HIV Risk and Circumcision in Developed Countries
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Abstract Data accumulated over the past several years has shown a protective effect for male circumcision against heterosexual transmission of HIV from women to men. In this study the author used observational data from English-speaking developed countries to determine if infant male circumcision rates are associated with an expected decrease in HIV rates. Infant circumcision was used as a proxy for circumcision prevalence in the young adult population who are at higher risk for HIV infection. Univariate and bivariate linear regression was used to analyze the data, which showed a strong correlation between infant circumcision rates and HIV infection rates (R^2 = 0.973) and lower correlation between population and HIV infection rates (R^2 = 0.738). The association between circumcision and HIV prevalence was statistically significant for increased population risk from infant circumcision at p=0.0019 with an increase of 0.0085% (95% CI 0.010 – 0.0076) increase in HIV rate in the general population for each 1% increase in infant circumcision. Until this correlation can be explained, infant circumcision cannot be recommended as a prevention strategy for HIV in these countries.

Introduction – Circumcision of adult men has been shown in Africa to offer partial protection from heterosexually acquired HIV transmission from women to men. [1] [2] [3]

Since these studies were statistically significant, they raise the question whether circumcision would offer similar protection against HIV transmission in developed countries. The lower prevalence of HIV infection in developed countries would mandate an extremely large trial to replicate the results of the African trials, which is not feasible. Fortunately, circumcision rates among developed countries differ, offering a natural laboratory with millions of participants.

If male circumcision is effective in these countries, we would expect a negative correlation between circumcision prevalence and HIV prevalence. This is not what has been found, however. As shown in Figure 1, the prevalence of HIV closely tracks male circumcision prevalence in the study countries indicating the hypothesis is false. Since the three RCTs only studied heterosexual transmission in men with and without a foreskin, they did not address the population as a whole, nor did they assess risks to other groups or the efficacy of infant circumcision. This initial study addresses some of these factors in developed countries which were not demonstrated in the RCTs. It is notable that a recent follow-up study in Kisumu Kenya showed no correlation

between circumcision status and HIV prevalence in heterosexual men (OR= 1.0; 95% CI 0.5–2.0).[4] The value of any HIV intervention must be measured by its performance in the general population.

Methods

The data used in this study are all from calendar year 2007. Countries were selected from members of the Organization for Economic Cooperation and Development (OECD) and listed as high income countries by the World Bank. Of these, only countries where English is the predominant language were selected. Table 1 lists these countries with selected demographic data.

Table 1. Countries Selected For Study

Country	Circumcision Rate	Population [million]	HIV	
			Prev[5]	Peak Age
Australia	13%	21	0.2%	30-39
Canada	32%	33	0.4%	30-39
Ireland	N/A	4.3	0.2%	25-29
New Zealand	0.35%	4.2	0.1%	30-39
UK	3.1%	61	0.2%	30-39
USA	56%	301	0.6%	40-44

Infant circumcision rates were used for two reasons. First, and most important, this is the most accurate data available, as most countries do not track circumcisions done later in life or for cosmetic or religious reasons. Second, infant circumcision is a proxy for the adult prevalence in the younger 20- to 44-year-age groups where the HIV diagnosis rates peak. [6] [7] [8] [9] [10] [11]

Infant circumcision rates were estimated based on published data from national hospital discharge surveys and National Health Service records.[12] [13] [14] [15] [16] Data for Ireland were very limited and not available for 2007, which was not included in further analysis. It is of note that circumcision rates as indicated by national health statistics and OECD population structure records from 2002 – 2004 indicate Ireland's circumcision and HIV rates are similar to the UK's so in effect Ireland is included.

