aggravation of asthma exacerbations [27] by stimulation of type 2 immune response associated cytokine production in infected epithelial cells [28]. Allergic diseases might predispose

to viral infections or a deferred viral clearance due to delayed and deficient production of the innate type I and type III interferons and/or deficient epithelial barrier function [29] [30].

Until now, limited knowledge has been available on the differences in the course of COVID-19 infections in allergic compared to non-allergic patients. Three studies from Wuhan reported allergic diseases (asthma, allergic rhinitis, atopic dermatitis, urticaria or drug hypersensitivity) as co-morbidities of COVID-19 patients [8] [31] [5]. In a study from Lombardy including over 1,500 patients, 13% of COVID-19 patients admitted to intensive care had asthma [4]. In none of these studies a prolonged or aggravated disease course was reported for patients with allergic disease compared to the included non-allergic cases. In COVID-19 patients from the Seattle area, 3 out of 24 patients developed severe respiratory failure after systemic glucocorticoid treatment due to asthma exacerbation [32]. In the US, higher asthma rates were found in COVID-19 hospitalized adult patients, especially those between 18 and 49 years. However, no information was available as to whether the asthma was caused by allergies [33]. A recent preliminary report suggested modulation of ACE-2 receptor levels by type 2 inflammation, which might shed new light on the role of type 2 immunity in SARS-CoV2 infections and the COVID-19 disease course [34]. Without any doubt, more scientific evidence is needed to answer the question as to whether allergic diseases or the treatment of allergic diseases might predispose patients for COVID-19 development and disease course.

Conclusions: Viral infections, including infections with Coronaviruses, are associated with aggravation of allergies such as asthma exacerbations. Limited knowledge is available on the differences in the course of COVID-19 infection in allergic compared to non-allergic patients and further clinical evidence is needed.

III. Care of allergic patients: preclinical setting and triage of patients

Provision of the appropriate level of necessary medical care for patients with allergic diseases and asthma needs to be based on the following principles:

1. Delay elective ambulatory provider visits
    a. Assess the patient's ability and resources to engage in home monitoring

b. Select the patients needing direct consultation based on proper screening protocols
c. Re-schedule any non-essential procedure that might impact on the safety of the patient and the HCP (e.g. lung function testing, airway samplings, rhinoscopy, surgery, drug/food/venom provocation tests)

2. Implement remote health care tools

Many clinics and medical offices already use these remote health care tools to triage and manage patients after hours and as part of usual practices. However, there are several core procedures that need to be taken into account. Primarily, sufficient numbers of health care providers (HCP) should be identified to conduct telephone and telehealth interactions with patients to identify COVID-19 symptoms. They should be assigned and followed by proper advice on the basis of the differentiation of COVID-19 symptoms from symptoms due to the common cold, flu, allergic rhinitis, chronic rhinosinusitis and allergic asthma (Table 1). For this purpose, telemedicine is a useful instrument, but should be provided by a dedicated HCP [35] [36] strictly following the general prerequisites of Information Technology (section IV). The triage of urgent cases is highly important to determine those needing in-person consultation and diagnostic procedures and those who can be managed effectively via telemedicine or scheduled for later dates. However, this important triage should not be undertaken by a medically untrained call centre operator. Individual demands for allergy testing need to be evaluated by experienced nurses or doctors with dedicated skills in taking an allergological history [36]. The technique of documenting allergological history in telemedicine follows generally accepted principles of medical conversation. Standardized and validated questionnaires for quantifying symptoms can complement the analysis of the history, be prefilled by the patient before telemedicine consultation, document the collected data and facilitate computer-assisted evaluation [37]. Patients with a clear need for in-person consultation in the allergy clinic (Figure 1) should be identified, triaged to the clinic and instructed on the procedures to be followed in the clinic.

INSERT: Figure 1 here

Figure 1: Proposed criteria for in-person consultation of allergic patients. These recommendations should be considered as general guidelines that always need to be adapted to suit the needs of individual patients, the capabilities of the facility itself, and must comply with the relevant and current rules from the responsibility government agency. (ACT, Asthma Control Test; AD, Atopic Dermatitis; ARIA, Allergic Rhinitis and its Impact on Asthma; AR, Allergic Rhinitis; CRS, Chronic Rhinosinusitis; EOE, Eosinophilic Esophagitis; EPIT, epicutaneous immunotherapy; PEF, Peak Expiratory Flow; OIT, oral immunotherapy; SCIT, subcutaneous AIT).

For milder forms, patients should be offered alternative solutions whenever possible to avoid any unnecessary risks associated with a real-life consultation, e.g., shipping electronic inhalation monitoring devices, peak-flow meters, and providing prescription for medication (see section "*clinical setting*"). In particular, allergic patients with mild symptoms regularly attending the outpatient clinic should be instructed to continue their medication including inhaled corticosteroids (ICS) and intranasal corticosteroids (INCS), AIT and biologicals targeting the T2 immune response as prescribed. Whenever possible, on-site administration in clinics for sublingual AIT and biologicals should be replaced by (self) administration at home with close monitoring, and sufficient supplies of medication should be provided. Local community organisations and health services could be engaged to assist patients who are treated at home and who may need support services in order to ensure optimal care. In some cases, trained clinic nurses can assist by telephone. Additionally, these patients should be well instructed regarding proper prevention measures for allergen exposure control, e.g. using peak-flow measurements or Apps [38] [39] [40], and food avoidance [41] (especially with on-line ordering and shipping where no individual selection of food is feasible). They should also be motivated to notify their HCPs in the case of exacerbation or deterioration of symptoms which cannot be appropriately managed at home.

Conclusions: Many clinics and medical offices already use these remote health care tools to triage and manage patients after hours and as part of usual practices. These

measures can ideally be used to prioritize and triage allergic patients on the basis of the severity of the allergic disease, the need for in-person consultation and the differentiation of allergic symptoms from clinical symptoms of COVID-19.

IV. Challenges and Chances of Information Technology (IT)

Combining the need for regular consultations and the highest degree of protection for both patients with allergic conditions and healthcare workers is a significant challenge in the current pandemic. Digital health solutions, especially the use of telemedicine, have been previously proposed as a useful tool to provide medical advice remotely when physical presence is impossible [42] [36] [43] [44]. These technologies are now significantly gaining momentum [45]. However, certain limitations need to be considered.

As such, Electronic Health Records (EHRs) have now been adopted by most major healthcare organizations. They facilitate remote access and offer greater flexibility than paper-based medical records, a factor that is particularly important during the major clinic restructuring that is occurring during the current COVID-19 pandemic. Here we discuss some of the online tools and apps that can aid researchers, clinicians and other healthcare staff in working with each other (team communications) and with patients (clinical encounters) while working at different locations.

Cybersecurity

Every internet connection to other communication partners also involves a certain risk. Normally, clinical and company IT networks are secured from external networks - e.g. the internet - by a complex security infrastructure such as firewalls, separate security zones (DMZ = demilitarized zones), web content filters, intrusion detection systems and virus scanners. These systems protect internal clinical networks and also protect from hacker attacks and insecure processes from the internet.

If a videoconferencing system has security gaps, the ‘own network’ can become compromised, up to the installation of malware. A few weeks ago, the US Federal Bureau of Investigation (FBI) issued a warning on the security gaps in video

conferencing systems [46]. Security gaps were discovered in the popular communication platform ZOOM ("*Zoom vulnerability would have allowed hackers to eavesdrop on calls*"[47]). The use of dedicated computers only for this purpose which are operated in a separately secured DMZ is recommended for video conferencing.

Data protection and legal regulations

The use of messenger and / or video services in the healthcare sector is particularly worrying from a data protection perspective. It is a classic area handling particularly "sensitive" and protected data. The processing of healthcare data is even prohibited for the time being according to Art. 9 Para. (1) of the General Data Protection Regulation (GDPR) [48]. Exceptions to this may be for data processing, insofar as processing is necessary for medical diagnostics, care or treatment in the health or social field; exceptions may be possible according to Art. 9 Para. (2) of the GDPR [48].

In this context it should be noted that:

- When using videoconferencing apps, the terms and conditions and privacy policies of the providers must be observed.
- Usage should be conducted in compliance with institution-specific policies and country-specific laws
- Most of these apps prohibit commercial use of the service without a separate agreement. This may call into question the lawful use of these apps for healthcare communications.
- If the user agrees to the Legal Infos of the apps, he/she often grants the manufacturers of the apps the rights of use of the transferred data, images etc.. When transmitting personal data, this means a violation of the basic data protection regulation and, if applicable, of medical confidentiality, since unauthorized third parties have access to this data [49].

Team communication

Commonly-used team communication applications include Microsoft Teams "Teams"[50], Zoom[51], Box[52], WhatsApp[53], and Slack[54] (Table 3). However,

these services should not be used to talk about sensitive health data of identifiable persons, but only for team organizational matters.

Communication Activity	Technology
Team communications	Microsoft Teams, Zoom, Box, WhatsApp, Slack
Educational forums	Zoom, Microsoft Teams
Patient encounters/communication	Telephone, messenger services *, secure email, Telemedicine (Amwell, Doctor on Demand, Healthtap, MDLive, Teladoc, ZocDoc, Video visits via EHR and others)
Research/ Quality Initiatives	REDCap, Box, R markdown

Table 3: Commonly-used team communication applications. *The use of these services for patient communication is only lawful in the case of very well informed written consent of the patient who must be aware of any risks.

Easy accessibility, reliability, video conferencing, private messaging, creation of distinct channels for relevant discussion, and privacy are all important considerations. There exist popular tools that enable online video conferencing, screen sharing, chats, and file sharing. Only the apps approved by the hopitals' legal department should be used. They can be used for small teams or for larger and more formal meetings, such as weekly unit meetings covering inpatient activity and consultations with relevant educational background. Post-clinic Multi-Disciplinary Meetings (MDM) remain achievable and desirable to ensure that best practice standards are met and can be hosted on "Teams". Another popular tool is "Box," where private health information can be stored and the password encrypted. Folders and documents can be shared and different levels of access can be provided. Document versions can be managed and archived in an easily accessible and convenient manner. There are also a number of

cell phone apps that can be used to communicate with smaller groups. In addition to individually owned cell phones, additional cell phones can be shared by members of nursing and administration staff. Office phones can be forwarded to these 'hot' phones. Call forwarding between cell phones should be utilized based on a roster for receiving incoming calls.

Many of these tools allow the generation of distinct channels to capture relevant discussions and to ensure patient follow-up. These can include clinic-specific channels to capture logistics of billing, scheduling, rebooking and deferring patients, as well as patient-specific channels to capture follow-up required by nurses and doctors. For all channels, the ability to 'tag' staff and reply to comments can be utilized.

