

Re: Nicoll A, Sprenger M. Learning lessons from the 2009 pandemic: putting infections in their proper place. *Eur J Epidemiol* 2011; 26:191–194

Ulrich Keil · Peter Schönhöfer · Angela Spelsberg

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The article by Nicoll et al. [1] claims that learning lessons from the 2009 swine-flu pandemic means placing infectious diseases in proper perspective. We do not find a single proof for that. Moreover, the article misinterprets our paper [2].

The authors [1] agree that “sound infectious disease epidemiology must be applied to the surveillance of influenza epidemics” and that “data currently provided by the Global Influenza Surveillance Network are insufficient.” However, they do not respond to the cited work by Jefferson [3] that “the data on the seasonal influenza are similarly weak and the estimates of disease frequency, mortality, and case fatality are vague. Consequently, the effectiveness of seasonal influenza vaccination campaigns and of antiviral medications is more than questionable [3]”.

WHO’s changing of the definition or description of a pandemic in May 2009, removing the phrase “enormous numbers of deaths and illnesses” from WHO’s website, is not a myth [1] but has been documented [4].

To imply the invention of a new myth by proposing that the improvement of social conditions prevents epidemics

of non-communicable (NCD) and communicable diseases (CD) alike, is remarkable, but contradicts the literature [5, 6, 7]. Tuberculosis is an example; although no effective drug or vaccination against tuberculosis was available in the nineteenth and first half of the twentieth century, this major scourge declined dramatically with the improvement of social conditions.

Life expectancy “in the record holding countries” increased linearly from 1840 to 2000 by 40 years, i.e. 2.5 years per decade [8]. The life expectancy increase of 20 years from 1840 to 1920 cannot be linked to the invention of effective drugs or vaccinations but to the improvements in social conditions such as income, housing, working conditions, nutrition, education and sanitation.

Nowhere did we criticise “the modern public health approach to tuberculosis control such as case finding and ensuring completion of proper antimicrobial treatment”; nowhere did we question the present strategies of public health bodies to combat tuberculosis or vaccinations against diseases such as measles, mumps, whooping cough, etc. The attempt to label us vaccination opponents is unfounded.

On the other hand, side effects of vaccinations must be monitored and investigated: Why do the authors not mention two epidemiological studies from Sweden and Finland indicating a four- to nine-fold increased risk of narcolepsy in children vaccinated with adjuvant containing Pandemrix as compared to unvaccinated children [9]. Deaths associated with Pandemrix vaccination have been reported from Sweden [10].

The willingness of the public to accept influenza vaccination depends primarily on the credibility, quality, and independence of advising institutions [11, 12]. Fear-mongering such as performed by industry-dependent marketing

U. Keil (✉)

Institute of Epidemiology and Social Medicine, University of Münster, Domagkstrasse 3, 48149 Münster, Germany
e-mail: keilu@uni-muenster.de

P. Schönhöfer

Institute of Clinical Pharmacology, Klinikum Bremen-Mitte
St.-Jürgen-Strasse 1, 28177 Bremen, Germany

P. Schönhöfer · A. Spelsberg

Transparency International, German Chapter, Berlin, Germany

A. Spelsberg

Tumor Zentrum Aachen e.V., Pauwelsstrasse 30,
52074 Aachen, Germany

agents, WHO, and some national health administrations proved to be deleterious to any preventive activities [13]. Fear-mongering based on misleading interpretations of experiments with ferrets, claimed dangers due to serious or fatal pneumonia by A/H1N1 [14]. It is deplorable that the ECDC seems to be misinformed about the lack of efficacy of antiviral drugs [15].

What is needed is an agenda for public health which strikes a balance between fighting CDs and NCDs. We feel that CD specialists often do not have a proper public health perspective [6] not knowing the burden from NCDs. “Four NCDs, namely cardiovascular diseases, cancers, chronic respiratory diseases and diabetes are the world’s biggest killers, causing an estimated 35 million deaths each year—60% of all deaths globally—with 80% in low and middle-income countries. As these diseases are largely preventable it is time to concentrate resources and invest in the prevention of these NCDs by elimination of shared risk factors,... [16].”

Scarce resources should not be wasted on ill-founded pandemic scenarios.

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Drs. Nicoll and Sprenger reply:

In their letter Keil et al. [1] state that infectious disease specialists lack a public health perspective and are unaware of the burden of non-communicable disease. ECDC possesses a strong public health perspective and fully acknowledges the burden of non-communicable diseases. However, the mandate the Centre has been given is prevention of and responding to infectious diseases in the European Union. With novel threats like Shiga-toxin producing enterohaemorrhagic *Escherichia coli* [2] and emerging antimicrobial resistance [3] adding to the existing prevalent infectious conditions (HIV, tuberculosis, measles etc.) these are topics of importance to Europe.

