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LETTER TO THE EDITOR

Reply to Letter by Dr. Christoph Kupferschmid: Commentary on "Countries with high circumcision prevalence have lower prostate cancer mortality"

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Dear Editor,

We thank Dr. Kupferschmid for his interest in our study, which examined male circumcision (MC) and prostate cancer mortality.^{1,2} Considerable strong evidence has been accumulated since 1951.³ Most of his references^{4–10} do not address MC and the risk of death from prostate cancer. That is a different question than MC and the risk of developing prostate cancer, which none of his references validly assess. One reference addressed bacterial colonization,⁶ not prostate cancer. Another⁷ concerned sexually transmitted infections and prostate cancer. The US article he claims calculated number of circumcisions required to circumvent one prostate cancer death¹¹ had no death statistics. Since 14% of American men get prostate cancer and the Wright study found circumcision reduced risk by 13% in Caucasian and 36% in African American men, 54 Caucasian and 19 African American men would need to be circumcised prior to sexual debut to prevent one prostate cancer diagnosis.

Epidemiological studies in and of themselves can no more prove MC reduces prostate cancer mortality than they can prove cigarette smoking increases lung cancer mortality. They do, however, provide evidence scientists and officials might use to direct scientific investigation and government policy. We specifically stated that our findings to do not prove a causal relationship.¹

Dr. Kupferschmid asserts our study used data from "different heterogeneous sources and different years." Each information source provisioned estimates for a particular year for prostate cancer mortality rates,¹² MC rates,¹³ gross national incomes per capita and male life expectancies at birth,¹⁴ and proportions of Muslims¹⁵ and Jews in countries.¹⁶

Dr. Kupferschmid infers we evaluated differences among continents without taking into account potential biases. Vital, in our view, was taking into account differences among large geographic regions that might have biased the analysis of countries' mortality rates. Evidence of differences in cancer incidence and other relevant matters among continents is readily available.¹⁷⁻²⁰ Using the WHO region as a covariate mitigated potential study bias arising from factors unrelated to MC. In our study, the "Americas" is not only limited to the USA, where MC is common, but also includes Central and South America, where MC is low.

Our study¹ took into account male life expectancy at birth and gross national income per capita. These covariates in part adjust for factors such as access to clean water and medical care. Higher-income countries have increased levels of prostate cancer, possibly due to sedentary lifestyle, obesity, and high red meat consumption, as we discussed.¹ Differences in proportions of Muslims and Jews, while of direct importance as respects MC, also reflect differences in dietary habits, as we discussed.¹ Social factors, a concern of Dr. Kupferschmid, were taken into account.

With these factors taken into account, our analysis revealed an association between increased MC rates and decreased prostate cancer mortality rates that could not be explained by chance.¹ The three categories used for MC prevalence, 0%–19%, 20%–80%, and 80%–100%, were designated by the WHO.¹³ The threshold for significant protection against prostate cancer mortality could be well below 80% and requires further research.

Since more men die with prostate cancer than die of it, death from prostate cancer is a harder endpoint. By revealing an association of MC with prostate cancer mortality, our study adds to the existing data.

COMPETING INTERESTS

All authors declare no competing interests.

REFERENCES

- Wachtel MS, Yang S, Morris BJ. Countries with high circumcision prevalence have lower prostate cancer mortality. *Asian J Androl* 2016; 18: 39.
- 2 Kupferschmid C. Commentary on "Countries with high circumcision prevalence have lower prostate cancer mortality." *Asian J Androl* 2016. Doi: 10.4103/1008-682X.182816.
- 3 Ravich A, Ravich RA. Prophylaxis of cancer of the prostate, cervix and penis by circumcision. *NY State J Med* 1951; 51: 1519–21.
- 4 Kaplan GW, O'Connor VJ Jr. The incidence of carcinoma of the prostate in Jews and Gentiles (research letter). JAMA 1966; 196: 123–4.
- 5 Gibson E. Carcinoma of the prostate in Jews and uncirumcised gentiles. *BJU* 1954; 26: 227–9.
- 6 Lai FC, Kennedy WA, Lindert KA, Terris MK. Effect of circumcision on prostatic bacterial colonization and subsequent bacterial seeding following transrectal ultrasound-guided prostate biopsies. *Tech Urol* 2001; 7: 305–9.
- 7 Rosenblatt KA, Wicklund KG, Stanford JL. Sexual factors and the risk of prostate cancer. Am J Epidemiol 2001; 153: 1152–8.
- 8 Rotkin ID. Studies in the epidemiology of prostate cancer: expanded sampling. Cancer Treat Rep 1977; 61: 173–80.
- 9 Jackson MA, Kovi J, Heshmat MY, Ogunmuyiwa TA, Jones GW, et al. Characterization of prostatic carcinoma among blacks: a comparison between a low incidence area, Ibadan, Nigeria and a high incidence area, Washington, DC. Prostate 1980; 1: 185–205.
- Wynder EL, Mabuchi K, Whitmore WF. Epidemiology of cancer of the prostate. Cancer 1971; 28: 344–60.

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- 11 Wright JL, Lin DW, Stanford JL. Circumcision and the risk of prostate cancer. Cancer 2012; 118: 4437–43.
- 12 Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, et al. GLOBOCAN 2012: Estimated Cancer Incidence, Mortality, and Prevalence Worldwide in 2012. Lyon, France: International Agency for Research on Cancer; 2014.
- 13 World Health Organization and Joint United Nations Programme on HIV/AIDS. Global map of male circumcision prevalence at country level, as of December 2006. Male circumcision: global trends and determinants of prevalence, safety and acceptability. Geneva, Switzerland: World Health Organization; 2007.
- 14 World Bank. World Bank Open Data. 2014 ed. New York, United States: The World Bank Group; 2014. Available from: http://www.data.worldbank.org/.
- 15 Pew Research Religion and Public Life Project. The Future of the Global Muslim Population. Washington, DC: Pew Research Center; 2011.
- 16 Della Pergola S. World Jewish Population, 2010. Storrs, Connecticut: University

of Connecticut; 2010.

- 17 Martel-Jantin C, Filippone C, Tortevoye P, Afonso PV, Betsem E, *et al.* Molecular epidemiology of merkel cell polyomavirus: evidence for geographically related variant genotypes. *J Clin Microbiol* 2014; 52: 1687–90.
- 18 Piel FB, Tatem AJ, Huang ZJ, Gupta S, Williams TN, et al. Global migration and the changing distribution of sickle haemoglobin: a quantitative study of temporal trends between 1960 and 2000. Lancet Glob Health 2014; 2: E80–9.
- 19 Mendizabal AM, Younes N, Levine PH. Geographic and income variations in age at diagnosis and incidence of chronic myeloid leukemia. *Int J Hematol* 2016; 103: 70–8.
- 20 Mahdavifar N, Ghoncheh M, Pakzad R, Momenimovahed Z, Salehiniya H. Epidemiology, incidence and mortality of bladder cancer and their relationship with the development index in the world. Asian Pac J Cancer Prev 2016; 17: 381–6.