



Schweizerische Gesellschaft für Notfall- und Rettungsmedizin  
Société Suisse de Médecine d'Urgence et de Sauvetage  
Società Svizzera di Medicina d'Urgenza e di Salvataggio  
Swiss Society of Emergency and Rescue Medicine

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The German version is the root version

## Prehospital triage and care under resource scarcity in the hospital sector (particularly in intensive care) during the COVID-19 pandemic

***Recommendations from the Swiss Society of Emergency and Rescue Medicine SSER***

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The following text is meant to be gender neutral.

## 1 Situation

The current COVID-19 pandemic has placed Switzerland in an extraordinary situation.<sup>1</sup> In the hospital sector, various measures are being taken to cope with the influx of patients (restriction of elective procedures,<sup>2</sup> transfer of patients to Intermediate Care (IMC) units, increase in ventilator-equipped beds, avoidance of personnel-intensive treatments).<sup>3</sup> As soon as the additional resources made available are exhausted, not all patients can be provided with the treatment they need.

In this COVID-19 pandemic, the bottleneck arises in Intensive Care Units (ICU) in particular. Prehospital patient care, as well as the transport sector, is strained by the necessary protective measures. Adequate primary care of the critically ill is still possible, however, the limitations for follow-up treatment must be considered. Accommodating these patients in the hospitals most appropriate for their given condition(s) is severely limited.

The Swiss Society of Intensive Care Medicine (SSICM), together with the Swiss Academy of Medical Sciences (SAMS), has adopted (20.3.2020) amendments to chapter 9.3 of the SAMS Guideline for Intensive Care Interventions (2013).

This guideline describes the criteria and the process of assigning patients to an intensive care unit. It distinguishes between two stages: **Stage A:** intensive care beds ARE available, but capacity is limited (→ admission-triage) and **Stage B:** intensive care beds ARE NOT available (→ resource management through decisions on discontinuation of treatment). Even if it is not presently clear how these stages will be authorized, or if these stages will be a result of the reality, SSERM considers it important to support this concept of stages in the sense of a «unité de doctrine».

In a situation of resource scarcity, applying comparable criteria for all of Switzerland is not only important for admission to and remaining in an ICU, but is also central for the decision-making process in the prehospital phase. This concerns the extent of prehospital interventions and measures, especially the choice of destination hospital.

Due to the current circumstances, these recommendations have been written under great time pressure. They will be adapted if experience in practice and new scientific findings so require.

## 2 Applicability

The following recommendations are applicable when there is a scarcity of resources in hospitals (places in ICUs) that cannot be bridged either nationally or with the support of neighbouring countries and one of the stages mentioned under → 1 is present:

- **Stage A:** ICU beds ARE available, but capacity is limited
- **Stage B:** ICU beds ARE NOT available.

The rationing decisions affect all patient categories (COVID-19 infected patients to the same extent as other patients), which in the prehospital phase necessitates dispatch of an emergency doctor or, in regions where this service is unavailable, indicates that this patient requires intensive care.

The present recommendations are based on the following published SAMS guidelines: *Intensive Care Interventions (2013); Amendments to chapter 9.3 of the SAMS Guideline for Intensive Care Interventions (20.3.2020); Decisions on Cardiopulmonary Resuscitation (2017)*.

### **3      Fundamental ethical principles**

The fundamental principles of medical ethics are taken from the above-mentioned SAMS guideline:<sup>4</sup> "The four widely-recognized principles of medical ethics (beneficence, non-maleficence, respect for autonomy and equity) are also crucial under conditions of resource scarcity".

Other relevant points are:<sup>5</sup>

- **Early knowledge of patient's wishes** with regard to emergency treatment and intensive care. No treatment if a patient does not wish to receive it.
- **Equality**  
Justified equal treatment: age, sex, residence (town/country), regional hospitalization structure (central hospital/cantonal hospital/regional hospital), nationality, ethnicity, religious affiliation, social status, insurance status, chronic disability.  
The allocation procedure must be fair, objectively justifiable and transparent so that arbitrary decisions can be avoided.
- **Preserving as many lives as possible**  
Objective: decisions should be made in such a way that as few people as possible become severely ill or die.
- **Protection of the professionals involved**  
Involved professionals should be protected from infection and also from excessive physical and psychological stress. Those belonging to a risk group with regard to COVID-19 should especially be protected. If intensive care patients are transferred between institutions for reasons of resource allocation, it would be preferable to transfer patients not infected with COVID-19.

