More than a thousand studies on coronaviruses summarized by researchers

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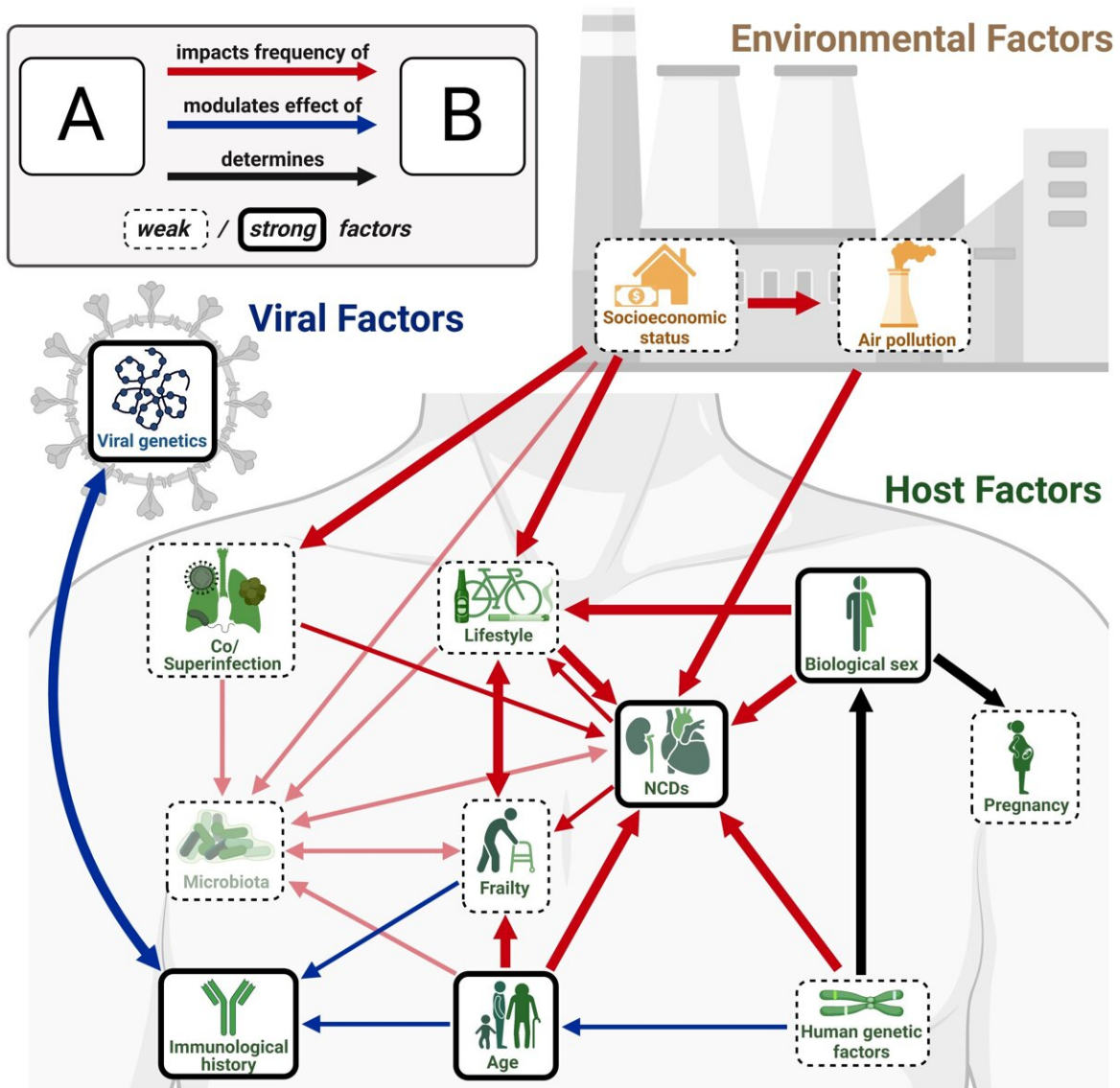
Researchers at Eötvös Loránd University (ELTE) have processed the scientific findings on COVID-19 disease severity, which reveal the risk factors and possible causes of the differential course of the disease. Their study was published in Viruses. Credit: Müller Viktor, Zsichla Levente / Eötvös Loránd University

Researchers at Eötvös Loránd University (ELTE) have processed the scientific findings on COVID-19 disease severity, which reveal the risk factors and possible causes of the differential course of the disease. Their study was published in *Viruses*.

The COVID-19 pandemic has affected the whole world, but the number of cases and deaths is very unevenly distributed between geographical regions and individual risk has been significantly influenced by the infected individual, the infectious virus strain and some characteristics of the environment.

The clinical course and outcome of COVID-19 is highly variable.