Clinical Encounters

Virtual doctor consultations as an alternative to on-site clinical encounters are increasing amid the coronavirus pandemic. Patient communications can take place via telephone, telemedicine/video, secure email, and texting apps (Figure 2):

INSERT: Figure 2 here

Figure 2: Remote communication between the HCP and the patient. EHR, Electronic Health record

Video visits with a virtual care environment within the EHR platform are also being offered [55]. It is recommended that an approved, certified procedure should be used for the patient-related video consultation. These are subject to the respective legal regulations in the individual countries. It is important that the patient should be informed and should give his/her consent for the video consultation. This must be documented in order to have legal security in the case of complaint by the patient. Furthermore, it is important to have a direct "peer to peer" connection between the doctor's video workplace and the patient's workplace in order to prevent unauthorised third parties from recording the video stream. Corresponding security aspects must be taken into account (see also "cybersecurity").

Conclusions: Digital health solutions, especially the use of telemedicine, has been previously proposed as a useful tool to provide medical advice remotely when physical presence is impossible or should be limited to a strict minimum such as in the current COVID-19 pandemic. However, certain limitations of this technology need to be considered and special emphasis should be placed on data-security and –protection.

V. Clinical Setting

Public transport to and from a COVID-19 hospital

Transportation to and from the hospital should follow common healthcare recommendations. Public transport should have clear signs that it is going to the COVID-19 specialty hospital. At the last stop, the bus should be thoroughly disinfected. The driver's seat should be protected by a transparent plastic wall and the patients should be at least 2 metres away [56]. The front door of the bus should not open for passengers; only the middle and back doors should be used.

General hygiene rules

SARS-CoV-2 is an enveloped virus, which means it is susceptible to common hard-surface disinfectants such as soap and alcohol. Hand sanitizers should be provided in every patient room (ideally both inside and outside of the room), in other patient care and common areas, and at all entrances to the building. Sinks should be well stocked with soap and paper towels. High-touch surfaces, such as door handles, need to be regularly cleaned with hospital grade approved disinfectant solutions or diluted bleach.

Entrance to the Clinic

A hospital should have only two entrances for the patients: one for emergencies and one for non-emergencies. The emergency entrance should have full patient isolation equipment. The triage doctor should immediately determine the need for full isolation of the patient. Patients who present with an acute respiratory illness and require hospital admission should be tested for SARS-CoV-2 RNA expression by RT-PCR on

admission and placed in isolation until the results are ready [57]. Healthcare, cleaning and kitchen staff should all use a separate entrance. The entrance should be near the dressing rooms with two doors. At the non-emergency entrance to the hospital, masks and gloves should be provided for anyone who enters and it should be obligatory to wear these items. Visitors should be actively discouraged from entering the hospital if possible and in line with local recommendations and outpatients should be pre-assessed and triaged accordingly (see section III). Patients should wear a surgical mask and gloves, and perform strict and repeated hand hygiene. A separate toilet/bathroom/commode should be used for virus RNA RT-PCR positive patients.

Staff organization

In order to reduce the risk of the healthcare workers becoming infected, which would result in service disruption, new forms of staff deployment need to be elaborated. The personnel in the triage area should wear a FFP2/3 mask as well as a face shield, goggles, gown, gloves, and closed shoes.

A two-team approach has been adopted in many large hospital-based departments with no or minimal contact between the two teams. A popular method involves:

1. “Team One”: Inpatient COVID-19 deployment including Consultant, Senior Registrar, Junior Medical Officer. Several such groups could form a roster depending on unit and hospital size.
2. “Team Two”: Outpatient allergy/asthma/immunology predominantly operating a virtual call centre approach and ideally remotely operating in staff homes.

A designated deputy head of department and subleads for Allergy/Asthma/Immunology provide a backup framework for key personnel in the case of staff infection requiring substantial self-isolation and resulting in workforce disruption. In COVID-19 patient-overloaded clinics, day and night shifts can be decreased to 6 hours in order to avoid extreme fatigue and thus reduce the risk of HCP errors and infection. Moreover, there is an urgent need for staff training resources and mechanisms to ensure a constant re-training of the most important policies. This regular training has to involve all of the staff members.

Patient organization

Any service that does not require a diagnostic or onsite therapeutic procedure should be undertaken via telemedicine consultation [58].

For regular non acute care: only patients requiring a timely diagnostic or therapeutic procedure should be seen in the hospital. A history of identifying potential infected contacts, recent travel and early symptoms such as anosmia and dysgeusia [59] [60] should be obtained from all patients before any in-person consultation in the clinical setting [61]. There is now ample evidence that COVID-19 may be contagious before the onset of the classical symptoms of cough and high fever [8]. Therefore, identifying the early symptoms of COVID-19 is of particular importance and is a health system priority. Recently, a probable association between COVID-19 and altered olfactory and gustatory function has been reported by several groups, often as the presenting symptom [60] [62]. To evaluate whether this could be a first symptom of COVID-19 can be particularly challenging when treating allergic and rhinosinusitis patients.

Establishing COVID-19 free zones in the hospital includes a strict screening protocol to ensure that patients who are entering the clinic are not infected by COVID-19.

Patients who have indications of potential COVID-19 infection (classical COVID-19 symptoms, fever, but also anosmia, and/or recent contact with a COVID-19 positive subject) should not be admitted to these areas [63]. These patients should be guided to the COVID-19 clinic for further screening evaluation.

To decrease the density of patients, the waiting area should be separate from the treatment area, the number of appointments reduced, and appointments should be scheduled with ample time intervals and online consulting services whenever possible [64].

Precise appointment times are particularly important during the COVID-19 pandemic as this can greatly reduce patient-patient and patient-HCP hospital-acquired cross-infections. Also, precise appointments can ensure that patients stay in the hospital for a minimum amount of time and that the medical staff are fully prepared with personal protective equipment. Moreover, the patient should be admitted to a consulting room with good ventilation and, at the same time, there should not be more than one patient in the waiting area for visiting or post-immunotherapy observation.

In the consultation room

All physical contact with the patient should be limited to a strict minimum. When caring for a patient with suspected COVID-19, staff are recommended to wear a gown, gloves, and either an FFP/FFP2 (or local equivalent) respirator plus face shield and goggles, or a powered air-purifying respirator. However, in hospital areas outside potential SARS-CoV-2 contaminated zones, there is conflicting advice on the necessary level of personal protective equipment (even when available), and evidenced-based recommendations are scarce. Gloves and face masks [22] may be considered for use near entrances and in common areas. Personal protective equipment should be available at the entrance of patient rooms and in other areas where patient care is provided. Signs at the entrance of patient rooms should clearly indicate the level of personal protective equipment required.

Diagnostic procedures involving upper airway manipulation like anterior rhinoscopy and, even more, nasal endoscopy, or nasal provocation should be considered as high risk for viral transmission. These procedures should therefore be limited to patients with an urgent need of examination during the initial phase of the COVID-19 outbreak. For further details, see nasal endoscopy during COVID-19 [24].

Conclusions: General hygiene rules should be followed, especially in the preclinical and clinical setting. The entrance, which is the first point of contact, further patient traffic organization as well as the triage of allergic patients should be organized to minimize the risks of viral infection. Moreover, the organization of staff should be optimized and regular training of procedures should be provided. Any physical contact with the patient should be minimized, and effective preventive measures should be carried out for any further examination and diagnostic.

VI. Specific considerations for diagnostic procedures in allergic patients

The following sections overview the specific considerations for diagnostic procedures in different allergic diseases in a clinical setting during the current pandemic. The indication and the urgency for these tests should be taken into account and can be confirmed, for example by an initial visit performed via telemedicine. Contraindications for skin tests, provocation tests and lung function tests can be clarified, and this can help to avoid unnecessary in-person consultation with patients during the COVID-19 pandemic.

ENT examination, nasal provocation testing and sampling procedures

SARS-CoV-2 spreads primarily through respiratory aerosols, and higher viral loads have been detected in nasal swabs compared to other locations [65]. Thus, rhinoscopy, nasal endoscopy, nasal provocation testing, smell- and taste testing and samplings are high-risk procedures. Nasal provocation tests should be avoided, whereas rhinoscopy, endoscopy and nasal samplings should be limited to patients with an urgent need for examination [64]. A tower with camera, screen and light source can maximize the examiner-patient distance during endoscopy [24]. The use of anaesthetic spray can be replaced by a soaked pledget, thus avoiding virus atomization [24]. The examiner should wear the adequate personal protective equipment recommended for HCPs: FFP2 or FFP3 face mask, goggles or disposable face shield covering the front and sides of the face, clean gloves, and clean isolation gown [66].

Lung Function Testing, bronchoprovocation tests and lower airway sampling

Aerosols can be generated during spirometry, bronchoprovocation testing, fractionated exhaled nitric oxide (FeNO) measurement and other lower airway sampling procedures [67] [68] [69]. Therefore, routine lung function testing and related procedures should be generally suspended during the current pandemic. In cases of extreme need, the personnel should use personal protective equipment and follow the other safety measures as described above [66] [70].

Skin testing and blood-sample collection for diagnostic use

Skin testing should be generally suspended during the current pandemic. Nevertheless, exceptions can be considered after a careful/proper risk-benefit assessment or may be replaced by laboratory tests. When collecting biological samples or conducting skin testing, the personnel must use the recommended personal protective equipment [66] and also follow the standard precautions (SP) when handling clinical specimens, all of which may contain potentially infectious materials [71]. In this case, a laboratory gown and a single-use waterproof apron may replace the isolation gown [72] [73]. After collection, samples should be placed in a leakproof primary container, and inserted into watertight secondary packaging with absorbent material. This package should be placed in a rigid outer packaging with appropriate labelling [74]. Sample processing should be performed following biosafety level 2 (BLS-2) practices, the current standard in clinical laboratories. Aerosols can originate from centrifugation, pipetting, vortexing, mixing, decanting liquids, loading and spilling samples or cleaning up spills. Therefore, these procedures should be performed inside a biological safety cabinet and using centrifuge safety cups and sealed rotors [71]. Work surfaces and equipment should be appropriately decontaminated and laboratory waste should be handled as biohazardous agents [75]. The inactivation of serum samples suspected to be contaminated with SARS-CoV-2 should be carried out by following the procedure recommended by WHO for serum samples for ELISA-based analysis [76].

Sample collection for research use

Research procedures involving virus isolation and propagation in cell culture should be conducted in a BSL-3 laboratory [77]. The appropriate minimum containment measures for research procedures other than virus propagation (e.g. flow cytometry) are currently unclear. The addition of a virus-neutralizing agent to research samples might be considered to ensure safe processing under BSL-2 conditions [77].

Drug Provocation Tests

Cough, sneezing or rhinorrea may occur during drug provocation tests [78] [79]. Therefore, these procedures should not be generally conducted during the current pandemic [79]. Nevertheless, exceptions can be considered after a proper risk-benefit

assessment. Examples of these include chemotherapy in oncologic patients, perioperative drugs or radiocontrast media in subjects needing urgent procedures, or antibiotics in infected individuals without any alternative effective drug [80] [81].

