We urgently need to understand the medication histories of COVID-19 victims, writes Dr. Stefan Ecks

On March 18, 2020, Dr. Anthony Fauci and Dr. Howard Bauchner discussed a possible link between common hypertension medications and a heightened risk of dying with a coronavirus infection. Dr. Fauci directs the National Institute of Allergy and Infectious Diseases and is a key advisor on the White House Coronavirus Task Force. Dr. Bauchner is the Editor of *JAMA*, the *Journal of the American Medical Association*. Not exactly lightweights, as Walter Sobchak would say. Fauci and Bauchner responded to reports of a link between ACE (angiotensin converting enzyme) inhibitors and COVID-19 fatalities. Fauci said that ACE inhibitors can increase "the expression of the receptors for the virus" (JN Learning 2020). Fauci was struck by reports from Italy that the vast majority of those who died with COVID-19 suffered from hypertension. Italy is a rich country with excellent access to care, so chances are that most of the patients had been taking ACE inhibitors to treat their hypertension. "Why should someone who has hypertension that's well controlled have a much greater chance of dying than somebody else with any other kind of underlying condition?," Fauci asked. "We really need to get data and we need to get data fast" (JN Learning 2020).

As the SARS-CoV-19 pandemic is unfolding, strong links between the infection and "underlying health conditions" have become evident. Studies of mortality rates in China show that almost all the people who died with the virus had pre-existing disorders (Novel Coronavirus Response Team 2020). COVID-19 is

an acute infection with mild to moderate flu symptoms in most people. But in combination with noncommunicable disorders such as heart disease, diabetes, chronic respiratory disease, high blood pressure, and cancer, the infection can be fatal. Multimorbidity is the first key to understanding COVID-19 mortality rates. What is not yet known is if COVID-19 victims also have similar patterns of medication use. Multimorbid patients tend to be on several chronic medications simultaneously. It is likely that some of these medications put people at a heightened risk of dying from the infection. The data that we urgently need, but completely lack, are the medication histories of COVID-19 victims. Medication profiles could prove to be the second key to understanding COVID-19 mortality patterns.

Multimorbidity occurs when the same person suffers from two or more chronic disorders. The disorders can be noncommunicable, infectious, or mental. Noncommunicable diseases are cancer and heart disease; mental disorders are depression and dementia; long-term infectious diseases are HIV and tuberculosis (Academy of Medical Sciences 2018: 6). There is no agreed definition: some classify multimorbidity by the number of disorders that occur together, others look for recurrent clusters (Busjia 2019). What comes into the clusters varies, some consider only a handful of chronic disorders (Dugravot et al. 2020), while others capture dozens of conditions (Payne 2020).

Multimorbidity is increasing across the world. In rich countries, multimorbidity makes up 25-50% of the overall disease burden (Garin et al. 2016; van der Aa et al. 2017). Longer lifespans mean more multimorbidity: the older people get, the more chronic health problems they have. Up to two thirds of people over 65 are multimorbid. Treating older patients accounts for a large chunk of all health expenditures (Kaufman 2015). The pharmaceutical industry promotes the chronic consumption of five or more medications as necessary

for the maintenance of “normal” health (Dumit 2012).

Multimorbidity is not a new condition, there have always been people with more than two health issues at the same time. Yet the medical focus on multimorbidity is new. According to Dr. Chris Whitty, the UK government’s chief advisor on COVID-19, multimorbidity did not come into view for so long because biomedicine is organized “vertically” on specific diseases, while a “horizontal” understanding of simultaneous disorders is lacking (Whitty et al. 2020: 1). Biomedicine is founded on specific aetiology and specific treatment. The “medical model” tries to capture the specific causes of disorders and to develop therapies that target unique pathogens or other similarly specific causes (White 2006: 141-142). It is almost impossible for individual clinicians to control for all possible side effects of multiple medications taken over a long period of time. In an era of rising multimorbidity, biomedical specificity has serious limitations.

Iatrogenesis takes three forms: (1) polypharmacy, when too many different treatments are given at the same time; (2) drug-drug interactions, which happen when two or more drugs together produce adverse side effects; and (3) inappropriate treatments that harm instead of heal (Novaes et al. 2017). Different forms of iatrogenesis can happen together and augment harmful effects. Patients with multiple chronic disorders are at a particularly high risk of iatrogenesis because they are consuming different medications simultaneously and for a long time. Multimorbidity exacerbates the risks of iatrogenesis. For example, beta-blockers prescribed for heart disease or high blood pressure can worsen asthma and mask dangerously low blood sugar levels in diabetics (Onder 2013). Public health researchers are speaking of the first iatrogenic epidemic in history (Mangin & Garfinkel 2019). “Polyiatrogenesis” is the deepening of multimorbidity through isolated vertical interventions. In an era of rising multimorbidity, the adverse effects of taking

different medications for different chronic conditions are increasing.

Medical researchers have done excellent work in teasing out the various chronic conditions of people who died with the coronavirus infection, but a deeper examination is needed. In the next step, we need to go beyond specific conditions and look for nonrandom clusters among the patients' chronic conditions. In a further step, medication histories of COVID-19 victims should be recorded and analysed. There are a myriad of possible interactions between SARS-CoV-19, existing comorbidities, and medication histories. The possible link between taking ACE inhibitors and an increased risk of dying with a SARS-CoV-19 infection might just the tip of the polyiatrogenic iceberg. There are potentially dozens more such interactions. We need to know what drugs people take and if there are nonrandom clusters of medication use and fatal COVID-19 trajectories.

Tracking medication histories of multimorbid patients will also help to model population-based mortality rates with greater accuracy. By early April 2020, the impact of SARS-CoV-19 is far more severe in rich countries than in low-income countries. The United States now have the highest number of confirmed infections and are on course to overtake Italy and Spain in the number of fatalities. This pattern is surprising, because infectious diseases usually strike much harder in low-income countries. One reason why Europe and North America are the current epicenters of the COVID-19 pandemic could be that patients have longer life expectancies and, therefore, higher rates of multimorbidity. But it is also possible that COVID-19 strikes harder in multimorbid patients with a long and complex medication history. The world map of COVID-19 victims does not show a Global North/South distribution of wealth gaps or lack of healthcare. Instead, the COVID-19 map looks like an atlas of industrialized countries with a deep presence of biomedicine. Monitoring victims not just for underlying health

conditions but also for their medication histories is the only way of knowing if COVID-19 mortalities might be linked to medication use patterns. Finding clustered relations between COVID-19, underlying conditions, and medication use will save thousands of lives.

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