### **4      Considerations regarding prehospital primary care of patients under resource scarcity in hospital ICUs**

- As long as sufficient resources are available, the regular algorithms and "state-of-the-art" supply concepts apply. In case of imminent or existing regional scarcity of resources in the hospital sector, the **supra-regional and not the local conditions apply**, as long as transport capacities are available. Clarification of bed capacity in the hospital sector is carried out via the SNZ (emergency call centre) using the IES (information and deployment system) of the CMS (coordinated medical services).<sup>6</sup> As a back-up, the various emergency call centres (SNZ) dynamically exchange information on the number of intensive care beds still available and the personnel capacity, particularly in the emergency units, via a common platform/hotline etc. In this way, the SNZ provides logistical support to the teams on site. This requires active communication between the hospitals with their responsible emergency call centres.
- Prehospital patient evaluation, respectively triage, must be carried out individually according to valid medical criteria.<sup>7</sup> It is important that prehospital care on site and during transport is oriented to the needs and requirements of the patient. However, restrictions in the hospital sector influence decisions regarding the destination hospital (→ 5).
- Chronological age *per se* is not a main criterion that can be used in the decision-making process. It accords less value to older than to younger individuals (→ 3). Age, however, is indirectly taken into account under the main criterion "short-term prognosis".<sup>8</sup>

- COVID-19 positive patients are treated in the same way as those who are COVID-19 negative provided self-protection is guaranteed.
- In allocating the destination hospital, a supra-regional view is fundamental. It is not only necessary to minimize the time lost in caring for the patient, but also to take into account overstretched hospital structures and to avoid secondary transport<sup>9</sup> (→ 5 Stage B).
- Critically ill patients who cannot be assigned to a hospital that corresponds to the appropriate category of care in a normal situation must be treated as well as possible when assigned to a subordinate hospital category. In a palliative situation, adequate care can be provided, if necessary, in cooperation with a responsible general practitioner, thus, potentially avoiding hospitalization.
- The information available in the prehospital setting is often minimal or even contradictory. Diagnostic options are very limited. In addition, the prehospital patient's condition, (particularly in the context of hypotension, hypothermia, intoxication, etc.) can both very dynamically improve and worsen. Therefore, serious and fair decisions can only be made at a later point in time, if at all, by obtaining additional information. For these reasons, critically ill or injured patients almost always must be brought to an emergency ward even if there is a known lack of ICU capacity.
- Frailty is a relevant prognostic factor in critically ill patients. The prehospital setting often allows the opportunity to obtain objective parameters regarding frailty of a patient from patients themselves or from their relatives. After admission to the hospital, this may be more difficult due to deterioration of the patient or inability to contact the responsible next of kin. Frailty-Scores are typically validated for people > 65 years and should reflect the patient status in the period before the acute deterioration.

## 5 Triage

### 5.1 Principles

If there is an existing scarcity of resources, Stage A or Stage B, the below-mentioned considerations and criteria (→ 5.3.1 and 5.3.2) should be taken into account with regard to prehospital care.

These considerations and criteria relate to the initiation of care facility measures, to their omission, or to possible discontinuation of interventions that have already been started. In principle, in this situation, which is similar to a prehospital mass influx of patients, the initiation of interventions with a very poor prognosis must be critically reviewed.<sup>10</sup>

In justified cases, the proposed limitations can and should be waved despite a major shortage of resources in the hospital sector.

The considerations and criteria relating particularly to all facilities providing in-hospital medical treatment (**hospitalization zone**): Patients who under normal conditions would be admitted to maximum care centres, may not be able to receive this optimal care if resources are scarce. The aim, from a collective perspective, is to maximize benefits for all patients.<sup>11,12</sup>

The decision to admit a patient to a destination hospital with an less than sufficient level of care (→ 5), must be made by a physician (emergency doctor/GP on emergency duty) and be documented accordingly.