Oral food challenges and esophageal examination

Oral food challenge may induce respiratory symptoms with aerosol-generating potential, together with vomiting and diarrhoea [82]. Importantly, the virus can persist in gastrointestinal fluids for a longer period than in the respiratory specimens [83]. Therefore, oral food challenges should be avoided during the current pandemic, as they lack urgency [84]. The diagnosis of eosinophilic esophagitis requires a gastroscopy-guided esophageal biopsy [85]. The performance of a gastroscopy is not recommended during the current pandemic, due to the possible persistence of virus in biological fluids [86]. In the case of extreme need (e.g. frequent food impaction), a proper risk-benefit assessment should be conducted [87].

Conclusions: Specific considerations in a clinical setting are necessary for the diagnostic procedures of different allergic diseases during the current pandemic. As SARS-CoV-2 spreads primarily through respiratory aerosols, airways but also other allergy-related organs are affected and preventive measures should be ensured. These comprise ENT exams (including endoscopy), bronchoscopy, nasal or bronchial allergen provocation tests, tissue-sampling, lung function tests, skin testing and blood-sample collection, drug provocation tests, oral food challenges and esophageal exams.

VII. Specific considerations in the management of different allergic diseases

General treatment recommendations for selected allergic diseases during COVID-19

According to WHO, patients at risk of or with diagnosed COVID-19 should continue their treatment for any other disease (this includes allergic disease) in line with current guidelines. Special consideration should be given to the interference of drugs with COVID-19 or vice versa [25]. It is generally recommended that patients should have a supply of the medication they need for at least a 14-day quarantine. Where more stringent or lengthy measures of isolation are enforced, consideration must be given to

availability of medicines and potential substitutes for current treatments if particular medications cannot be obtained. Patients should have an action plan to ensure that these issues are covered.

Telemedicine visits cannot replace all personal consultations, notably those mandatory for the administration of subcutaneous allergen immunotherapy (SCIT). Nevertheless, prior to the consultation, questions identifying actual contraindications can be clarified by a telemedicine consultation. Many of the biologics used for the treatment of allergic diseases (e.g. Omalizumab, Benralizumab, Mepolizumab and Dupilumab) are registered for self-application if the patients are adequately trained in the injection technique and in the assessment and management of allergic side effects. During telemedicine visits, injection techniques may be rechecked, and patients' questions answered regarding the treatment. Peak flow protocols can be discussed during a telemedicine visit, and treatments can be adapted.

In general, patients can be instructed on allergen avoidance measures and treatment modalities. They can show the drugs they have at home, and can be instructed on the use and especially on the application techniques of inhalers and topical nasal sprays. Patients suffering from anaphylaxis may be trained to use adrenaline auto-injectors for self-administration; this improves safety and may also improve the patient's quality of life.

As a general rule, patients with severe allergic disease who are on biologicals and have a SARS-CoV-2 infection should pause the biologicals. Proper management and background controller treatment (topical steroids or other controller medications as recommended by current guidelines) should be continued as prescribed. If resolution of the disease is established (e.g. via a negative SARS-CoV-2 test) at a minimum of 2 weeks post onset/positive testing, the re-administration of the biological should be re-initiated [9].

Avoidance measures

Importantly, self-identified and physician-diagnosed (via skin prick test, blood test, provocation testing) triggers of asthma exacerbation and allergies (seasonal, food allergies, etc.) need to be understood for each patient. Targeted messages to patients who have a known allergen sensitivity may be a meaningful way of connecting with patients during a time of limited in-person clinic visits (e.g. reminder alerts that the spring season has arrived). Educational outreach messages or tele-visits can include instructions on allergen avoidance, indoor air purifiers, proper medication use (e.g. reviewing the appropriate use of inhalers with spacers). Food scarcity during pandemic operations may adversely impact food-allergic families and strategies for planning and stocking safe foods should be discussed. Medication supply should also be addressed in conversations with patients to plan for adequate controller and rescue medication with the possibility of substituting or switching medications as needed.

COVID-19 in the light of different allergic diseases

The following section overviews recommendations for selected allergic diseases (Table 4):

Disease	Recommendations for COVID-19-diagnosed individuals or for cases with suspected SARS-CoV-2 infection	Recommendations for noninfected individuals during the COVID-19 pandemic or for patients having recovered from COVID-19 infection
Allergic rhinoconjunctivitis [88] [10]	- Continue INCS - Continue second-generation H1-antihistamines - Stop SCIT until resolution of the disease is established - Stop SLIT until resolution of the disease is established	- Continue INCS - Continue second-generation H1-antihistamines - Continue SCIT and SLIT -Consider supplying patient with a sufficient amount of SLIT medication for home self-administration (for a 14-day quarantine at least)

	- biologicals *	-biologicals *
Asthma [13]	- For severe attacks, pressurized metered dose inhaler (pMDI) via a spacer is the preferred treatment instead of nebulizers -While a patient is being treated for a severe asthma attack, their maintenance inhaled asthma treatment should be continued (at home and at hospital) -For *acute asthma attacks*, patients should take a *short course* of oral corticosteroids (if instructed in their asthma action plan or by their healthcare provider), to prevent serious consequences. -Additional treatment should be based on the individual patient and on the underlying disease. - biologicals *	- Continue all inhaled medication, including ICS (containing therapies), as prescribed by the physician and in line with the personal asthma action plan. - If needed, OCS should be continued at the lowest possible dose in patients at risk of severe attacks/ exacerbations. - Routine *spirometry* testing should be suspended to reduce the risk of viral transmission, and, if absolutely necessary, adequate infection control measures should be taken. -biologicals *
Atopic dermatitis	- Continue topical treatment - Systemic immune-modulating therapy may be paused based on interdisciplinary risk assessment. Optimize the topical treatment after pausing systemic treatment.	- Continue topical treatment - Continue systemic immune-modulating treatment

	-biologicals *	-biologicals *
Chronic Rhinosinusitis [11]	-Like in other upper airway viral infections (common cold or flu), the loss of smell is a frequent symptom in COVID-19 patients. But a sudden and severe loss of smell (anosmia) and/or taste may also be present in COVID-19 patients who are otherwise asymptomatic [62] [59] -Surgery for CRS should be avoided unless patients are proven COVID-19 negative -Patients with CRS should continue using their INCS -biologicals *	-Anosmia in COVID-19 patients often improves within 14 days -Patients with CRS should continue using their INCS -biologicals *
Drug Allergy [89]	Quick and accurate diagnostic and therapeutic decisions are mandatory in the case of DHRs induced by COVID-19 drugs.	Severe allergic reactions must be treated immediately. Diagnostic testing may be urgently indicated in the case of suspicion of allergic reaction to highly necessary drugs. When validated and reliable, in vitro test may be preferred for diagnosis. If not immediately required, drug allergy diagnostic must be postponed until pandemic is locally under control, and alternative drugs should be used until then.

Food allergy	Severe allergic reactions must be treated immediately. Diagnostic testing should be postponed. In vitro diagnostic tests can be preferred for diagnosis in severe anaphylaxis cases. Strict avoidance measures must be taken and an adrenalin auto-injector must be carried. - OIT or EPIT: adapt dosing as indicated in the dosing plan and in coordination with the treating physician.	Severe allergic reactions must be treated immediately. Diagnostic testing should be postponed. In vitro diagnostic tests can be preferred for diagnosis in severe anaphylaxis cases. Strict avoidance measures must be taken and an adrenalin auto-injector must be carried. - Continue OIT or EPIT
Urticaria	-Continue second-generation H1-antihistamines. - Systemic immune-modulating therapy may be paused based on interdisciplinary risk assessment. -biologicals *	-Continue second-generation H1-antihistamines. -Continue systemic immune-modulating treatment. --biologicals *
Venom allergy	Severe allergic reactions must be treated immediately. Diagnostic testing is postponed. Strict avoidance measures must be taken and an adrenalin auto-injector must be carried. - Stop SCIT until resolution of the disease is established.	Mastocytosis and grade 3 or 4 anaphylaxis patients need to be diagnosed and venom IT initiated. Strict avoidance measures must be taken and an adrenalin auto-injector must be carried. -Continue SCIT.

Biologicals*	**Recommendations for COVID-19-diagnosed individuals or for cases with suspected SARS-CoV-2 infection**	**Recommendations for noninfected individuals during the COVID-19 pandemic or for patients having recovered from COVID-19 infection**
Recommendation applies for biologicals in the context of all diseases [9]	- Stop until resolution of the disease is established (e.g. via a negative SARS-CoV-2 test in connection with clinical recovery), but for a minimum of 2 weeks from onset/positive testing. - Ensure re-administration after recovery	Continue the application of biologicals - if possible as home self-administration.

Table 4: Key-recommendations from recently-published EAACI- / ARIA-statements. These recommendations are conditional and should be adapted regularly on the basis of more clinical data. epicutaneous immunotherapy (EPIT) ; CRS, chronic rhinosinusitis; INCS, intranasal corticosteroids; OCS, Oral corticosteroids, OIT, oral immunotherapy; SCIT, subcutaneous immunotherapy; SLIT, sublingual immunotherapy

Atopic Dermatitis

Atopic dermatitis is one of the most common skin disorders. The lifetime prevalence varies between 0.2% and 25% worldwide, the most effected area being the northern part of Europe [90]. The disease most often starts in early childhood and persists into adult life in up to 50% of affected patients [91]. Co-morbidities with other atopic diseases including asthma, allergic rhinitis and food allergy are common [92]. Most with mild to moderate atopic dermatitis can be controlled on topical treatment. However, in the severe cases, systemic immune-modulating treatments including immuno-suppressive therapy is needed [93]. Conventional systemic immuno-suppressive treatment, such as Ciclosporin, may interact with the human body's defense

mechanisms against viral disease, while Dupilumab, which is registered in many countries for the treatment of moderate to severe atopic dermatitis, selectively interferes with type 2 inflammation and is in general not considered to increase the risk for viral infections.

It is well known that viral and bacterial infection may complicate and exacerbate atopic dermatitis including infections with Staphylococcus aureus (impetigo), poxvirus (molluscum contagiosum) and Herpes Simplex virus (eczema herpeticum) [92]. Severe and untreated atopic dermatitis is a known risk factor for disseminated viral skin disease [94].