Data were analyzed in two ways. First, a univariate linear regression was performed on the HIV prevalence with infant circumcision rate as the independent variable. Second, a bivariate linear regression was performed with infant circumcision rate and country population as independent variables. Pearson correlation and r-squared were determined in both cases. Significance was determined using Student's t-test with a null hypothesis of slope = 0 or no relationship between infant circumcision and HIV prevalence. The circumcision studies showed a protective effect only for heterosexual men; specific data from the study countries regarding heterosexual transmission was taken from HIV surveillance reports published by the various National Health Services[17],[18],[19],[20]. These data were controlled for infections from countries where HIV is considered endemic to allow for a more direct comparison of the native circumcision rate with the native HIV rates among this subpopulation. Data from 2000 to 2007 were used because both Canada and Australia published data for males and females with source of infection indicated (endemic country or not). The

US did not allow immigration of HIV positive individuals prior to 2007 so this data too represents a good estimate of the native HIV rates. Correction factors for the UK data had to be based on estimates from ethnic data, which did indicate if the source was an endemic country. These data were then broken down by sex ratio and used to adjust the greater population data to remove cases from endemic countries. New Zealand did not publish sufficient data to perform this analysis.

Data prior to 2000 was not used due to potential data quality issues regarding testing and collection. Further, not all countries supplied information regarding endemic countries all the way back to 2000 so only data with this breakdown was used.

Results

Figure 1 and Table 2 show the results of the univariate regression. The coefficient of correlation (R^2 = 0.973) showing a significant positive correlation between infant circumcision rates and HIV. The slope of the fit line is 0.0085 (p=0.0019), which is statistically significant

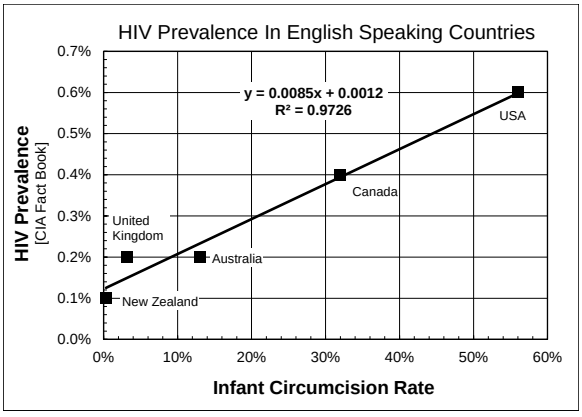

Figure 1. Circumcision and HIV Rates in OECD member English speaking countries – 2007 data.

Table 2. Results of Univariate Analysis

Parameter	Value
Slope	0.0085
Std Error [slope]	0.0008
p [slope]	0.0019
Slope t parameter	10.3
Critical t parameter (p=0.05)	3.18
Std Error [regression]	0.0004
Pearson's correlation	0.986
Coefficient of correlation [R^2]	0.973

The results of the bivariate analysis, which included country population, are presented in Table 4. A significant correlation (R^2=0.973) between infant circumcision and HIV prevalence persisted. The slope of the linear relationship between infant circumcision and HIV prevalence remained almost unchanged at 0.0077 (p=0.047), which is still statistically significant. The relationship between population and HIV rate was not statistically significant (p=0.66).

Table 4. Results of Bivariate Analysis

Parameter	Circumcision Rate	Population [million]
Slope	0.0077	1.7E-6
Std Error [slope]	0.0017	3.29E-6
p [slope]	0.047	0.66
Pearson's correlation	0.986	0.859
Slope t parameter	4.43	0.517
Critical t parameter (p=0.05)	4.3	
Std Error [regression]	0.00044	
Coefficient of correlation [R^2]	0.976	

Figure 2 shows the results of the analysis of HIV infections from the study countries in heterosexuals. The positive correlations hold across all heterosexual

groups tracked by the surveillance reports. The groups of interest are HIV rates among heterosexual men and women. These data were summed across all years prior to 2007 but after 2000 where data were available. Percentages of the total reported HIV positive population, including those from endemic countries, were computed based on this cumulative data. Final population percentages in heterosexual were then computed based on the total HIV prevalence from the CIA Fact Book. Since the data reported by the CIA Fact Book are cumulative totals of all individuals, we performed a quality control test to verify that this was a reasonable estimator of the population prevalence of HIV positive heterosexual men and women. We examined the data for consistency over the years in question and found all years had similar rates of infection among heterosexuals. Thus, the study years were not unusual and the rates were consistent over all the years for which data were available (Authors note: we have continued this investigation and found that thru 2010 this consistency remains unchanged). The data were analyzed using linear regression with best fit line and correlation inset in the chart. The positive correlation holds for both male and female HIV prevalence among heterosexuals. The top chart is for all HIV-positive individuals who reported themselves heterosexual. The second chart plots male HIV-positive heterosexual against infant circumcision rate (ICR). The third chart shows female HIV prevalence. The last chart plots the ratio of female to male.