## 5.2 Definitions

### 5.2.1 Resource stages

- Resource scarcity Stage A: ICU beds ARE available, but capacity is limited
- Resource scarcity Stage B: ICU beds ARE NOT available

### 5.2.2 Destination hospital categories

(Classification of destination hospitals according to categories of care in accordance with the Swiss Task Force on the *New Triage Tag / Patient Tracking System ("neues PLS")*)<sup>10</sup>

- $H_{Base}$  Regional or cantonal hospital without ICU and/or without own blood bank
- $H_{Intens}$  Hospital with ICU, 24hr OR-/lab/x-ray facilities, own blood bank (limited capacity for artificial blood products)
- $H_{Max}$  University hospital/maximum-care hospital (e.g. trauma centre)

## 5.3 Recommendations

### 5.3.1 Scarcity of resources, **Stage A**

The following considerations and criteria should be considered:

- **Advance directive** (living will, etc.) with patient's wishes: do not resuscitate (DNR)/no mechanical ventilation/no intensive care treatment
- **Resuscitation measures in case of cardiac arrest**
  - Do NOT take any steps in case of:
    - cardiac arrest without effective resuscitation measures for more than 10 minutes
    - asystole or pulseless electrical activity (PEA) as initial rhythm
    - known severe comorbidities and/or poor health status prior to cardiac arrest
    - specific circumstances of cardiac arrest with poor prognosis (e.g. polytrauma, strangulation)
  - Resuscitation:
    - start in case of witnessed collapse (self-observed, by a bystander) with immediately initiated resuscitation measures
    - continue with shockable rhythm up to max. 4 cycles (= 10 minutes)
    - without return of spontaneous circulation (ROSC), resuscitation must be interrupted on site. No patient with ongoing resuscitation should be brought to a trauma bay or resuscitation room
  - ROSC: Hospitalization →  $H_{Intens}$  /  $H_{Max}$  with PTA-option
- **Other invasive measures**
  - Restrained use of endotracheal intubation (ETI)  
ETI may still be necessary in specific situations, e.g.:
    - suspected acute epidural haematoma in therapeutic time interval
    - mid-facial fracture with acute threat of suffocation
    - anaphylaxis with acute threat of airway obstruction
  - Restrained use of mechanical resuscitation systems (Autopulse®, Lucas®, etc.)
  - No prehospital usage of extracorporeal cardiopulmonary resuscitation (eCPR) systems

- **Choice of destination hospital**
  - In the phase with only very limited intensive care resources, supra-regional allocation is of maximum importance. For as long as possible, the hospital category should correspond to the patient's care needs
  - Restrictive hospitalization in categories  $H_{Max}/H_{Intens}$  in cases of poor long-term prognosis, e.g.
    - known metastatic oncological disease
    - known neurodegenerative disease in the final stage, severe dementia
    - clear indications of an irreversible, central-neurological impairment
    - home oxygen therapy<sup>13</sup>
    - Clinical Frailty Scale score  $\geq 6$ <sup>14</sup>
- **Choice of alternative care/support options**

It should be considered whether adequate care can be provided at the place of residence (at home/in an institution) with the help of established primary care providers and "Spitex"/other care services. It is important to ensure that at least palliative measures are guaranteed.

If this form of care cannot be provided or cannot be provided within a reasonable period of time, the patient is allocated to a destination hospital of the category  $H_{Base}$ .

### 5.3.2 Scarcity of resources, **Stage B**

In the event that ICU capacity is totally overloaded, the short-term prognosis is decisive for prioritizing interventions as well as for allocating the destination hospital category. This means that the prehospital measures and consecutive hospital interventions either on their own or together with intensive treatment, of only a short duration, stabilize the condition and a good outcome can be expected. The long-term prognosis is already taken into account in the proposed catalogue of criteria (→ 5.3.1).

For most **trauma patients**, prehospital decisions should primarily focus on surgical-operative care. This also applies to **burn victims** with a non-fatal prognosis. The extent of the burn surface can usually only be validly estimated after evaluation by experienced surgeons. If necessary, until the patient is stabilized, respiratory assistance can be provided by anaesthesiologists without the need for intensive care.

In addition to the criteria already mentioned under Stage A, the following restrictions are recommended:

- **Invasive measures**
  - **Extreme restraint** for endotracheal intubation (ETI)
  - **No use of** mechanical chest compression devices (Autopulse®, Lucas®, etc.)
- **Choice of destination hospital**

In the stage (Stage B) where national (including bordering countries) intensive care resources are no longer available, allocation of a patient with an unquestionable need for intensive care, leads to an enormous burden for the responsible teams in emergency and ICUs, as this additional patient must be carefully considered against the already selected intensive care collective. This results in the following recommendations for the selection of hospitalization category:

  - Extremely restrictive hospitalization in  $H_{Max}/H_{Intens}$
  - No assignment to  $H_{Max}/H_{Intens}$ : Age  $>85$  years and mandatory ventilation

- No hospital admission in cases of a Clinical Frailty Scale score  $\geq 5$ , if alternative care/support options are available
- Consider a reduction in the level of care ( $H_{Max} \rightarrow H_{Intens}$  resp.  $H_{Intens} \rightarrow H_{Base}$ )
- Ultimately, allocation to the appropriate hospital is carried out according to cantonal/regional guidelines, reported to the respective (SNZ) emergency call centre (cantonal doctor, COVID-19 task force of the hospitals involved). Ideally, the hospitals are served sequentially in order to distribute the enormous burden on the responsible emergency and ICU teams.