In the current SARS-CoV-2 pandemic, the European Task Force on Atopic Dermatitis (ETFAD) recommends to continue all immune-modulating treatment since exacerbations of underlying diseases can have a large negative impact on the patient's immunity [30]. However, patients at risk are advised to strictly follow the recommendations issued by the local health authorities in each European country [30]. The British Association of Dermatologists (BAD) has addressed potential issues regarding the COVID-19 infection of patients undergoing immune-modulating treatment [95]. Other countries will follow. A thorough hygienic procedure is recommended with hand washing and disinfectants. Non-irritant soap substitutes should be used following the same instructions as those for regular soap. Moisturizers should be applied afterwards. In the case of COVID-19-infected atopic dermatitis patients, interdisciplinary risk assessment should be carried out and, in accordance with current guidelines on active infections and systemic therapy, the immune-modulating therapy may or may not be paused afterwards [30]. If systemic treatment is paused, it is important to optimize the topical treatment. Furthermore, if the paused systemic treatment also has an effect on co-morbidity such as asthma, then the co-morbidity also has to be treated by other drugs. According to a letter from Italy regarding 245 patients on therapy with Dupilumab, only two developed COVID-19 [96]. An abnormal course of COVID-19 was not observed in these 2 patients. More clinical data are needed for this specific treatment.

Urticaria

Urticaria is characterized by the development of wheals (hives), angioedema or both [97]. Acute urticaria is defined as the occurrence of wheals, angioedema or both for less than 6 weeks. Chronic urticaria is defined as wheals, angioedema or both for 6 weeks or more [97]. Viral infection has been found as a potential trigger - and sometimes as the main etiologic agent - in causing acute or chronic urticaria [98].
In Italy, 88 patients with COVID-19 were studied by a group of dermatologists. 20% developed cutaneous symptoms including erythematous rash and urticaria. It was concluded that the skin manifestations related to the COVID-19 infection are similar to those occurring during common viral infections [99]. In France, among 103 out- and in-patients with confirmed COVID-19 infection, two had urticaria [100]. In a study from China, 1.4% of the COVID-19 patients reported an underlying urticaria. However, skin symptoms during the infection were not described [5]. The manifestation of urticaria could appear before the onset of fever or respiratory symptoms [101].

As a consequence of these observations, the manifestation of acute urticaria could be an indication to test for SARS-CoV-2. According to the guidelines, second-generation H1-antihistamines are the base of urticaria treatment [97] and should be continued during the pandemic. If urticaria cannot be controlled on antihistamines in four-fold dose, Omalizumab is recommended as an add-on treatment. Omalizumab is registered for self-administration after patients have received training on the injection technique and on the assessment of allergic side effects. Only the first two injections need to be administered in hospital, due to the risk of anaphylaxis. Therefore, especially during the COVID pandemic, treatment at home is favourable. By telemedical visits, the efficacy of the treatment can be evaluated and patients' questions regarding the treatment may be reviewed. This is currently recommended by the BAD [95]. As for all COVID-19 infected patients, interdisciplinary risk assessment should be performed and, in accordance with current guidelines on active infections and systemic therapy, the immune-modulating therapy may or may not be paused afterwards.

Food Allergy

Many reactions to foods are mild-moderate and can be self managed by the patient, given the availability of an up-to-date action plan and adequate rescue medication.

During periods of isolation, it is vital that children and adults with food allergy have access to suitable foods according to their dietary recommendations [102]. Patients with a history of severe anaphylactic reaction urgently need an emergency health card providing information on the diagnosis, eliciting (causative) allergens, and necessary treatment in the case of a severe reaction and / or an unexpected hospital admission due to COVID-19 [103]. Oral (OIT) and epicutaneous immunotherapy (EPIT) for Food Allergy should follow the general rules of EAACI/ARIA for AIT during COVID-19 pandemic (description in subchapter "allergic rhinoconjunctivitis").

Venom allergy

In the case of an anaphylactic reaction due to an actual insect sting, patients should be treated according to the guidelines. Especially in high-risk patients (e.g. high risk for subsequent stings, patient suffering from mastocytosis, patient with grade 3 or 4 anaphylaxis), the diagnosis of insect venom allergy must be proved urgently. Venom immunotherapy should be initiated without any delay in order to prevent severe reactions in the case of further stings in the future [104]. The treatment should follow the general rules of EAACI/ARIA for AIT during COVID-19 pandemic (description in subchapter "allergic rhinoconjunctivitis"). Patients must be informed regarding avoidance strategies and provided with drugs for self-administration. Adrenaline autoinjectors must be prescribed, and patients must be trained to use these devices. Prior to the initiation of venom immunotherapy, contraindications and requirements for treatment can be discussed with the patient in a telemedicine consultation.

Drug allergy

Severe allergic reactions to drugs must be treated immediately. Diagnostic testing may be urgently indicated in the case of a suspicion of allergic reaction to highly necessary drugs. This may be the case for example in patients suffering from reactions to antibiotics which may be necessary to treat bacterial superinfection in COVID-19 pneumonia. In the case of an immediate need for treatment with a drug that is suspected to be responsible for systemic allergic reactions, drug desensitization is a

therapeutic procedure whose aim is to induce a temporary state of unresponsiveness to a drug in a patient with confirmed allergy. During drug desensitization, respiratory and gastrointestinal symptoms occur commonly [105] [106] with a subsequent risk of spreading infectious aerosols. Therefore, the decision to conduct the procedure during the current pandemic must consider both the expected benefits obtained from the drug administration, as well as the potential risks of severe reaction and infection spread [89]. Absolute indications for desensitization may include chemotherapeutic agents in oncologic patients, aspirin in subjects with ischemic diseases and antibiotics in infected individuals when no effective alternative is available [107].

Chronic rhinosinusitis

Chronic rhinosinusitis (CRS) affects approximately 5-12% of the general population worldwide and is regarded as a chronic airway disease, that, according to WHO recommendations, may be a risk factor for COVID-19 patients [6] [11]. The inflammatory changes affecting the nasal and paranasal mucous membranes in CRS with nasal polyps (CRSwNP) are, in most cases, of the type 2 (T2) inflammation endotype. They are typically associated with epithelial damage and tissue destruction [108], which can promote viral infections [109]. Asthma often coexists with CRSwNP and it is known that deterioration in the control of CRSwNP can promote asthma exacerbations [109].

Symptoms of nasal obstruction, rhinorrhea, facial pressure and smell problems regularly occur in CRS. Recently, a number of reports have been indicating that a sudden and severe (anosmia) isolated onset of loss of smell (ISOA) and/or loss of taste may also be present in COVID-19 patients who are otherwise asymptomatic. This is considered a marker symptom in screening for SARS CoV-2 infection [110] [111] [62], but may also interfere with loss of smell in CRS [11]. CRS is treated with intranasal corticosteroids (INCS), systemic corticosteroids or specific, T2 endotype-driven anti-inflammatory therapies according to the severity of disease [112]. INCS remain the standard treatment for CRS in the COVID-19 pandemic and also for patients with SARS-CoV-2 infection [11]. Surgical treatments should be reduced to a minimum and surgery should be preserved only for patients with local complications and those for whom no

other treatment options exists. Systemic corticosteroids should be avoided. Treatment of severe uncontrolled CRSwNP patients [112] with biologicals can be continued with careful monitoring in non-infected patients. However, it should be temporarily discontinued in patients having tested positive for SARS-CoV-2 (RT-PCR), until recovery. We suggest that physicians assess the risks vs. benefits in low-risk patients before initiating biologics therapy on a case-by-case basis. However, it should not be initiated in high-risk patients [11] [9].

Allergic rhinoconjunctivitis

There have been reports that topical applied "corticosteroid preparations" may increase the risk of developing COVID-19 or may cause a more severe course of the disease. This opinion massively unsettled numerous patients suffering from allergic rhinitis (AR), CRS or asthma. A current Position Paper by ARIA and EAACI on AR treatment [88] states that INCS are the therapeutic standard for the treatment of AR regardless of symptoms and inflammation, thus avoiding mucosal damage. In approved doses (see package leaflet), INCS do not increase the risk of infections in patients with SARS-Cov-2, nor do they trigger a more severe course of COVID-19 disease [88]. Reducing allergic mucosal inflammation by INCS may even shorten the duration and decrease the severity of symptoms in upper respiratory tract virus infections of AR patients [113], but seems not to have any marked effects on the common cold symptoms of patients without AR. Therefore, it is recommended that patients with AR should continue to regularly use their INCS at the individually-prescribed dose. Hence, it is not advised that they change or even stop their treatment without consulting their doctor [88]. Discontinuation of INCS may worsen AR symptoms with increased secretion and sneezing which may promote viral droplet transmission from SARS-Co-2 infected patients to healthy individuals [88]. In addition, worsening of AR can trigger an exacerbation of asthma [88], which is regarded by WHO as a risk factor for severe courses of COVID-19. Systemic glucocorticosteroids in general have several adverse effects if given long term [114]. For AR, they should be used with even more caution during the current COVID-19 pandemic and only when no therapeutic alternatives are available [88] because of a potential temporary immunosuppression and a possible increased risk of contracting a SARS-CoV-2 infection or progression to severe disease [114].

Allergen immunotherapy (AIT) is the only disease-modifing treatment option for patients with allergic diseases as applied through the subcutaneous (SCIT) or sublingual route (SLIT) [115] [116]. During the current pandemic, special considerations should be introduced to the management of AIT [117] [10]. **All** in-person consultation may be preceded and prepared by a telemedicine visit, during which information is obtained about the patient´s health status and possible contraindications for AIT. Since SLIT is self-administred at home during the maintenance phase, telemedicine visits may be helpful for advising patients and increasing their adherence to treatment.

In noninfected individuals during the COVID-19 pandemic or in patients having recovered from COVID-19 infection, it is recommended to continue SCIT in potentially life-threatening allergies, such as venom allergy [10]. The possibility of expanding injection intervals in the continuation phase should be evaluated and may be beneficial. SLIT should also be continued, and the patient must be supplied with sufficient medication.

For both application routes a continuation of AIT is possible in principle under the following prerequisites [10]: (i) asymptomatic patients without suspicion of SARS-CoV-2 infection and/or contact with SARS-CoV-2 positive individuals, (ii) patients with a negative test result (RT-PCR), (iii) patients after an adequate quarantine or (iv) patients with detection of serum IgG to SARS-CoV 2 without virus-specific IgM. In COVID-19-diagnosed cases (positive RT-PCR), in patients suspected of SARS-CoV-2 infection, or in symptomatic patients with exposure or contact to SARS-CoV-2-positive individuals, EAACI recommends interrupting SCIT and SLIT until recovery [10].

If AIT is stopped due to signs of a potential SARS-CoV-2 infection (such as fever, cough, dyspnea), or due to other signs of ill health, or due to local restrictions on clinic operations, it should be resumed after recovery but with proper dosage adjustment and under medical supervision when appropriate. To maintain social distancing procedures in the clinic, the following methods could be considered: stretching out the interval of IT or organizing different clinic hours to limit the number of patients attending for IT [10] [118].