Keil et al. [1] mention concerns expressed by some over the levels of influenza burden and the effectiveness of influenza antivirals and vaccines. The burden of new (post 2009 pandemic) seasonal influenza needs to be determined [4] but the initial indications are that it will be significant. Deaths due to laboratory confirmed influenza are recognised to be only a proportion of all of the premature deaths caused directly or indirectly by influenza viruses. Despite that, the winter of 2010–2011 saw over 600 confirmed influenza deaths in one European Country [5]. The majority of them were in young adults and of those 40% in

seemingly previously healthy people without risk factors [5]. Recently an independent reanalysis of randomised trials has reconfirmed the effectiveness of the most used antiviral in Europe in preventing respiratory complications of seasonal influenza [6]. ECDC has developed and led European studies on the effectiveness of pandemic and seasonal influenza vaccines. These have demonstrated that the pandemic vaccines were very effective [7]. However, with collaborating member states, we have found the effectiveness of the seasonal vaccines, while still significant also show considerable need for improvement [8].

Keil et al. [1] continue to allege that WHO changed the definition of the pandemic. Rather than continue that debate we refer readers to a set of articles published on this topic in the July 2011 edition the Bulletin of WHO [9]. However, we must point out how the definition of a pandemic is unchanged, straightforward and well-established in the Dictionary of Epidemiology “an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people” [10].

Keil et al. comment that ECDC did not mention potential side effects of influenza immunisation in our last writing. That was because it was not raised by Keil et al. originally and we were responding to their article [11, 12]. Those who have followed ECDC’s work and publications will know the Centre has been active in this field, working within our mandate and closely with national authorities, the European Medicines Agency and WHO. Since observed associations of vaccination and adverse events in recipients can be due to chance or causation, determining what are not side effects has to be approached scientifically. Guidance on how to distinguish chance association from causation has been laid down by WHO [13]. The correct term for these events is Adverse Events Following Immunisation (AEFIs) and these are carefully monitored, evaluated and when necessary investigated by national regulatory bodies, European Agencies, the relevant manufacturers and WHO. That has been happening intensively since the pandemic vaccines were deployed, with ECDC playing its part and following its policy of transparency.

Concerning the narcolepsy-cataplexy AEFIs ECDC has been active since they were first reported by the Swedish and Finnish authorities, especially through the VAESCO project. But we are not rushing to judgement because investigations are ongoing and the science is unclear. ECDC published an early risk assessment and multiple updates in the form of *Public Health Developments* (the latest was on July 21, 2011 and contains links to the others) [14]. We have been advising the Commission and the European Medicines Agency (the lead EU Agency for vaccine safety). We have repeatedly reminded member

states and the public of which vaccines should be used against seasonal influenza [14, 15] and have funded and co-directed the one pan-European investigation into these cases in a case–control study conducted in nine EU member states, the ECDC-VAESCO study [14]. We do not pretend to understand the epidemiology and the mechanisms underlying them or why the cases are appearing mostly in three counties and not in other EU countries where the vaccine was used. But we are certainly part of a determined collaboration to understand the phenomenon [14, 15].

In addition, in preparation for the pandemic vaccination campaigns, the ECDC called for and funded (1.1 million €) several activities facilitating possible upcoming reports on AEFIs; developing background rates for a number of adverse events identified by the European Medicines Agency of specific interest [16] and two prospective pharmacoepidemiological studies (case–control and self-control case series) addressing Guillain–Barre’ syndrome and pandemic vaccines [17].

Finally Keil et al. demonstrates the particular difficulty in determining causation of AEFIs with influenza vaccines by mentioning deaths associated with influenza vaccination in Sweden [18]. The most important group that was immunised in Europe in the pandemic (and the 2010–2011 season) were people with chronic and sometimes life-threatening conditions. When that happens, some will die in the period following vaccination by chance alone. The report cited by Kiel et al. from the Lakemedelsverket (the Swedish Medicines Agency) following influenza immunisation does as they say mention deaths that took place following immunisation [13, 16]. What is important is that the detailed assessments undertaken by the Lakemedelsverket and the expert group *Pandemic Pharmacovigilance Rapid Response Group* (PREG) convened by the European Medicines Agency to investigate and evaluate difficult cases concluded that no causative association could be identified [19].

Angus Nicoll

Marc Sprenger

European Centre for Disease Prevention and Control (ECDC)

Stockholm 17183, Sweden

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