## 6 Decision-making procedure

- When making triage decisions, trust must be maintained despite the most difficult circumstances. For this reason, rationing criteria must be fair, and applied decisions must be transparent at all times. Clear reasons for granting or not granting priorities must be documented. Deviations from the defined criteria must be permissible and must be documented accordingly.
- Triage decisions with rationing elements that have a direct impact on the patient's quality of care require great professional competence. Emergency physicians deployed in Switzerland are often still in the training phase for the qualification in Prehospital Emergency Medicine/Emergency Physician SSERM. The supplementary guidelines to chapter 9.3 of the *SAMS Guidelines on Intensive Care Interventions* (20.3.2020) adopted by the SAMS-SSICM requires that the decision-making process must be under the direction of experienced personnel. In order to ensure that this seniority can also be guaranteed during the prehospital phase, the medical director (or designated medical team) of the emergency services should be consulted by telephone if possible in the event of uncertainty regarding the triage decisions mentioned in → 5. If an on-site assessment is necessary, incident command emergency physicians, if necessary, can provide a back-up function and support the medical directors of the emergency rescue services, provided they are not deployed in their actual function. If none of the above options is available, the support of the prehospital teams must be arranged by the SNZ 144 (emergency call centre) responsible for their area (at least a telephone consultation with an experienced physician).
- Whenever possible, decisions must be made within the interprofessional team.
- Mechanisms must be provided for the subsequent resolution of conflicts.

## 7 Secondary transport

In the extraordinary circumstance of the COVID-19 situation, the resource bottleneck is in the ICU sector of the hospital rather than in the prehospital field where it usually is. The mass influx of patients is currently affecting ICUs, therefore, in order to allow a fair allocation of resources, in solidarity with the entire population of Switzerland, secondary transport remains necessary.

So that self-protection of the professionals involved, as mentioned under → 3, is respected as far as possible, primarily non-COVID-19 patients requiring intensive care should be transferred to other hospitals.

## 8 References

<sup>1</sup>Verordnung 2 des Bundesrats über Massnahmen zur Bekämpfung des Coronavirus (COVID-19) vom 13. März 2020 (Fassung vom 16. März 2020), sich auf Artikel 7 des Epidemiengesetzes abstützend. Dieser Artikel regelt die Ausserordentliche Lage. Art 10a Abs. 2. verfügt, dass Gesundheitseinrichtungen wie Spitäler und Kliniken, Arztpraxen und Zahnarztpraxen auf nicht dringend angezeigte medizinische Eingriffe und Therapien verzichten müssen. <https://www.admin.ch/opc/de/official-compilation/2020/783.pdf>; last accessed: 22.3.2020

<sup>2</sup>Erläuterungen zur Verordnung 2 des Bundesrates vom 13. März 2020 über Massnahmen zur Bekämpfung des Coronavirus (COVID-19-Verordnung 2), Fassung vom 20. März 2020: <https://www.bag.admin.ch/bag/de/home/krankheiten/ausbrueche-epidemien-pandemien/aktuelle-ausbrueche-epidemien/novel-cov/massnahmen-des-bundes.html>; last accessed: 22.3.2020

<sup>3</sup>Bundesgesetz über die Bekämpfung übertragbarer Krankheiten des Menschen (Epidemiengesetz, EpG) vom 28. September 2012 (Stand am 1. Januar 2017) <https://www.admin.ch/opc/de/classified-compilation/20071012/index.html#a7>; last accessed: 23.3.2020

<sup>4</sup>COVID-19-Pandemie: Triage von intensivmedizinischen Behandlungen bei Ressourcenknappheit. Hinweise zur Umsetzung Kapitel 9.3. der SAMW-Richtlinien Intensivmedizinische Massnahmen (2013). [www.samw.ch/de/corona](http://www.samw.ch/de/corona). last accessed: 23.3.2020