Asthma

To date, there is very little information available on patients with asthma who have COVID-19. In general, viruses, including rhinoviruses and respiratory synctial viruses, have been shown to induce asthma episodes or exacerbations [119] [120]. Mounting evidence implicates that particular viral pathogens, namely the human rhinovirus and respiratory syncytial virus, are among the most likely culprits in asthma inception [120]. Bacterial infections and colonization have also been associated with exacerbation and recurrent wheeze, an effect that may be independent, or a cofactor with viruses. In addition, certain individuals may have a genetic predisposition towards viral-induced wheezing and the development of asthma [120]. Whether this also applies to SARS-CoV-2 infection remains to be seen. Interestingly, according to initial reports, allergic airway disease including asthma did not appear to be a risk factor for COVID-19 or for a severe clinical course [5] [8] [121]. However, more recent reports from the USA show asthma as an underlying condition in 13-27% of patients hospitalized with COVID-19, within the COVID-NET hospitals [33]. Additionally, immunocompromised patients - including the elderly, those with diabetes mellitus or those on (systemic) corticosteroids in conjunction with the underlying immune disorders - may be at an increased risk of being infected and more severely affected by SARS-CoV-2 [5] [122].

Optimal disease control is the first defense against respiratory triggers including infections in patients with inflammatory airway disease such as allergic rhinitis and asthma. Inhaled maintenance therapy with bronchodilators and ICS should not be stopped during the COVID-19 pandemic [13]. The termination of inhaled treatment may in fact imply an increased risk for asthma symptom worsening and acute airway exacerbations. Furthermore, the risk of asthma deteriorating in a threatening manner and necessitating (otherwise unscheduled) doctor visits or hospital stays - potentially responsible for contact with COVID-19 patients - is far more dangerous for asthmatic patients than a possible increased risk of SARS-Cov-2 infection due to a theoretic local immunodepression induced by ICS. Given the lack of current evidence that ICS negatively affect the COVID-19 outcome, experts and professional societies within the respiratory and allergy field - including the Global Inititiative on Asthma (GINA), the American Academy of Allergy, Asthma and Immunology (AAAAI), the European

Respiratory Society (ERS) and EAACI – all stress the importance of disease control, especially since many countries are now entering the spring pollen season [13]. Apart from the generally applicable avoidance measures issued by the governments, the societies recommend that patients continue taking their corticosteroid-containing controller medications and other controllers (including biologicals), as detailed in their personal asthma plan and that they should seek medical help if disease control deteriorates [88] [123] [124] [125] [126]. This applies both for adults and children with chronic inflammatory airway disease and for with COVID-19 or a suspicion of having the infection. Contact with health care providers should be digital as much as possible.

Treatment of severe asthma with biologicals should also be continued [9]. A discontinuation of biologicals can lead to a worsening of the underlying disease, which in turn could have a negative impact on the course of a COVID-19 infection [9]. Virus-related asthma exacerbations occur less frequently or are less severe under biologicals, as demonstrated for Omalizumab, but not in the context of COVID-19 [127] [128]. However, when authorized by international regulatory bodies (i.e. the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA)), self-administration should always be advised in order to reduce exposure to high-risk environments such as hospitals and primary care settings.

In the absence of biological therapy, patients would have to be switched to therapy with systemic glucocorticosteroids, especially those with severe asthma. This can have negative effects on the immune defense against SARS-CoV-2. In a study performed on patients from the Seattle area, severe respiratory failure was observed in 3 of 24 COVID-19 patients after systemic glucocorticoid treatment due to asthma exacerbation [32].

Post-COVID-19 routine care

For patients who have recovered from moderate to severe COVID-19 infection, particular attention should focus on lung, kidney, cardial and liver recovery before re-instituting usual medications [129] [130] [131] [132] (Figure 3). Some patients infected with SARS-CoV-2 have a severe systemic inflammatory response, with marked elevation in CRP, d-dimer, and ESR in addition to multi-organ dysfunction. Patients may have

participated in COVID-19 clinical trials and it is important to note which medication was potentially administered (see section "Considerations for performing clinical trials"). When resuming allergy care, clinical judgement should determine whether additional labs (complete blood count, liver function test, kidney function) or lung function testing are necessary before restarting the treatment of allergic diseases and this decision should be based on a multidisciplinary consultation. In some cases, a close follow-up to assess pulmonary rehabilitation may be warranted.

INSERT: Figure 3 here

Figure 3: General diagnostic measures in post-COVID-19 routine care. The decision on the diagnostic tests or additional labs before restarting allergy care should be based on an interdisciplinary consultation.

Conclusions: Though avoidance measures during the COVID-19 pandemic are similar in different allergic diseases, specific aspects should also be followed in optimal care for allergic rhinoconjunctivitis, asthma, atopic dermatitis, chronic rhinosinusitis, drug allergy, food allergy, urticaria and venom allergy. Different recommendations can be provided for patients with suspected SARS-CoV-2 infection or diagnosed COVID-19 disease versus noninfected individuals or patients having recovered from COVID-19 infection.
After recovery from COVID-19, allergy care has to be resumed, but an interdisciplinary consultation is recommended before any further diagnostic or therapeutic procedure.

VIII. Socio-psychological considerations for allergic patients and optimal care during and after the pandemic

Allergic responses are affected by psychological factors such as stress and anxiety and can be modulated by interventions other than conventional drug therapy [133]. These psychological mechanisms play a role in terms of symptom development, symptom exacerbation and perception [134, 135]. The reactions of other people to patients showing allergic respiratory symptoms during the COVID-19 pandemic are amplified.

These reactions, along with the governmental regulations (e.g., social distancing) for dealing with the pandemic, induce further stigmatization and thus enhance psychosocial stress for allergic patients.

Symptom development and symptom perception are only partially caused by the biological mechanisms of the allergy, and many patients report bodily symptoms that are mainly developed via psychological effects (nocebo effects). Relevant psychological mechanisms for symptom development include: negative expectations, increased self-observation of somatic reactions, catastrophizing of perceived symptom (dysfunctional appraisal), as well as fears and negative affect [136]. For many patients (and sometimes even for their physician), the reported symptoms are a conglomerate of potential allergic symptoms, potential symptoms of COVID-19, and correlates of concern that are almost impossible to disentangle. These nocebo symptoms can account for up to 80% of patients with medical conditions [137].

During the COVID-19 pandemic, the general population is highly sensitive to the perception of people showing respiratory symptoms. This increases the risk of stigmatization of patients with allergies, further increasing the psychosocial stress of the patients. The neuroendocrine and immunological consequences of stress exposure are in turn able to amplify the development of allergic symptoms [134] [138]. Negative effects on the willingness to expose oneself to those contacts (e.g. at work, in private social networks) are further potential consequences with negative impact on health conditions. This is even more problematic, because social contact and social support can dampen negative stress effects and reduce disease symptoms [139]. Several recommendations to improve medical care for patients with allergies during the COVID-19 pandemic can be given (Table 5).

- Manage the increased potential for the development of nocebo symptoms: patients should be informed about the potential detrimental effects of nocebo mechanisms, such as increased self-observation or negative expectations. Patients should be encouraged to work against them, and to disentangle stress effects from symptoms of clinical conditions.

• Despite public encouragement for social distancing and increased social stigmatization in the public, patients should be encouraged to maintain an active social network employing the available communication channels. Social support is a crucial factor for improving health in general.
• Encourage patients to do regular physical exercise. Regular physical activities induce anti-inflammatory responses.
• An empathetic, reliable and predictable doctor-patient relationship guarantees patient compliance with medical recommendations and lowers nocebo effects.
• Encourage engagement in stress reduction activities such as relaxation techniques, mindfulness, yoga.

Table 5: improving medical care for patients with allergies during the COVID-19 pandemic

Conclusions: Socio-psychological mechanisms play a major role in terms of symptom development, symptom exacerbation and perception in allergic patients. Besides, the general population is highly sensitive to the perception of people showing respiratory symptoms during the COVID-19 pandemic. This increases the risk of stigmatization of patients with allergies, further increasing the psychosocial stress of patients. Therefore, optimal medical and psychological care for patients with allergies during the COVID-19 pandemic is essential.

IX. Considerations for performing non-COVID-19-related clinical trials

Many of the ongoing non-COVID-19-related clinical trials have been suspended during the current COVID-19 pandemic for safety and feasibility reasons as recommended by guidance from the US Food and Drug Agency as well as the European Medicines Agency [140] [141]. While it is imperative that clinical trials on COVID-19 be prioritized and quickly implemented following local regulatory policies and fullfiling highest quality standards [142] [143], it is also critical that other essential clinical research programmes, such as those involving study drugs or clinical assessments, should safely continue as much as possible. However, the social distancing measures put into place

by different governments (e.g. close-down of clinical units and public transportation, etc.) complicate the implementation of certain protocol-related procedures, scheduled visits, or hospital / clinic procurement of study medication. Nevertheless, with proper adjustments, some studies can be continued safely without loss of data integrity. In the following, we discuss safety and regulatory measures as well as logistical issues that should be taken into consideration when amending non-COVID-19 related clinical trial protocols during the COVID-19 pandemic (Table 6).

• Provide written and oral instructions on disease symptoms and signs and for the prevention of disease spread.
• Study participants, research and laboratory staff may need to monitor their temperature and check for symptoms and signs of the pandemic during participation in the trial and if entering the clinical research unit/workplace.
• Study participants, research and laboratory staff should frequently wash their hands with disinfectants, wear PPE (e.g., laboratory garments, gloves, face masks, eye protection), and clean work surfaces and equipment with appropriate disinfectants.
• Consider which visits can be conducted via remote solutions (phone check-ups, tele-consulting and monitoring) [36].
• Provide specific instructions on clinical trial unit procedures, particularly those that generate aerosols/droplets (e.g., sputum and nasal fluid collection, nasal and bronchial provocation testing). All isolations of peripheral blood mononuclear cells (PBMC) and bronchoalveloar lavages (BAL) should be performed in a BSL2 bench. For centrifugation steps, the use of closed beakers should be mandatory.
• Provide specific instructions for the collecting, handling and processing/testing of specimens from clinical trial participants.

Table 6: General consideration when amending non-COVID-19 related clinical trial protocols during the COVID-19 pandemic

Immediate contact is indicated with all involved parties - sponsor, institutional review board (IRB), institutional ethics committee (IEC), participants, investigators and staff -

as well as with all enrolled participants, to inform them of the changes related to the pandemic. All immediate actions should take place as long as the pandemic-related policies are in place and documented. Otherwiese, conventional amendments are required.

Essential non-COVID-19-related research can be continued safely during the COVID-19 pandemic while maintaining data integrity with appropriate amendments to the protocols. These adjustments should take into consideration modern technological communication tools (between hospital staff and patients), IP delivery, appropriate laboratory safety guidelines, and proper source (case report form (CRF)), statistical analysis plan and regulatory documentation (Figure 4).

