Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

survival and of recovering from the infection, if provided the treatment under discussion. This criterion was that previously adopted in the case of school of the conjoined twins Mary and Jodie.[9] Separation was required to prevent the death of both but was certain to cause the death of the weaker twin. The England and Wales Court of Appeals considered prevailing the interest of Jodie because Marie was self-designated for a very early death.

We are aware that even case-by-case criteria cannot ultimately avoid discrimination, for example, when dealing with patients with similar chances of recovery. In such cases, inevitably the "first-come, first-served" rule is in force, a seemingly impersonal fact that is not, however, a value judgment.

A case-by-case approach that depends on chance of recovery avoids a priori categorization, providing health operators with objectifiable, medical criteria. Therefore, it has universal value, freeing physicians from the burden of conscience and exposure to possible legal ramifications, as well as freeing legislators from making partisan decisions. Furthermore, it could help patients and families better comprehend the medical choices to which they are subjected.

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The COVID Grim Reaper

To the Editor:

The articles "COVID-19 in Italy: Ageism and decision making in a pandemic" by Cesari and Proietti[1] and "The geriatrician: The frontline specialist in the treatment of COVID-19 patients - Gemelli against COVID-19 Geriatrics Team" by Landi et al.[2] clearly discuss the topics to be considered to best manage the care of sick older individuals in COVID-19 outbreaks.

Multimorbidity, frailty, physical disability and cognitive impairment, and alterations of the biological background all may play an additional role in worsening the prognosis and increasing the risk of adverse outcomes more than the mere number of years lived.

Whatever the causes, the mortality rate in older patients is remarkably high: in our hospital located in Brescia, in the region of Lombardy (the area with the highest rate of SARS-CoV-2 infection and death in Italy), in patients older than 80 the mortality rate is 54%, in patients older than 85 the mortality rate is 75%, and in those with severe to terminal dementia [Clinical Dementia Rating (CDR3) to CDR5] the mortality rate is 100%.

The use of cutpoints based on chronological age as guidance of clinical decision of treatment may put most older patients at risk for second-class care, but very old patients in the COVID-19 pandemic have a negligible survival hope; they are "de facto" a doomed population.

A community that abandons their older citizens is a hateful community; if we want to save older lives we must absolutely avoid COVID-19 infection. COVID-19 infection for an aged person is the "Grim Reaper," and age should therefore be taken into account mainly to incentivize an obligation toward prevention.

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Plasma Therapies and Parabiosis in the COVID-19 Era

To the Editor:

A novel coronavirus (SARS-CoV-2), likely spilled over from bats, is causing a nightmarish global pandemic and has ignited a worldwide race for the discovery of effective therapies against COVID-19. The disease severity and lethality are clearly higher in older adults, with notable sex-specific differences. The impact of age on COVID-19 outcomes is reflected by case fatality rates in older patients being up to 100-fold higher than in infants.[1] At all ages, men are more severely affected than women.[1] An ageism-guided reallocation of medical resources to prioritize assistance of younger patients may contribute to the excess mortality in older citizens.[2] Yet, the combined effect of age and gender on COVID-19–related morbidity and mortality mirrors what is commonly encountered in aging research and in major chronic diseases.

According to the geroscience paradigm, some molecular pathways, collectively called "hallmarks of aging," underpin age-related

derangements in physiological systems and cellular processes.[3] Noticeably, these pillars of aging are also involved in the pathogenesis of conditions that increase COVID-19 severity and lethality (e.g., hypertension, cardiovascular disease, diabetes). Geroprotective treatments targeting inner mechanisms of aging might therefore be exploited to improve disease outcomes in older adults with SARS-CoV-2 infection.[4]

Among the treatments under investigation for COVID-19, convalescent plasma transfusion has aroused a great deal of interest in the medical community.[5] Preliminary findings from 2 small-scale studies[6,7] have also been welcomed with enthusiasm and hope by the public, as witnessed by their wide media coverage. The US Food and Drug Administration has approved the use of convalescent plasma under compassionate use rules, and dozens of trials have been registered in ClinicalTrials.gov to test its efficacy and safety for the treatment of COVID-19. The downsize of this therapeutic approach is that plasma transfusions are neither inexpensive nor risk-free; plus, the large-scale distribution of convalescent plasma is logistically challenging. Risks associated with plasma transfusion include infections (e.g., human immunodeficiency virus, and hepatitis B and hepatitis C viruses), anaphylactic shock, transfusion-related acute lung injury (TRALI), and transfusion-associated circulatory overload (TACO).[8] Although the hazards of transfusion-transmissible infections is very low, risk factors for TACO (e.g., cardiovascular disease, lung disease, kidney failure, advanced age) are common in patients with severe COVID-19, which calls for careful recipient selection and judicious fluid volume management. The risk of TRALI is low when antibody screening of donors with prior history of pregnancy or transfusion is performed; however, TRALI is especially worrisome in patients with severe COVID-19 because their pulmonary vessels may already be compromised by the viral infection and associated microembolism. Risks and limitations associated with plasma therapies may be overcome through the use of hyperimmune globulin (HIG) preparations and monoclonal neutralizing antibodies (mNAbs) against SARS-CoV-2. These alternative approaches are now viewed as true game changers in the fight against COVID-19,[9] although the risk of antibody-dependent enhancement following infusion of HIG or mNAbs may not be negligible.[10]

Convalescent plasma is much more than an antibody "soup." Rather, it contains all the "molecular tools" the recipient will harness to heal from COVID-19. The repertoire of plasma-based factors that are transfused alongside with neutralizing antibodies includes anti-inflammatory cytokines, anticlotting factors, natural antibodies, specialized pro-resolving mediators (e.g., resolvins, protectins, maresins), defensins, pentaxins, collectins, plus an undefined number of unknown mediators.[5] This molecular arsenal enhances viral clearance, engages B and T lymphocytes, limits the inflammatory cascade, prevents microembolism, and promotes tissue repair.[5] Anti-SARS-CoV-2 non-neutralizing antibodies that bind to the virus without impeding its replication may still promote recovery through recruitment of innate immune cells.[5]

The foreseeable increasing use of convalescent plasma to treat COVID-19 may also allow the exploration of an intriguing hypothesis in the geriatric field. In heterochronic parabiosis experiments, multiple organs, including lungs, liver, heart, kidney, and brain, can be "rejuvenated" in old mice by synergistic actions of young blood constituents.[11] Indeed, the plasma proteome harbors key regulators of aging.[12] Because of the plausible interaction of aging biology with SARS-CoV-2 infection, the geroprotective properties of plasma from young convalescent donors could mitigate COVID-19 severity in older adults to a greater extent than one might expect from the sole antibody titer. Whether older men experience additional benefits from receiving plasma from young women is also worth being explored. In conclusion, the ongoing COVID-19 pandemic and the lack of effective pharmacological therapies have set the stage for the unprecedented opportunity to test one of the tenets of contemporary geroscience on a large scale.

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Addressing Rehabilitation Needs During a Pandemic: Solutions to Reduce Burden on Acute and Post-Acute Care

To the Editor:

The letter by Valenzuela et al "Coronavirus lockdown: forced inactivity for the oldest old?,"[1] calls for the need to address the

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