<sup>5</sup>Bundesamt für Gesundheit (BAG). Influenza-Pandemieplan Schweiz, Strategien und Massnahmen zur Vorbereitung auf eine Influenza- Pandemie, 5. Auflage 2018, Kap. 6.1. sowie insb. Teil III «Ethische Fragen des Influenza-Pandemieplan Schweiz 2006», Stellungnahme der Nationalen Ethikkommission NEK-CNE Nr. 12/2006. <https://www.bag.admin.ch/dam/bag/de/dokumente/mt/k-und-l/hygiene-pandemiefall/influenza-pandemieplan-ch.pdf.download.pdf/bag-pandemieplan-influenza-ch.pdf>. last accessed: 23.3.2020

<sup>6</sup>Informations- und Einsatz-System (IES) des Koordinierten Sanitätsdiensts. <https://www.vtg.admin.ch/de/organisation/astab/san/ksd/mehr-zum-ksd/ueber-den-ksd.html#informations-und-einsatzsystem-ies>. last accessed: 23.3.2020

<sup>7</sup>Consistency of Triage in Victoria's Emergency Departments Guidelines for Triage Education and Practice. July 2001, ISBN 0 7326 3006 1

<sup>8</sup>Murthy S, Gomersall CD, Fowler RA. Care for critically ill patients with COVID-19. JAMA published online, March 11, 2020. <https://jamanetwork.com/journals/jama/fullarticle/2762996>

<sup>9</sup>Totondo MF et al. Resources for optimal care of the injured patient. Committee on Trauma. American College of Surgeons; 2014

<sup>10</sup>Arbeitsgruppe neues PLS Schweiz (2019). Gebrauchsanweisung PLS Schweiz, Ittigen Geschäftsstelle KSD.

<sup>11</sup>Persad G, Wertheimer A, Emanuel EJ. Principles for allocation of scarce medical interventions. Lancet 2009; 373: 423–31. [https://doi.org/10.1016/S0140-6736\(09\)60137-9](https://doi.org/10.1016/S0140-6736(09)60137-9)

<sup>12</sup>Biller-Andorno N, Monteverde S, Krones T, Eichinger T (Ed). Medizinethik. Grundsätze für die Allokation knapper medizinischer Interventionen. Springer 2020. ISBN 978-3-658-27696-6

<sup>13</sup>Bagshaw SM et al. Association between frailty and short- and long-term outcomes among critically ill patients: a multicenter prospective cohort study. CMAJ 2014; 186:E95

<sup>14</sup>Lee KC, et al. Defining serious illness among adult surgical patients. J Pain Sympt Manage 2019; 58:844

## **9      Information on the preparation of these recommendations**

### **Authors**

PD Dr. med. Mathias Zürcher, SGNOR, SZRNK (Head)  
Dr. med. Thomas von Wyl, SGNOR  
Dr. med. Kaspar Meier, SGNOR  
Prof. em. Dr. med. Wolfgang Ummenhofer, SGNOR

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The authors have no financial or personal conflicts of interest to declare.

### **Correspondence address**

PD Dr. med. Mathias Zürcher  
Member of the board SGNOR  
Head Swiss Center for Rescue, Emergency and Disaster Medicine (SCRED)  
Department for Anesthesia, Prehospital Emergency Medicine and Pain Therapy  
University Hospital Basel  
Spitalstr. 21  
CH-4031 Basel

[mathias.zuercher@sgnor.ch](mailto:mathias.zuercher@sgnor.ch)  
Tel.: +41 31 332 41 11

## **10     Appendix**

- 1       Short version SSERM COVID-19 recommendations incl. algorithm
- 2       Clinical frailty scale

# COVID-19: Prehospital triage and care under resource scarcity in the hospital sector

Summary of the SSERM recommandations of 06.04.2020 (original text: <https://www.sgnor.ch/home/covid-19>)

## Fundamental ethical principles

- **Ascertain the patient's wishes at an early stage** with regard to emergency treatment and intensive care.  
Do not employ treatments, which a patient does not want to receive.
- **Equality = equal treatment**  
Distribution of resources must be fair, objectively justifiable and transparent: no arbitrary decisions
- **Preserve as many lives as possible:** collective point of view!
- **Protection of the professionals involved** from infection, but also from physical and psychological stress