INSERT: Figure 4 here

Figure 4: Ensuring data integrity in non-COVID-19-related research

Participant interactions:

In conducting non-COVID-19-related trials (i.e., in apparently non-infected individuals), the safety and well-being of the participants and hospital and research staff during physical interactions and specimen handling should be considered and risks evaluated. When possible and appropriate, remote options for participant visits using telemedicine or video consulting may facilitate the conduct of the clinical trial. Contact scripts to standardize messages are recommended. In general, these scripts do not require approval during lockdown. Study procedures that generate aerosols or droplets, such as spirometry or nebulization of agents or medication, may require special considerations on how to perform similar assessments safely or may need to be reconsidered. Staffing considerations should include the minimal essential personnel required to carry out study visits, and staff should be cross-trained and added to Delegation of Authority logs, as appropriate.

Regulatory guidance

Regulatory aspects of protocol amendments need to be considered [140, 141]. Changes to protocols after Institutional Review Board (IRB) approval are only allowed without prior approval in cases where there is a need to eliminate immediate hazards for the participants. Regulations allow protocol adjustments for participant safety and minimization of risks for data integrity in line with good clinical practice (GCP). In light of the COVID-19 pandemic, certain study visits or procedures may need to be paused or re-designed. This could facilitate ongoing research while maintaining safety and also allow time for evaluating the benefits of continuing investigational products for enrolled participants versus the disadvantages (harm incurred) of discontinuing. New strategies for safety assessments, monitoring, and data collection should be considered. Proper and detailed documentation of updates to procedures and operations is critical and protocol amendments should be communicated to research staff, participants, sponsors and regulatory agencies as soon as possible. Changes that may impact efficacy assessments, data management and/or statistical analysis plans should be discussed, when necessary, with the appropriate EMA-/FDA-division review. Records of all deferred procedures need to be kept and documented.

Investigational Product

Depending on the clinical trial, adjustments to investigational product (IP) administration may be possible with the use of telemedicine. These decisions must involve conversations with protocol chairs, sponsors, medical monitors and regulatory authorities as applicable. If participants are not able to come into the Clinical Research Unit (CRU), other options to continue IP intake include curb-side dispensing or direct shipping of pharmaceuticals. The research pharmacy staff should ensure that all local and federal regulations are followed with regards to the documentation and transport of study medication. In parallel, any necessary rescue medications should be provided to study participants, and documented with prior communication to relevant parties. Further guidance for the investigational product should be followed (table 7).

○ Treatment initiation and dose increases only performed in clinic; levels maintained at a stable dosage (e.g. for oral immunotherapy) when clinic visits not possible
○ Training of at-home administration of biologics and injectables, where applicable [9]

○ Ensuring participants maintain adequate IP supply to continue at-home dosing as needed without disclosing identity via research pharmacy (direct-to-participant shipments or curbside dispensing)
○ Ensuring integrity between pharmacy and participant in the case of shipping (secure chain of custody and monitoring of storage conditions in transit)
○ Necessary rescue medication provision with written instructions and emergency phone numbers

Table 7: General consideration on investigational products when performing a non-COVID-19-related clinical trial during the COVID-19 pandemic

Laboratory safety and precautions

Laboratory staff should follow Standard Precautions (SP) when handling clinical specimens, all of which may contain potentially infectious materials (see also section v) [71]). SP include hand hygiene and the use of PPE, such as laboratory coats or gowns, gloves and eye protection. All new arriving samples can be potentially infected. Isolations have to be performed with closed centrifuge beakers which will be loaded and unloaded under the biosafety cabinet. Material carriage should be performed with aerosol tight transport boxes. The usage of BSL2 benches for all arriving patient material is mandatory during and after the pandemic times. Handling of open vessels may only be performed inside of class II biosafety cabinets.

Antibody tests and procedures that utilize samples that are formaldehyde fixed or virus-inactivated, or those that concentrate viruses (via precipitation or membrane filtration), may be performed in a Biosafety Level 2 (BSL-2) laboratory. BSL-3 facilities and procedures are recommended for virus isolation in cell culture, initial characterization of viral agents recovered in cultures of SARS-CoV-2 specimens, and virus neutralizing antibody assays (Table 8). All work surfaces and equipment should be decontaminated with appropriate disinfectants.

Biosafety level 2 (BSL-2) precautions	Biosafety level 3 (BSL-3) precautions

○ Flow cytometry of formaldehyde-fixed specimens	○ Procedures with human or animal primary specimens to intentionally concentrate or isolate SARS-CoV-2 for research purposes (e.g., ultracen-trifugation of a sample)
○ Cell sorting with FACS Sorter has to be performed in the closed tube system. If a plate sort is necessary, the aerosol protection has to be used	○ Culturing specimens (e.g., propagated virus)
○ Assays with virus inactivated specimens	○ Preparatory work for *in vivo* activities
○ Concentration of samples prior to inactivation	○ Processing a culture (i.e., propagated or cultivated) known to contain SARS-CoV-2 for packaging and distribution to laboratories
○ Sample preparation for nucleic acid extraction, flow cytometry analysis, molecular testing of nucleic acids	○ Preparing inoculum, inoculating animals, and collecting specimens from experimentally infected animals.
○ Antigen and antibody assays	○ Virus neutralization tests for blocking activity against SARS-CoV-2 (with live virus)

Table 8: Laboratory procedures that may require different biosafety level precautions [71]

Conclusion: Clinical trials to combat the COVID-19 pandemic currently have top priority. However, a number of non-COVID-19 trials are also essential and should be continued if they can be conducted in a safe manner. Safety measures and new guidelines need to be established for participants, and research/laboratory staff dealing with non-COVID-19 related clinical trials to ensure the continuation of essential and critical non-COVID-19 trials.

Discussion

In view of the ongoing and emerging novel coronavirus (COVID-19) pandemic spreading worldwide [2], the safety and well-being of our patients, personnel, and colleagues globally are of primary importance. EAACI and ARIA are closely monitoring the situation. They recommend aligning any diagnostic and treatment operations with guidance from WHO [25] and ECDC [26], in accordance with all applicable national/regional/local government and public health authority requirements.

Allergists and other health care providers (HCPs) in the field of allergies and associated airway diseases are on the front line in taking care of patients potentially infected with SARS-CoV-2. Hence, strategies and practices to minimize risks for infection of both HCPs and the treated patients have to be developed and followed by allergy clinics [20]. This is especially important in high-risk patients for the course of a SARS-CoV-2 infection e.g. of older age or with comorbidities.

If patients are diagnosed with COVID-19 or are suspected to have COVID-19, they should follow the local area treatment and quarantine guidance. In general, most medications should be continued [88] [10]. Patients may be unable to attend clinic visits, have examinations and/or receive prescriptions. E-Health and telemedicine can assess the value of specialized treatments, provide education for self-management without the risk of infection [44], and triage patients for urgent in-person consultations. Examples for the latter are diagnostic testing in drug allergy in the case of suspicion of allergic reaction to highly necessary drugs [89] or the application of medication (e.g., SCIT or biologicals) through a HCP.

Clinic staff should keep in contact with the patient preferably through telephone calls or video conferences to maintain awareness of their status in the case of symptom exacerbations. Dispensing a sufficient amount of medication is a way of enabling the patient to self-treat. In treatment with biologicals, the decision to continue or discontinue a treatment should be made on a case-by-case basis by the attending physician, since the safety and efficacy of the mentioned biologicals in COVID-19 patients are currently unknown [9]. Besides, psychological care for patients with allergies during the COVID-19 pandemic is essential.

Non-COVID trials may be able to be continued according to regional regulations. However, special emphasis should continue to be placed on the safety of the participants and research/laboratory staff. The same safety precautions used in clinical routine for aerosol-generating procedures and handling of samples should also be applied in the non-COVID trials.

Conclusion

According to WHO and ECDC, patients at risk or with diagnosed COVID-19 should continue to be treated for all other diseases according to current guidelines, if there are no interferences of treatment with COVID-19 or vice versa. Preparedness of the allergy clinic, specialized centre or practice is imperative in order to cope with COVID-19 correctly. The recommendations in this Position Paper are conditional since there is a paucity of data. They should be revised regularly with new incoming information on COVID-19.

As doctors, scientists and specialist societies, we are required to observe our patients, to provide optimal advice and treatment based on the current state of medical knowledge, and to inform them accordingly when new evidence is available, making it possible to adapt the therapies. EAACI has a prevailing requirement to protect the safety and welfare of our patients, allergists and staff and is working diligently to ensure responses to new recommendations as quickly as possible.

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Alhabash S, Aleksic A, Aloulah M, Al-Qudah M, Alsaleh S, Baban MA, Baudoin T, Balvers T, Battaglia P, Bedoya JD, Beule A, Bofares KM, Braverman I, Brozek-Madry E, Richard B, Callejas C, Carrie S, Caulley L, Chussi D, de Corso E, Coste A, El Hadi U, Elfarouk A, Eloy PH, Farrokhi S, Felisati G, Ferrari MD, Fishchuk R, Grayson W, Goncalves PM, Grdinic B, Grgic V, Hamizan AW, Heinichen JV, Husain S, Ping TI, Ivaska J, Jakimovska F, Jovancevic L, Kakande E, Kamel R, Karpischenko S, Kariyawasam HH, Kawauchi H, Kjeldsen A, Klimek L, Krzeski A, Kopacheva Barsova G, Kim SW, Lal D, Letort JJ, Lopatin A, Mahdjoubi A, Mesbahi A, Netkovski J, Nyenbue Tshipukane D, Obando-Valverde A, Okano M, Onerci M, Ong YK, Orlandi R, Otori N, Ouennoughy K, Ozkan M, Peric A, Plzak J, Prokopakis E, Prepageran N, Psaltis A, Pugin B, Raftopulos M, Rombaux P, Riechelmann H, Sahtout S, Sarafoleanu CC, Searyoh K, Rhee CS, Shi J, Shkoukani M, Shukuryan AK, Sicak M, Smyth D, Snidvongs K, Soklic Kosak T, Stjarne P, Sutikno B, Steinsvag S, Tantilipikorn P, Thanaviratananich S, Tran T, Urbancic J, Valiulius A, Vasquez de Aparicio C, Vicheva D, Virkkula PM, Vicente G, Voegels R, Wagenmann MM, Wardani RS, Welge-Lussen A, Witterick I, Wright E, Zabolotniy D, Zsolt B, Zwetsloot CP, European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology 2020;58: 1-464.

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CONFLICT OF INTEREST :

Agache, Ioana

Dr. Agache reports : Associate Editor Allergy.

Akdiz, Cezmi

Dr. Akdis reports grants from Allergopharma, Idorsia, Swiss National Science Foundation, Christine Kühne-Center for Allergy Research and Education, European Commission's Horison's 2020 Framework Programme, Cure, Novartis Research Institutes, Astra Zeneca, Scibase, advisory role in Sanofi/Regeneron, outside the submitted work.

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Dr Ansotegui reports personal fees from Mundipharma, Roxall, Sanofi, MSD, Faes Farma, Hikma, UCB, Astra Zeneca, Stallergenes, Abbott, outside the submitted work.

