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Gross Domestic Product (GDP) and productivity of schizophrenia trials: an ecological study

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Abstract

Background: The 5000 randomised controlled trials (RCTs) in the Cochrane Schizophrenia Group's database affords an opportunity to research for variables related to the differences between nations of their output of schizophrenia trials.

Methods: Ecological study – investigating the relationship between four economic/demographic variables and number of schizophrenia RCTs per country. The variable with closest correlation was used to predict the expected number of studies.

Results: GDP closely correlated with schizophrenia trial output, with 76% of the total variation about the Y explained by the regression line (r = 0.87, 95% CI 0.79 to 0.92, r2 = 0.76). Many countries have a strong tradition of schizophrenia trials, exceeding their predicted output. All nations with no identified trial output had GDPs that predicted zero trial activity. Several nations with relatively small GDPs are, nevertheless, highly productive of trials. Some wealthy countries seem either not to have produced the expected number of randomised trials or not to have disseminated them to the English-speaking world.

Conclusions: This hypothesis-generating study could not investigate causal relationships, but suggests, that for those seeking all relevant studies, expending effort searching the scientific literature of Germany, Italy, France, Brazil and Japan may be a good investment.

Background

Most randomised trials are produced in the USA. Certainly, when it comes to trials relevant to the care of people with schizophrenia, certain countries have a strong tradition of trialling, and others have not [1]. This study investigates whether certain accessible economic and/or demographic variables are, in some way linked, and can be predictive of productivity of schizophrenia trials.

Methods

The Cochrane Schizophrenia Group has constructed a unique collection of reports of randomised controlled trials relevant to schizophrenia [2]. In this collection a single electronic record is made per study and the multiple references/reports/presentations of that study are appended to that single record. This attempt to decrease the confusion caused by 'salami' publication is made possible using custom made specialised reference/study management

Table 1: Top 10 producers of schizophrenia trials

Country	Simple frequency of trials (n)
USA	2363
United Kingdom	669
Canada	275
Germany	256
Japan	113
France	108
Netherlands	104
Sweden	101
Italy	91
China	87
TOTAL	4167

Table 2: Correlation of number of trials (if >0) vs each variable

Variable	r	95% CI for r	r^2
GDP (in million US $)	0.87	0.79 to 0.92	0.76
Population (in thousands)	0.14	-0.11 to 0.38	0.02
GDP/Capita (US $)	0.31	0.06 to 0.52	0.10
Telephones/per 100 inhabitants	0.30	0.06 to 0.52	0.09

software [3]. A study-based register affords an opportunity for research. Each study record in the Cochrane Schizophrenia Group's database has been coded for 'country of origin'. This has had to be defined as the country from which the first author originates. These data were extracted from the database (currently 5062 studies), and the number of trials undertaken in each country calculated.

Data for gross domestic product (GDP), population, GDP/Capita, and the number of telephones/100 people, for all countries, were acquired from the United Nations website [4]. A second website was used to supplement the first dataset where gaps were apparent [5]. Both datasets were figures from 1997. These particular sets of data were chosen as they are widely accessible, and because the authors felt they each add some qualities worthy of consideration. GDP is a measure of the sheer wealth of a nation. The population is the number of people, and, with a lifetime prevalence of 1% for schizophrenia, it represents the numbers of people with the illness who live in the country. GDP/capita is a measure of potential individual affluence, and number of telephones/100 people, is a crude estimate of technical development.

Statistical analysis was performed using StatsDirect, Statistical Software [6]. Number of randomised controlled trials relevant to schizophrenia was correlated against each of the four economic/demographic variables using simple and linear regression and Pearson's correlation calculated (Appendix 1 [see Additional file 1]). Finally, the best-fit plot was used to interpolate X (economic/demographic variable of best fit) to Y (calculated number of trials). In this way it was hoped to estimate the expected output of schizophrenia trials and compare this to the actual output.

Results

Of the 5062 studies, 61 (1.21%) were reported in such a way as to make reliable data extraction of country of origin impossible. Data extraction for 'country of origin' defined in the way used in this study has been found to be reliable in this sample with over 90% agreement [6]. Simple frequencies of studies by country verify that the USA is the most productive country of schizophrenia trials (Table 1).