## Considerations on prehospital primary care of patients during COVID-19 pandemic

- Bottleneck mainly in intensive care, not in prehospital setting
- Adequate primary care of critically ill patients is still possible
  - consider the limited possibilities for follow-up treatment
- Patient care and transport sector are strained by necessary protective measures
- With increasing difficulty in accommodating patients, supra-regional and not local conditions are decisive as long as transport capacity is available
- **COVID-19 patients** are treated the same as **Non-COVID-19 patients**
- Total overload of ICU capacity (Stage B, see page 2)
  - Best possible treatment in a subordinate category of hospital
  - In a palliative situation consider cooperation with patient's GP / organized home care → avoid hospitalization

### ATTENTION:

- » available prehospital information is often minimal or even contradictory.
- » diagnostic possibilities are limited.
- » patient's condition is initially often masked and dynamic: hypotension, hypothermia, intoxication....
  - Serious decisions are often possible only later with additional information/ diagnostic findings.
  - Hospitalization on an emergency ward is often necessary despite lack of intensive care capacity.

## Decision-making procedures

Faith in the health system must be maintained despite necessary triage decisions, therefore:

- fair criteria for rationing
- transparent procedures
- documentation of reasons for granting or not granting priorities

### IMPORTANT:

- » Deviations from defined criteria
  - o must be possible
  - o must be documented
- » Decision-making → within interprofessional team, if possible
- » Conflicts → provision of mechanisms for subsequent resolution of conflicts