Further analysis was not performed on these data sets owing to the relatively small number of individuals tracked in these narrow subcategories.

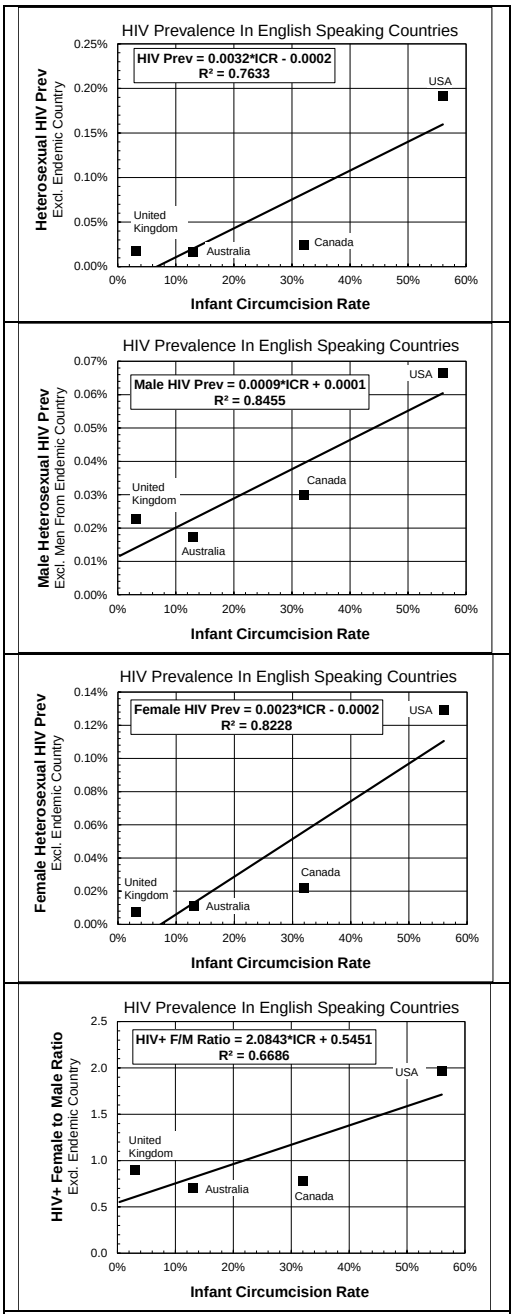

Figure 2. Heterosexual data from study countries shows positive correlation between infant circumcision rates and HIV rates in study countries.

Discussion

These data demonstrate a significant positive correlation between infant circumcision rates and HIV prevalence in English-speaking countries in the OECD. While correlation does not prove causation, the narrow linear relationship of the data suggests a potential causal relationship or a closely related common causal factor. If the data regarding male circumcision from Africa were applicable in the developed world, we would expect the exact opposite relationship from what was found, particularly among heterosexual men. At the national level in these countries, infant circumcision has not provided any protection for the general population and is associated with higher HIV prevalence, especially among women in the US. The ratio of female to male HIV prevalence among heterosexuals is particularly troubling since it clearly indicates a potential increase in risk for women who have circumcised HIV positive partners.
In looking for explanation for the disparate results one possibility is suggested by the National Gay Men's Sex Survey and an RCT of HIV-infected men in Africa. [21],[22]These studies found an increase in HIV infection rate among the partners of circumcised HIV positive men.

In the Sigma Research study, men with foreskins were less likely to test positive for HIV (5.0%) than men without (6.1%). For white, British, gay men (the only group with enough members, 13,243, to have sufficient power) the risk ratio was 1.22 (95% CI 1.02-1.46, Fisher exact p=0.042). In this case, a risk ratio greater than one indicates increased risk for a circumcised man contracting HIV over one with a foreskin. Therefore, in this population circumcision is contraindicated. From these results a Number Needed to Harm (NNH) of 92 was computed. In this study, for every 92 gay men circumcised one will contract HIV that otherwise would not have.