Correlation of the number of trials by each of the four variables is shown in Table 2.

The correlation with GDP was by far the best fit with 76% of the total variation about the Y explained by the regression line (log transformation made little difference to the analysis). Having created the best-fit line, GDP data from

Table 3: Countries productive of schizophrenia trials ordered by level of productivity

country	GDP (mUS $)	actual trials > 100	predicted trials	% predicted output (95% confidence intervals)
Finland	119834	38	2	1900 (1312–2488)
South Africa	129094	26	5	520 (340–700)
Denmark	161455	79	12	658 (525–792)
Canada	607702	275	118	233 (212–254)
Norway	153362	24	10	240 (167–313)
Greece	118172	15	2	750 (397–1103)
Switzerland	172400	54	15	360 (278–442)
Sweden	227757	101	28	361 (301–421)
Poland	135623	17	6	283 (175–392)
UK	1283335	669	279	240(226–254)
Netherlands	363342	104	60	173(152–196)
Belgium	242508	49	32	153 (128–178)
Austria	206236	33	23	143 (117–170)
USA	7824008	2363	1831	129 (127–132)
Hong Kong	175200	18	16	113 (95–130)
Australia	402787	64	70	91 (85–98)
India	388649	48	66	73 (60–85)
Germany	2089845	256	470	54 (48–61)
Nigeria	142920	4	8	50 (1–99)
China	901981	87	188	46 (36–57)
Turkey	191865	8	19	42 (8–76)
Thailand	153909	4	10	40 (-8–88)
Italy	1145370	91	246	37 (27–47
France	1394124	108	305	35 (26–44)
Spain	531289	32	100	32 (16–48)
Russian Federation	447103	21	80	26 (7–45)
Mexico	402109	13	69	19 (-2–40)
Iran	159391	2	12	17 (-35–68)
Saudi Arabia	134825	1	6	17 (-56–90)
Republic of Korea	442543	13	79	16 (-4–37)
Brazil	806972	21	166	13 (-2–27)
Argentina	323548	6	51	12 (-14–38)
Japan	4192669	113	969	12 (6–18)
Taiwan	308000	4	47	9 (-19–36)

every country, whether or not they had been found to produce a relevant randomised trial, were interpolated to estimate the number of trials predicted by GDP.

The results of these interpolations fell into three distinct groups: i. Countries for which we had failed to identify any schizophrenia randomised trials; ii. Countries which had produced schizophrenia trials and which had a GDP that predicted trial activity; and finally, iii. Countries for which the GDPs predicted no trial activity, but that had undertaken a number of relevant studies.

Countries with no schizophrenia trials

We could not identify any randomised controlled trial research for people with schizophrenia for 132 (out of 192) countries. All of these countries, with the exception of Indonesia and Iraq had such low GDPs that trial activity would not be expected. Indonesia's GDP of $214593 million/year suggests that 25 studies could be expected, but wide confidence intervals do not exclude zero productivity (95% CI -16 to 66). The same applied for Iraq's $149036 million/year, with nine trials predicted but similarly wide confidence intervals (95% CI -32 to 51).

Countries productive of schizophrenia trials and also with a GDP that predicted trial activity (Table 3)

Finland is far ahead of other nations but numbers of both actual and expected studies are small. Denmark, however, is highly productive, as is Sweden, the UK, Canada and the Netherlands. Using these data, the USA's strong tradition of undertaking and disseminating trials still is outstanding, but it is the 14th most productive country of schizophrenia trials, according to percent of predicted output.

Table 4: Countries with GDPs that predicted no studies, but with >10 trials

Country	GDP (million US $)	Trials
Israel	92587	83
Czech Republic	52038	78
New Zealand	65291	14
Yugoslavia (Serbia/Montenegro)	17000	10
Hungary	45725	10

Countries for which GDP predicted no trial activity, but which had undertaken relevant studies

Twenty-five countries fell into this category, five of which produced more than ten studies when none were predicted by GDP (Table 4).