Bachert, Claus

Dr. Bachert has nothing to disclose.

Bedbrook, Anna

Mrs Bedbrook has nothing to disclose.

Bonini, Matteo

Dr. Bonini has nothing to disclose.

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Dr Bosnic Anticevich reports grants from TEVA, personal fees from TEVA, AstraZeneca, Boehringer Ingelheim, GSK, Sanofi, Mylan, outside the submitted work.

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Dr. Brehler reports personal fees from ALK, Allergopharma, Astra Zeneca, Bancard, GSK, HAL, Leti, Merck, Novartis, Stallergenes, Takeda, Thermo fischer Novartis, other from ALK, Allergopharma, Novartis, Takeda, Bencard, Biotech Tools, Circassia, Genentech, Leti, outside the submitted work.

Breiteneder, Heimo

Dr. Breiteneder has nothing to disclose.

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Dr. Brough reports speaker fees from DBV Technologies and Sanofi and research support from ThermoFisher Scientific

Brussino, Luisa

Dr Brussino has nothing to disclose.

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Pr Canonica has nothing to disclose.

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Dr Carreiro-Martins has nothing to disclose.

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Dr. Chinthrajah reports grants from NIAID, CoFAR, Aimmune, DBV Technologies, Astellas, Regeneron, other from Alladapt, Genentech, Novartis, personal fees from Before Brands, outside the submitted work.

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Dr. Chivato has nothing to disclose.

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Dr Czarlewski has nothing to disclose.

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Dramburg, Stephanie

Dr. Dramburg has nothing to disclose.

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Fokkens, Wytske J

Dr. Fokkens has nothing to disclose.

Fonseca, Joao A

Dr Fonseca has nothing to disclose.

Fritsch, Hans-Walter

Mr. Fritsch has nothing to disclose.

Gawlik, Radek

Dr. Gawlik has nothing to disclose.

Gelincik, Asli

Dr. Gelincik has nothing to disclose.

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Dr. Gotua has nothing to disclose.

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Pr Haahtela has nothing to disclose.

Hoffmann-Sommergruber, Karin

Dr. Hoffmann-Sommergruber has nothing to disclose.

Hox, Valeri

Dr. Hox reports personal fees from Consultant work for ALK, outside the submitted work.

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Jutel, Marek

Dr. Jutel reports personal fees from ALK-Abello, personal fees from Allergopharma , personal fees from Stallergenes, personal fees from Anergis, personal fees from Allergy Therapeutics , personal fees from Circassia, personal fees from Leti , personal fees from Biomay, personal fees from HAL, during the conduct of the study; personal fees from Astra-Zeneka, personal fees from GSK, personal fees from Novartis, personal fees from Teva, personal fees from Vectura, personal fees from UCB, personal fees from Takeda, personal fees from Roche, personal fees from Janssen, personal fees from Medimmune, personal fees from Chiesi, outside the submitted work.

Klimek, Ludger

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Knol, E. F.

Dr. Knol has nothing to disclose.

Kuna, Piotr

Pr Kuna has nothing to disclose.

Kvedariene, Violeta

Dr Kvedariene has nothing to disclose.

Larenas-Linnemann, Desiree

Dr Larenas-Linnemann reports personal fees from Allakos, Amstrong, Astrazeneca, Boehringer Ingelheim, Chiesi, DBV Technologies, Grunenthal, GSK, MEDA, Menarini, MSD, Novartis, Pfizer, Novartis, Sanofi, Siegfried, UCB, Alakos, Gossamer, grants from Sanofi, Astrazeneca, Novartis, UCB, GSK, TEVA, Boehringer Ingelheim, Chiesi, Purina institute, outside the submitted work.

Latiff, Amir

Dr. Latiff has nothing to disclose.

Lauerma, Antti

Dr. Antti Lauerma has nothing to disclose.

Matricardi, Paolo

Dr. Matricardi has nothing to disclose.

Morais-Almeida, Mario

Dr. Morais-Almeida has nothing to disclose.

Mortz, Gotthard Charlotte

Dr. Mortz reports grants from Novartis, outside the submitted work.

Mullol, Joaquim

Pr Mullol has nothing to disclose.

Naclerio, Robert

Dr Naclerio reports personal fees from Sanofi, Regeneron, GSK, AstraZeneca, American Chemistry Council, Lyra, TASC, outside the submitted work.

Nadeau, Kari Christine

Dr. Nadeau reports grants and other from NIAID, FARE, Novartis, AnaptysBio, Adare Pharmaceuticals, Stallergenes-Greer, NHLBI, NIEHS, EPA, WAO Center of Excellence, Iggenix, Probio, Vedanta, Centecor, Seed, Immune Tolerance Network, NIH, Sanofi, Astellas, Nestle, BeforeBrands, Alladapt, ForTra, Genentech, AImmune Therapeutics, DBV Technologies; personal fees and other from Regeneron; grants from EAT, Allergenis, Ukko Pharma; personal fees from Astrazeneca, ImmuneWorks, Cour Pharmaceuticals, outside the submitted work; In addition, Dr. Nadeau has a patent Inhibition of Allergic Reaction to Peanut Allergen using an IL-33 Inhibitor pending, a patent Special Oral Formula for Decreasing Food Allergy Risk and Treatment for Food Allergy pending, a patent Basophil Activation Based Diagnostic Allergy Test pending, a patent Granulocyte-based methods for detecting and monitoring immune system disorders pending, a patent Methods and Assays for Detecting and Quantifying Pure Subpopulations of White Blood Cells in Immune System Disorders pending, a patent

Mixed Allergen Compositions and Methods for Using the Same pending, and a patent Microfluidic Device and Diagnostic Methods for Allergy Testing Based on Detection of Basophil Activation pending.

O'Hehir, Robyn

Prof O'Hehir has nothing to disclose.

Ohta, Ken

Pr Ohta has nothing to disclose.

Okamoto, Yoshitaka,

Dr. Okamoto has nothing to disclose.

Ollert, Markus

Dr. Ollert has nothing to disclose.

O'Mahony, Liam

Dr. O'Mahony reports personal fees from AHL, grants from GSK, outside the submitted work; .

Onorato, Gabrielle L

Dr. Onorato has nothing to disclose.

Palomares, Oskar

Dr. Palomares received research grants from Inmunotek S.L. and Novartis Ð'dOscar Palomares has received fees for giving scientific lectures from:Úllergy Therapeutics, Amgen, AstraZeneca, Diater,

GlaxoSmithKline, S.A, Inmunotek S.L, Novartis, Sanofi-Genzyme and Stallergenes and participated in advisory boards from Novartis and Sanofi-Genezyme.

Papadopoulos, Nikos G

Dr. Papadopoulos reports personal fees from Novartis, Nutricia, HAL, MENARINI/FAES FARMA, SANOFI, MYLAN/MEDA, BIOMAY, AstraZeneca, GSK, MSD, ASIT BIOTECH, Boehringer Ingelheim, grants from Gerolymatos International SA, Capricare, outside the submitted work.

Patella, Vincenzo

Dr. Patella has nothing to disclose.

Pfaar, Oliver

Dr. Pfaar reports grants and personal fees from ALK-Abelló, Allergopharma, Stallergenes Greer, HAL Allergy Holding B.V./HAL Allergie GmbH, Bencard Allergie GmbH/Allergy Therapeutics, Lofarma, ASIT Biotech Tools S.A., Laboratorios LETI/LETI Pharma, MEDA Pharma/MYLAN, Anergis S.A., grants from Biomay, Circassia, Glaxo Smith Kline, personal fees from Mobile Chamber Experts (a GA^{2}LEN Partner), Indoor Biotechnologies, Astellas Pharma Global, EUFOREA, ROXALL, NOVARTIS, SANOFI AVENTIS, Med Update Europe GmbH, streamedup! GmbH, outside the submitted work.

Regateiro, Frederico

Dr Regateiro reports personal fees from AstraZeneca, Novartis, Lusomedicamenta, Sanofi, GSK, outside the submitted work.

Rief, Winfried

Dr. Rief has nothing to disclose.

Riggioni, Carmen

Dr. Carmen Riggioni has nothing to disclose.

Samolinski, Boleslaw

Pr Samolinski has nothing to disclose.

Sampath, Vanitha

Dr. Sampath has nothing to disclose.

Skypala, Isabel

Dr. Skypala has nothing to disclose.

Schedlowski, Manfred

Dr. Schedlowski has nothing to disclose.

Suppli Ulrik, Charlotte

Dr. Charlotte Suppli Ulrik has nothing to disclose.

Toppila-Salmi, Sanna

Dr Toppila-Salmi reports grants from GSK, personal fees from ERT, Novartis, Sanofi Pharma, Roche, outside the submitted work.

Torres, Maria Jose

Dr. Torres has nothing to disclose.

Traidl-Hoffmann, Claudia

Dr. Traidl-Hoffmann reports grants and personal fees from Töpfer GmbH, Danone Nutricia, personal fees from Sanofi, La Roche Posay, Lilly Pharma, Novartis, grants from Sebapharma, Thermofischer, outside the submitted work.

Untersmayr-Elsenhuber, Eva

Dr. Untersmayr has nothing to disclose.

Valiulis, Arunas

Pr Valiulis has nothing to disclose.

Ventura, Maria Teresa

Dr Ventura has nothing to disclose.

Walusiak-Skorupa, Jolanta

Dr. Walusiak-Skorupa has nothing to disclose.

Wang DY,

Dr. Wang has nothing to disclose.

Yorgancioglu, Arzu

Pr Yorgancioglu has nothing to disclose.