In 2007, gay men accounted for 51% of newly diagnosed HIV/AIDS cases in the US or 22,472. If, 80% were circumcised then the data from Sigma Research indicates that circumcision alone was directly responsible for 195 of these infections. It should be noted that other studies have not found this positive correlation among gay men.[23]

In the study, conducted by Wawer, et al, possible benefit to women in a stable relationship with HIV positive, circumcised and uncircumcised men was examined. The study used the standard two-tailed analysis to determine significance. However, when examining the data for harm to these women, where benefit and no effect are grouped, a single-tailed significance analysis is used. The author understands the limitations of this type of analysis but when the size of the study limits statistical power and the consequence of harm is death (in Africa) or a lifetime on antiretroviral drugs (in the OECD), this more conservative approach is appropriate.

Their data showed a potential increase in risk to women in a heterosexual relationship with a circumcised HIV positive man with relative risk ratio 1.55 (95% CI 3.373 – 0.710) {RR = 0.6462 (95% CI 0.2965-1.408) for comparison with the original study results which analyzed for benefit} and number needed to harm of 15. The study was halted by the study's Data Safety

Monitoring Board before there was sufficient power to demonstrate a statistically significant difference. Nevertheless, this data should not be ignored since heterosexual women constitute 21% of all HIV diagnoses in the US each year.[24]

If male circumcision does indeed increase risk in these two groups, this would explain the correlation demonstrated. Further studies are needed as gay men and heterosexual women are the two largest groups newly diagnosed in 2007 in most OECD countries. For example, the ratio of women to men who acquired HIV thru heterosexual contact in US is 2.0. [20] In Canada, this ratio is 0.78 and in Australia 0.70, which is consistent with the correlations identified. [25 26]

English-speaking countries in the OECD were selected for inclusion because of their similarities in economic development, general standard of living, medical and social infrastructure, language, predominant religion, and to lesser extents culture and political factors. These countries are also among the very few members of the OECD that have a history of circumcising infant males.

There are many other factors that impact HIV prevalence and infant circumcision rates. These include broadly held social attitudes towards sex, men, children, openness in discussing sexual matters, and social expectations of behavior and relationships, particularly among young heterosexuals. There are some differences between these countries that may be difficult control for.

Data Limitations

While high-quality estimates of the prevalence of circumcision in native-born adult males are not available, using infant circumcision rates as a proxy for adult prevalence is reasonable since most circumcision performed in these countries are on infants and preadolescent children and the rate of circumcision after this period is low. Moreover, infant circumcision rates will tend to represent native populations rather than immigrants who may bring other confounding factors to bear. Infant rates have been fairly consistent over the past four decades in the US, Canada and the United Kingdom and therefore are a reasonable proxy for the young adult prevalence. The prevalence in this age group is key because this portion of the population is at greater risk for HIV transmission. In addition, infant circumcision rates may measure cultural attitudes and biases that ultimately affect HIV rates as well. Neither circumcision nor HIV occur in a vacuum and social factors and cultural differences and expectations may affect both in some correlated and complex way. Obviously more work is required to fully understand these complex but interrelated phenomena.

Another potential limitation is the accuracy of national infant circumcision rates. The author used the rates that are believed to be the most accurate, yet some of these rates are best estimates.

Conclusion

These data show a strong and consistent correlation between infant circumcision and HIV rates among the general population and heterosexuals in English-speaking members of the OECD. This is particularly troubling

since the WHO and members of the US Centers for Disease Control and Prevention have stated that there is a benefit to infant male circumcision in the fight against HIV.[27] However, observational data in OECD countries do not substantiate that hypothesis and in fact show a strong correlation that infant circumcision may increase HIV infections. If circumcision were an effective prevention for HIV in developed countries, this association could not exist. From this we can draw only two possible conclusions for the study countries:

1) Infant circumcision is irrelevant to the HIV infection rate
2) Infant circumcision through some as yet unidentified causal chain increases the HIV infection rate.

Whether our findings are the result of a direct causal link of increasing risk to women and gay men or by maintaining and reinforcing cultural attitudes that lead to the higher HIV rates or some other factor has yet to be determined. Until there is an explanation for this correlation, infant circumcision as a preventative for HIV in these countries is unwise. Further research is needed to elucidate the complex interaction of culture, circumcision, and HIV before any recommendation can safely be made.

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