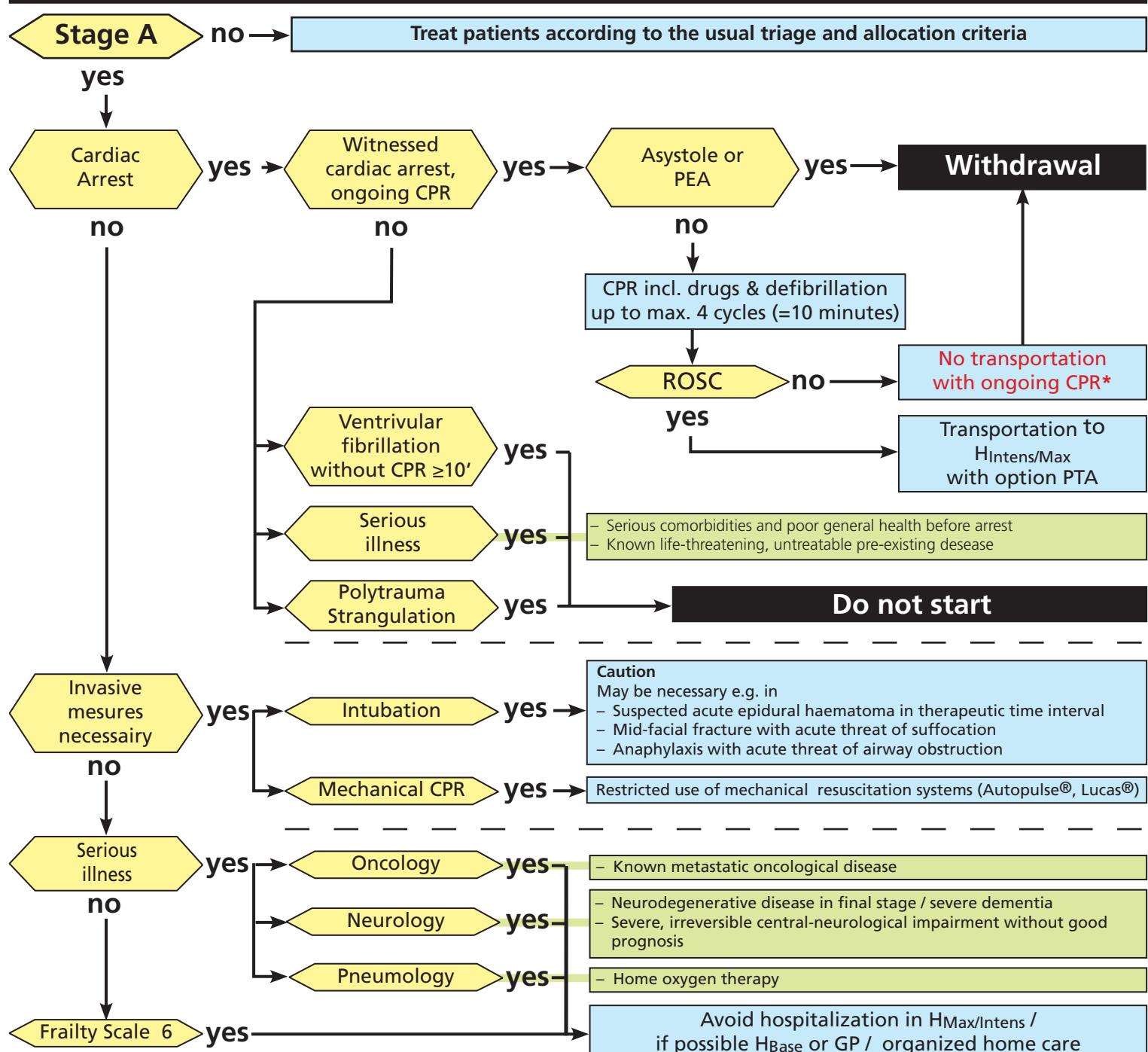
## Secondary transfer

- Fair allocation of resources for patients and solidarity-based protection of overburdened hospital structures → use transport capacities as long as possible
- Reduce danger for professionals involved / ensure functionality of rescue equipment
  - first and foremost, transfer Non-COVID-19 patients needing intensive care.

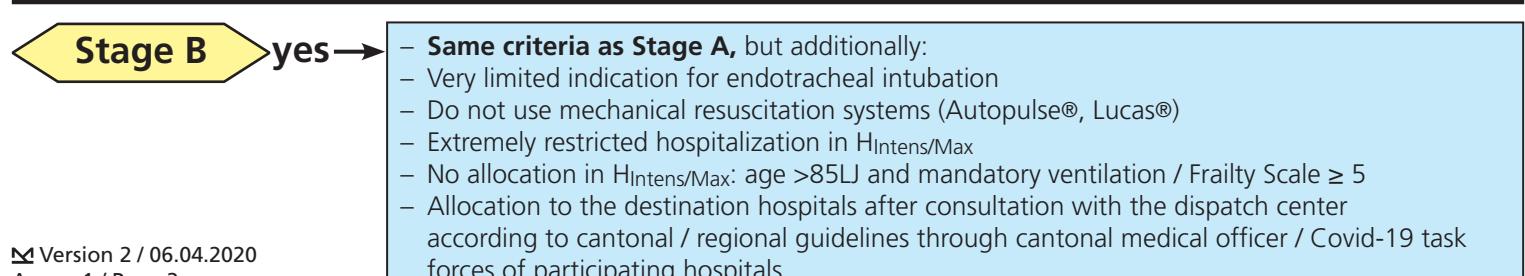
# COVID-19: Prehospital triage and care under resource scarcity in the hospital sector

Summary of the SSERM recommendations of 06.04.2020 (original text: <https://www.sgnor.ch/home/covid-19>)

- These recommendations only apply if a scarcity of resources in ICUs has been declared as follows:
  - Stage A: Beds available, but limited capacity**
  - Stage B: No ICU beds available**
- Categories of destination hospitals:
  - H<sub>Base</sub>** Regional hospital, cantonal hospital without ICU resp. own blood bank
  - H<sub>Intens</sub>** Hospital with ICU, 24hr OR/Lab./ x-ray facilities, own blood bank
  - H<sub>Max</sub>** University hospital/ maximum care hospital (e.g. trauma centre)
- Allocation decisions in consultation with dispatch centre according to cantonal/regional guidelines:
  - Supra-regional allocation must be taken into account
  - National capacity according to the national information and deployment system is decisive.
- Triage in situation without emergency physician → in consultation with experienced staff physician.



\* **Exception:** special cases like hypothermia, persistent ventricular fibrillation, see page 1



## Clinical Frailty Scale\*



**1 Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.



**2 Well** – People who have no **active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally** (e.g. seasonally).



**3 Managing Well** – People whose **medical problems are well controlled**, but are **not regularly active** beyond routine walking.



**4 Vulnerable** – While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being “slowed up” and/or being tired during the day.



**5 Mildly Frail** – These people often have **more evident slowing**, and need help in **high-order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.



**6 Moderately Frail** – People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.



**7 Severely Frail – Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~6 months).



**8 Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a mild illness.



**9 Terminally III** – Approaching the end of life. This category applies to people with a **life expectancy <6 months**, who are **not otherwise evidently frail**.

### Scoring Frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

\*1. Canadian Study on Health & Aging, Revised 2008.

2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005; 173: 489-495.

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