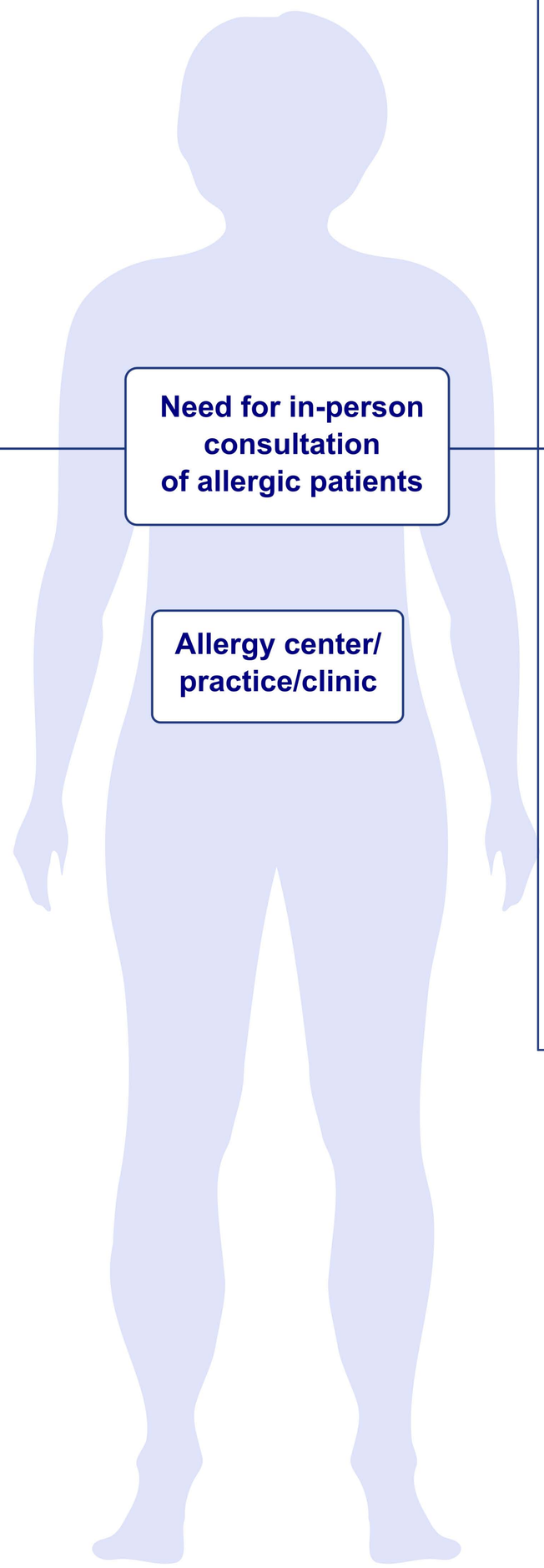
Zhang, Luo

Dr. Zhang has nothing to disclose.

Zuberbier, Torsten

Pr Zuberbier reports: Organizational affiliations: Commitee member: WHO-Initiative "Allergic Rhinitis and Its Impact on Asthma" (ARIA); Member of the Board: German Society for Allergy and Clinical Immunology (DGAKI); Head: European Centre for Allergy Research Foundation (ECARF); President: Global Allergy and Asthma European Network (GA^2LEN); Member: Committee on Allergy Diagnosis and Molecular Allergology, World Allergy Organization (WAO)

Pre-assessment for likelihood of COVID-19 ⟶ Triage accordingly



Need for in-person consultation of allergic patients

Allergy center/ practice/clinic

Asthma

- ACT <20
- Decrease in personal best PEF >20%
- Severe asthma
- Difficult to control asthma

Biologicals and subcutaneous AIT (SCIT) in non-infected patients*

Allergic rhinitis

- Severe symptoms (ARIA criteria)

Biologicals and subcutaneous AIT (SCIT) in non-infected patients*

Chronic rhinosinusitis

- VAS >7
- Suspicion for periorbital, endocranial and osseous complications

Biologicals and subcutaneous AIT (SCIT) in non-infected patients*

Atopic dermatits

- Involvement of large body surface areas
- Skin super-infection
- DD: Eczema herpeticum

Biologicals in non-infected patients*

Eosinophilic esophagitis

Complications like stictures, food impactions, malnutrition which require further workup

Food allergy

Anaphylactic episode

- Unknown elicitor
- First reaction
- Treatment plan and emergency training

OIT, EPIT

Complications which require workup such as EoE

Drug allergy

Anaphylactic episode

- No/few alternatives requiring challenge available
- Need for acute desensitization
- Urgent operation requiring workup based on history of drug allergy

Continuation of desensitisation protocol of the drug is needed and cannot be replaced

Vaccine allergy: vaccine application in a supervised setting in infants with a previous reaction

Venom allergy

Anaphylactic episode

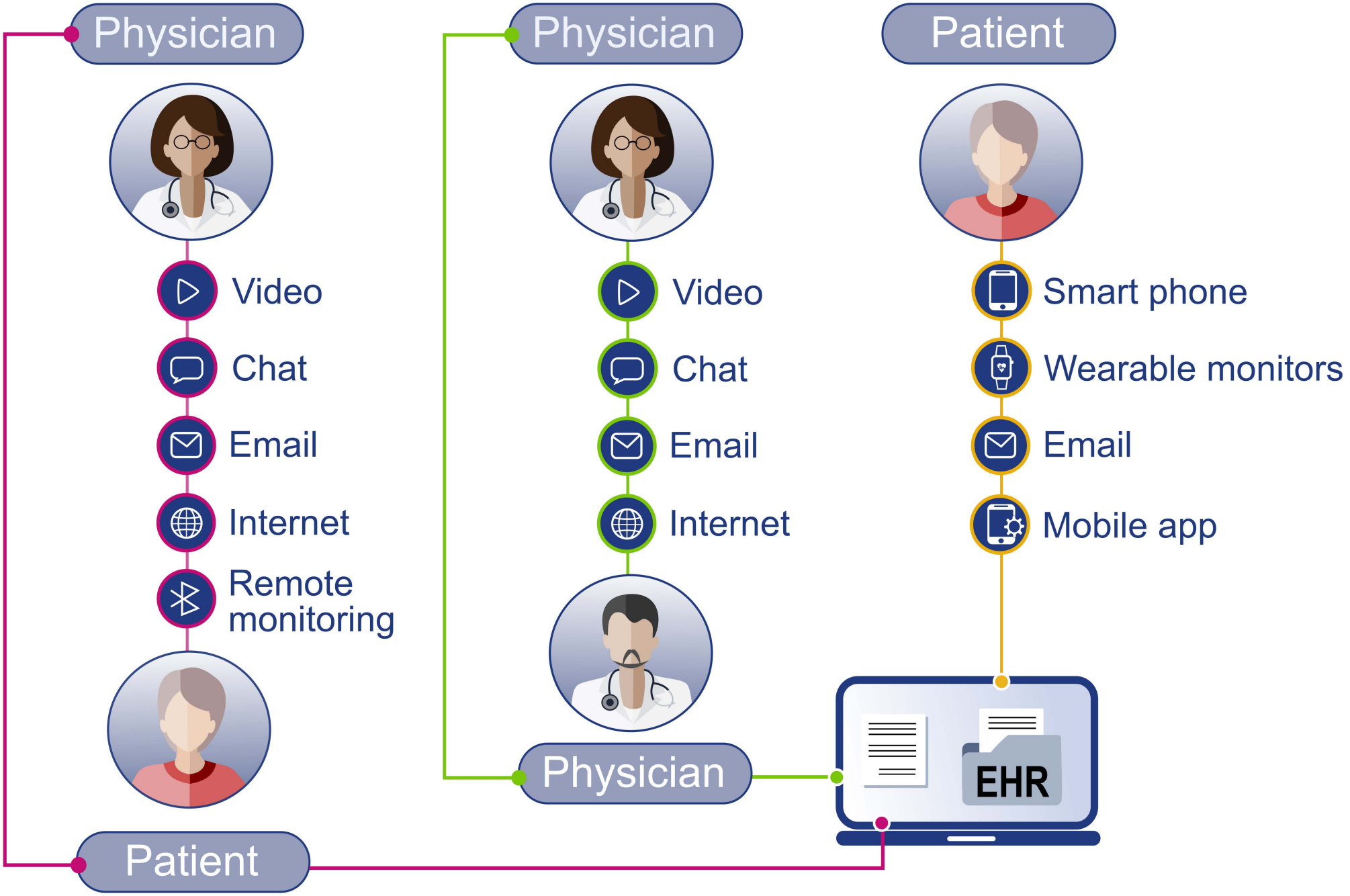
- Diagnostic confirmation
- Need for a rush-AIT early/pre-seasonal under special circumstances
- First reaction, epinephrine prescription, treatment plan and emergency training

Subcutaneous AIT (SCIT) in non-infected patients*

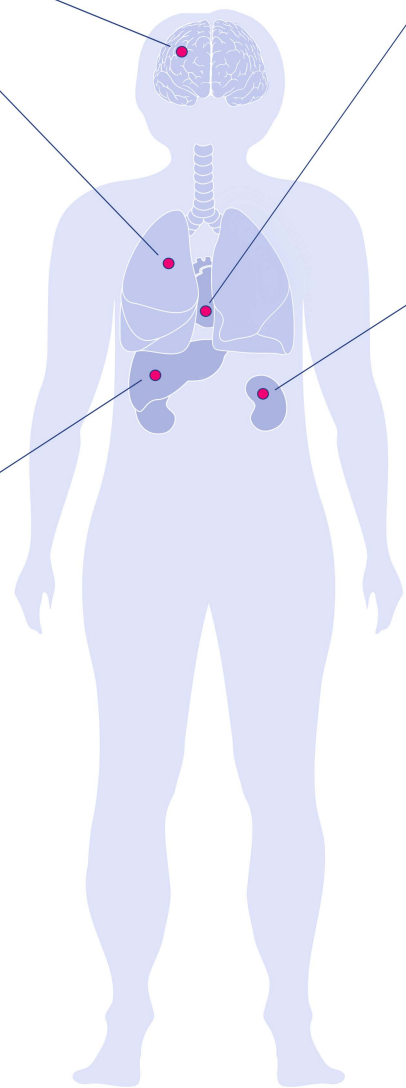
* some biologicals and sublingual immunotherapy can be administered at home (without supervision of physician), but these prerequisites a well-informed and compliant patient

Relevant for all diseases

- Consider severe psychological disturbance due to symptoms: evidence for socio-psychological impairment and suicide risk (section "Socio-psychological considerations for allergic patients and optimal care during and after the pandemic")
- Evidence for incorrect usage of prescribed medication and non-adherence, which requires in person training
- These recommendations are primarily for patients with severe clinical phenotypes who do not have the capacity to interact in a virtual setting


Physician
Video
Chat
Email
Internet
Remote monitoring
Patient
Physician
Video
Chat
Email
Internet
Physician
Patient
Smart phone
Wearable monitors
Email
Mobile app
EHR

Suggested follow-up test (on indication)



Mental health, CNS & psychosocial well being

Lungs
Respiratory system

- Spirometry/Peak flow
- Lung volume testing
- Diffusion test
- (FeNO)
- Chest imaging
- 6-minute walk test with O2 saturation monitoring

Liver
Liver system

- Liver function test
- Albumin
- Coagulation (PT, PTT, INR, thrombocytes)

Endocrinology system

- Hormonal balance
- Attend to weight and nutrition
- Blood sugars and gastric protection if on oral corticosteroids

Heart
Cardiovascular system

- Electrocardiogram
- Echocardiography
- Holter monitoring
- Exercise test

Kidney
Renal system

- Kidney function
- Electrolytes
- Urinanalysis

Immune cells & inflammation
Immune system

- Lymphocytes, eosinophils
- Consider following inflammatory markers for trend to resolution: CRP, ESR, d-dimer, fibrinogen

Skin
Dermatology

- Skin exams for resolution of rashes or thrombotic events

Patient interactions

Product delivery

Lab safety

Documentation