

rolinska stitutet

Pre-submission inquiry

2023-04-26

Dnr: Dnr

Dept. Medical Epidemiology and Biostatistics Karolinska Institutet Jonas F Ludvigsson, Prof. Eric J Rubin Mary Beth Hamel

Pre-submission inquiry

Dear Editors,

The Nordic countries have a long history of register-based research, with a substantial number of papers published in the *New England Journal of Medicine (NEJM)*¹⁻¹⁰. The basis of this research is the personal identity number^{11,12}, a unique number assigned to all residents, that allows for linkage of nationwide registers. The tax-funded public health care system allows for equal access to healthcare and minimizes selection bias ¹³.

Several of the Nordic healthcare registers started already in the 1940s and 1950s. With prospectively collected data over long time, and virtually no loss of follow-up, researchers in the Nordic countries can assess prognosis and etiology of a range of conditions, including rare diseases. This has become even more important in postmarketing studies of prescribed drugs¹⁴. Further, as many important questions in medicine and disease etiology cannot be addressed through randomized clinical trials, the Nordic multigenerational registers with complete family links offer unique opportunities for conducting family-based studies, e.g. where rates of disease among individuals with a particular exposure is compared to their non-exposed siblings, which inherently controls for inheritance and shared early environmental factors¹⁵⁻¹⁷.

We have written a large number of register-based papers including several publications on nationwide registers and research infrastructure ^{11,13,18-23}. We propose an article about registers in the Nordic countries and an overview of register-based research. Such a review article is lacking in major journals, and we believe it would be of substantial interest the readers of *NEJM*, and is likely to be highly cited. We look forward to hearing from you.

Best regards,

<i>Jonas F Ludvigsson</i> Karolinska Institutet (prof) Sweden	<i>Mika</i> <i>Gissler</i> Finnish In- stitute of Health and	<i>Giske Ursin</i> Oslo Univer- sity, (prof) Norway.	<i>Unnur</i> <i>Valdimarsdottir</i> University of Iceland (prof)	<i>Elisabete</i> <i>Weiderpass</i> Director (prof), of the Interna-	<i>Henrik Toft Sørensen</i> Aarhus University, (prof) Denmark
Adj. Prof. Colum- bia University.	welfare (prof), Finland	Prof. Em. Div. of Epidemio- logy, Keck School of	Adj. Professor, Dept. of Epidemiology, Harvard TH Chan	tional Agency for Research on Cancer,	Adj. Prof. Boston University, Darth- mouth University
President of the Swedish Soc. of Epidemiology 2011-14,	Karolinska Institutet Sweden. University of Turku, Finland.	Medicine, Univ Southern California. Director of the Cancer Registry of Norway	School of Public Health.	World Health Or- ganization	and University of North Carolina. Senior advisor at Stanford Univer- sity. Editor of <i>Clini-</i> <i>cal Epidemiology</i> (2008-)

1. Simon TG, Duberg AS, Aleman S, Chung RT, Chan AT, Ludvigsson JF. Association of Aspirin with Hepatocellular Carcinoma and Liver-Related Mortality. N Engl J Med 2020;382:1018-28.

2. Sorensen HT, Mellemkjaer L, Olsen JH, Baron JA. Prognosis of cancers associated with venous thromboembolism. N Engl J Med 2000;343:1846-50.

3. Lei J, Ploner A, Elfstrom KM, et al. HPV Vaccination and the Risk of Invasive Cervical Cancer. N Engl J Med 2020;383:1340-8.

4. Hofmann R, James SK, Jernberg T, et al. Oxygen Therapy in Suspected Acute Myocardial Infarction. N Engl J Med 2017;377:1240-9.

5. Lichtenstein P, Halldner L, Zetterqvist J, et al. Medication for attention deficithyperactivity disorder and criminality. N Engl J Med 2012;367:2006-14.

6. Momen NC, Plana-Ripoll O, Agerbo E, et al. Association between Mental Disorders and Subsequent Medical Conditions. N Engl J Med 2020;382:1721-31.

7. Sankila R, Olsen JH, Anderson H, et al. Risk of cancer among offspring of childhood-cancer survivors. Association of the Nordic Cancer Registries and the Nordic Society of Paediatric Haematology and Oncology. N Engl J Med 1998;338:1339-44.

8. Haberg SE, Trogstad L, Gunnes N, et al. Risk of fetal death after pandemic influenza virus infection or vaccination. N Engl J Med 2013;368:333-40.

9. Loberg M, Kalager M, Holme O, Hoff G, Adami HO, Bretthauer M. Long-term colorectal-cancer mortality after adenoma removal. N Engl J Med 2014;371:799-807.

10. Fang F, Fall K, Mittleman MA, et al. Suicide and cardiovascular death after a cancer diagnosis. N Engl J Med 2012;366:1310-8.

11. Ludvigsson JF, Otterblad-Olausson P, Pettersson BU, Ekbom A. The Swedish personal identity number: possibilities and pitfalls in healthcare and medical research. Eur J Epidemiol 2009;24:659-67.

12. Schmidt M, Pedersen L, Sorensen HT. The Danish Civil Registration System as a tool in epidemiology. Eur J Epidemiol 2014;29:541-9.

13. Laugesen K, Ludvigsson JF, Schmidt M, et al. Nordic Health Registry-Based Research: A Review of Health Care Systems and Key Registries. Clinical epidemiology 2021;13:533-54.

14. Stephansson O, Kieler H, Haglund B, et al. Selective serotonin reuptake inhibitors during pregnancy and risk of stillbirth and infant mortality. JAMA 2013;309:48-54.

15. Song H, Fall K, Fang F, et al. Stress related disorders and subsequent risk of life threatening infections: population based sibling controlled cohort study. BMJ 2019;367:15784.

16. Song H, Fang F, Arnberg FK, et al. Stress related disorders and risk of cardiovascular disease: population based, sibling controlled cohort study. BMJ 2019;365:11255.

17. Song H, Fang F, Tomasson G, et al. Association of Stress-Related Disorders With Subsequent Autoimmune Disease. Jama-J Am Med Assoc 2018;319:2388-400.

18. Cnattingius S, Kallen K, Sandstrom A, et al. The Swedish medical birth register during five decades: documentation of the content and quality of the register. Eur J Epidemiol 2023;38:109-20.

19. Wettergren B, Blennow M, Hjern A, Soder O, Ludvigsson JF. Child Health Systems in Sweden. J Pediatr 2016;177S:S187-S202.

20. Ludvigsson JF, Almqvist C, Bonamy AE, et al. Registers of the Swedish total population and their use in medical research. Eur J Epidemiol 2016;31:125-36.

21. Ludvigsson JF, Haberg SE, Knudsen GP, et al. Ethical aspects of registry-based research in the Nordic countries. Clin Epidemiol 2015;7:491-508.

22. Emilsson L, Lindahl B, Koster M, Lambe M, Ludvigsson JF. Review of 103 Swedish Healthcare Quality Registries. Journal of internal medicine 2015;277:94-136.

23. Ludvigsson JF, Andersson E, Ekbom A, et al. External review and validation of the Swedish national inpatient register. BMC Public Health 2011;11:450.