Discussion

Strengths and limitations

There are several limitations of the datasets used for this work. The study-based register is in its first draft. Many papers may be designated as a unique study when they only represent another report of an already identified randomised trial. Being fully confident of having minimised undisclosed multiple publications would take some time. This limitation will result in an overestimate of the number of studies. The overestimate probably is greatest for English language reports of industry-sponsored trials, the great majority of which originate from the USA. A second limitation is that the studies are from 1950 to the present day but the economic/demographic data are from 1997, disregarding the economic/demographic/political changes over time.

Economies that developed rapidly after World War II, such as China, Germany, Italy, Japan, Korea and Taiwan are being judged by the GDP of 1997. This technique could overestimate the expected output of trials from countries in which average GDP, or GDP relative to other countries, would have been considerably less than that of 1997. The crude definition of country of origin as country from which the first author originates is also a limitation. The author's origin may not represent the country where the study took place and we do not know the proportion of studies for which this accurately reflects where the work was undertaken. Lastly, the use of GDP is potentially a surrogate measure of one or many causal relationships. It could be a surrogate for the national investment of the pharmaceutical industry, the funding and activity of universities, or/and the degree to which fragmentation of the family had lead to public concern about the care of people with schizophrenia. As with any correlation study, this work is solely hypothesis-generating and not testing.

The USA produces more schizophrenia trials than any other country (Table 1). When the correlation of the four economic-demographic variables was undertaken GDP, whether logged or not, correlated highly with trial output (whether logged or not). Other variables did not (Table 2). This suggests that trial productivity may neither be a function of national burden of ill people, nor of individual prosperity, and not of technological development. Trial productivity seems more linked with the affluence of the country, irrespective of population, or technological development.

Every country that had not produced any randomised trials relevant to schizophrenia had a current GDP that predicted a study output of zero. The two exceptions (Indonesia and Iraq) had larger GDPs, but interpolation of which into the plot still predicted a study output compatible with zero (see 95% CIs). Every nation that can afford it, and many that cannot, undertake schizophrenia trials.

Table 3, highlights countries with what may be strong traditions of undertaking and disseminating trials, well beyond that predicted by GDP. On the other hand, the plot suggests that Japan, France, Italy, China and Germany are conducting only between 10–50% of trials predicted by their high GDPs. One reason for these poor results may be that those compiling the Cochrane Schizophrenia Group's database are not identifying relevant trials from non-Anglophone sources. These figures would suggest that those seeking as yet unidentified studies should focus efforts on these countries, where searching is likely to be fruitful. Investing effort in finding studies from Thailand, however, where only an additional six studies are predicted to have not yet been identified, may be considerable effort for little reward. Certainly, researchers in Japan are acutely aware of the problem of disseminating their work [7] and have recently created accessible registers to combat this [8]. The under-representation of schizophrenia trials from certain countries could also mean that the studies do not exist and that the tradition of evaluation of care for this client group is not strong in these states.

Twenty-five countries have a GDP that predicts no schizophrenia trial activity yet some is apparent. Table 4 shows those states where more than ten studies have been identified. Israel is out ahead, but with the Czech Republic, where GDP may be a more accurate representation of the state's affluence, a close second.

Conclusions

In summary, this hypothesis-generating study finds close correlation between current GDP figures and a country's production of schizophrenia trials. It suggests that some states have been remarkably generous in their commitment to evaluation of care of this group of people. For other wealthy countries, however, there is a suggestion that either substantial numbers of randomised trials remain unidentified, or that there is no great interest in randomised trials relevant to people with schizophrenia

Competing Interests

None declared.

Authors' contributions

CM – helped create the data set, extract data, analyse the results and write the paper

UG – helped create the data set, extract data, analyse the results and write the paper

SB – helped format and write the paper

HGE – helped create data, analyse results and write and format the paper

MF – helped create the data set, extract data, analyse results and write the paper

CEA – thought of the idea, helped create the data set, extract data, analyse results and write and format the paper

Additional material

Additional File 1

Appendix 1. One additional file reproduces the formulae employed for calculations in this study.
Click here for file
[http://www.biomedcentral.com/content/supplementary/1471-244X-3-18-S1.pdf]

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