Understanding why some people become asymptomatic while others lose their lives is essential both to cure the disease and to control the epidemic.

Levente Zsichla, a student of the Institute of Biology at ELTE and his supervisor, Dr. Viktor Müller, Associate Professor at the Institute of Biology at ELTE, analyzed more than a thousand studies to provide a comprehensive picture of how processes influence the severity of COVID-19 at the individual level.

In their study, they examined in detail the role of demographic factors (age and biological sex, and related pregnancy), the interactions of the

disease with other infectious and non-communicable comorbidities, and the influence of genetic polymorphisms, lifestyle, microbiota and established immune memory. In addition, the impact of genetic variation in the coronavirus (SARS-CoV-2) and environmental factors such as air pollution and socioeconomic status were reviewed.

For each factor, the evidence, sometimes conflicting, for the association with COVID-19 outcomes was examined and possible mechanisms of action were outlined. They also reviewed the complex interactions between different risk factors and the feedback effects of epidemic closures on these factors. We review some examples from their study.

What is already known—age and underlying diseases

Advanced age is among the strongest risk factors for COVID-19 mortality. This effect was first reported in early 2020 and has since been confirmed by numerous studies. These findings show that the risk of death in adults doubles approximately every 6-7 years of life, and (in the case of the first major wave of the pandemic) has already exceeded 1% in the 65-75 age group. Aging of lung tissue and the immune system, and the age-related increase in sterile systemic inflammation levels may also be responsible for this phenomenon.

Some chronic diseases also increase the risk of severe COVID-19, but there are exceptions and controversial cases. While obesity, diabetes, hypertension, chronic kidney disease and cardiovascular disease are certainly risk factors, the results for several immunological, neurological and mental diseases are still inconclusive. There is also such controversy within lung diseases.

While chronic obstructive pulmonary disease seems to have a clear aggravating effect, in the majority of studies allergic asthma has been found to be a neutral or even risk-reducing underlying condition. This

may be because, although both conditions are associated with shortness of breath, chest tightness, wheezing and coughing, the causes and mechanisms of the two conditions are largely different.

Men are more vulnerable, women have more complications

Data show that men are at about twice the risk of serious COVID-19 infection, not only among older people but also regardless of age. Similar associations have also been shown for other viral respiratory diseases (e.g. influenza) and infectious pneumonia, so the mechanism is probably not unique to COVID-19.

The role of several X-linked genes and the differential expression of other genes that play a key role in the immune system may underlie this phenomenon. In addition, men with severe COVID-19 often have immunological problems involving a family of immune molecules produced against viruses, interferons. In a significant proportion of patients, the production of these interferons is disturbed or the body starts to produce antibodies against them, inactivating the otherwise protective proteins.

Women have a lower risk of severe COVID-19 disease, but a higher rate of post-COVID-19 syndrome. Pregnancy is a particular risk factor for the course of the infection, with pregnant infected women more likely to develop gestational hypertension, more often being admitted to intensive care and the consequences for the fetus/infant.

Indirect effects of the environment

Poor socioeconomic status, including poverty, poor housing conditions or belonging to an ethnic minority, has been shown to be a risk factor in

many countries. It also affects people's lifestyle, nutrition, exposure to air pollution and infectious respiratory diseases, and the availability and quality of health care.

Unsurprisingly, and supported by research evidence, regular physical activity and a healthy diet are beneficial for overall health and COVID-19 outcomes, while excessive alcohol consumption increases the risk of serious disease. Even more surprisingly, the impact of smoking, which significantly impairs respiratory function, on the clinical outcome of SARS-CoV-2 infection remains undetermined. In contrast, a growing body of research links long-term exposure to high concentrations of particulate matter with severe coronavirus disease.

Significance of the review

There have been several summaries of factors influencing the outcome of COVID-19, but these have either covered a small area or provided only a sketchy summary of a wider range of risk factors. The new study provides the most comprehensive overview of risk factors, highlighting the dominant role of age, biological sex, certain chronic underlying diseases, previously acquired specific immunity, and the infectious virus strain in the course of the disease.

If you take the time to read it—and we recommend it to our brave and persistent readers—you will see how complex the science is and how often it is difficult to draw clear conclusions. It also reveals the amazing scientific collaboration that has taken place over the past few years as the international scientific community has joined forces to find answers and solutions to the pandemic threatening the world.

Fortunately, with the development of effective vaccines and the immunity of those who have been affected, the pandemic has gradually been pushed into the background. Nevertheless, as the virus is expected

to be with us for a long time to come, the conclusions of this study will be needed well into the future.

  More information: Levente Zsichla et al, Risk Factors of Severe COVID-19: A Review of Host, Viral and Environmental Factors, *Viruses* (2023). DOI: 10.3390/v15010175

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