Consistency of immigrant and country-of-birth suicide rates: A meta-analysis

Martin Voracek

University of Vienna, School of Psychology, Dept. of Basic Psychological Research and Research Methods
(martin.voracek@univie.ac.at)
Background

- Suicidal behavior: complex phenotype
- Psychological, psychiatric, social risk factors for a long time highlighted
- Pathways: multifaceted and intricate
- Also include genetic risk factors – increasingly recognized and investigated, most directly through molecular genetic studies
But also through classic behavior-genetic study formats (family, twin, and adoption studies)

As well as through less conclusive (i.e., merely suggestive), less direct, „exotic“, but nevertheless interesting and informative study designs (e.g., surname, geographic, and MIGRANT studies)

Totality of evidence from these distinctly different genetically informative research strategies suggests genetic risk factors for suicide

Such convergent evidence from very different approaches is corroborative, allows triangulation of probable truth
Family studies of suicide

- Background: design cannot disentangle (i.e., confounds) environmental and genetic effects

- Key finding (e.g., Baldessarini & Hennen, 2004, meta-analysis): suicidal behavior is highly familial ($RR = \text{approx. } 5$)

- Effect stronger for completed than for attempted suicide

- Effect largely independent (disassociated) from transmission patterns of major psychiatric disorders
Twin studies of suicide

- Background: best known and most widely applied classic design of behavior genetics

- Evidence (Voracek & Loibl, 2007, systematic review and meta-analysis): identical (monozygotic) twins much more concordant than fraternal (dizygotic) twins for suicide (concordance rates: 24% vs. 3%; OR > 5)

- Heritability ($h^2$) estimates: 30-55% (for broader phenotype of suicidal behavior)
Adoption studies of suicide

- **Background:** a powerful, classic design of behavior genetics to disentangle the contributions of heredity and environment (focusing on environmental influences)

- **Evidence** (Voracek, 2007, meta-analysis): suicide runs in the biological families of suicided adoptees, but not in those of demographically matched healthy control adoptees alive (rates: 4.0% vs. 0.3%; $RR > 8$)
Surname studies of suicide

- Background: surnames carry information about genetic relatedness vs. distance

- In patrilineal surname systems, a substitute for markers of haplotypes on the Y chromosome

- Surnames behave like a single Y-linked gene with numerous alleles

- Surname studies conceivable as macro-level family studies
Surname studies of suicide

- Design is common in population genetics, but only quite recently introduced to suicidology (by Marusic et al., 2006)

- Rationale: if suicidal behavior runs in families partly due to genetic factors, this should add up and be detectable on the aggregate (societal) level as well

- Key findings so far: different surnames have different suicide risk (Slovenia: Marusic et al., 2006); differences in regional suicide rates correspond to the intranational genetic population structure, as ascertained from surname similarity across regions (Austria: Voracek & Sonneck, 2007)
Geographic studies of suicide

- Background: rankings of national (and regional) suicide rates are conspicuously stable over time (100+ yrs.)

- Cross-national (and regional) variability of suicide rates is large

- These patterns seem not fully or sufficiently accounted for by ascertainment bias, socioeconomic factors, etc.

- There are known geographic (cross-national) differences in frequencies of risk alleles (5-HTTLPR, TPH1, etc.)
Geographic studies of suicide

- So – „Could genetic risk factors partly account for these differences?“ (Kondrichin, 1995; so-called „Finno-Ugrian Suicide Hypothesis“; inter alia, much work due to Andrej Marusic)

- Key findings (studies by Marusic, Farmer, Lester, Voracek, and others): spatial patterns (gradients) of suicide rates across Europe correspond to known gradients of the population genetic landscape of Europe
Migrant study design

- Background: yet another genetically informative design (conceivable as macro-level adoption study, i.e., naturally occurring „adoption“ of adults on a societal level)

- In genetic epidemiology: used to investigate genetic vs. environmental contributions to cancer, diabetes, multiple sclerosis, and other complex, chronic diseases

- In suicide research: underused, undervalued design
Migrant study design: its rationale

- Migrants bring with them specific genetic make-up (including nationally varying genetic risk configurations for diseases and certain behaviors, e.g., suicidality) and environmental factors (homeland culture, personal experiences).

- Homeland culture influence may fade over time spent in host country, but genetic factors do not fade.

- Migrants may well have been less ingrained in their homeland culture (at any rate, they emigrated).
Migrant study design: its rationale

- Migrants are exposed to host country culture and prevailing environmental factors there.
- Eventually, migrants reproduce – importantly, endogamy (marriage among own group) is strong.
- Hence, original genetic make-up (including genetic risk factors) more preserved in 2nd generation than expected by chance (i.e., with random mating).
- Conversely, homeland culture influence may well attenuate among 2nd-generation immigrants.
Migrant studies: their interpretation

- All of the above has obvious implications for evaluating disease frequencies in immigrants:

- Stable disease frequencies in various immigrant groups, continuing to resemble those of their home countries: suggest (albeit not conclusively) possible role of genetic risk factors

- Whereas changing disease frequencies, converging from those seen in home countries to the one of the host country: support environmental factors

- Clearly, test more conclusive when based on 2nd-generation immigrants
Migrant studies of suicide: past & present

- Early studies assessing the resemblance of country-of-birth (COB) and immigrant suicide rates: have originally been designed to demonstrate veridicality/validity of national differences in suicide rates (e.g., Sainsbury & Barraclough, 1968; Lester, 1972)

- Logic (and above interpretation) of migrant study design brought to suicidology by Ferrada-Noli (1997) and Sher (1999)

- We did the first migrant study of suicide for Austria (Voracek, Loibl, Dervic, Kapusta, Niederkrotenthaler, & Sonneck, 2009, *Psychiatry Research*)

- and did the first meta-analysis of migrant studies of suicide (Voracek & Loibl, 2008; *Acta Psychiatrica Scandinavica*)
Austrian migrant study of suicide: Database

- All registered suicides in Austria 1970-2006 ($n = 65206$)
- 2.6% of these ($n = 1724$) were by non-citizens
- Omitted: suicides of stateless persons, cases with unidentified or unclear nationality, and nationalities with <4 cases during study period
- Included: 1439 cases (2.2% of all), from 31 countries
- Successor states of CSSR, USSR, Yugoslavia merged (for clarity and according to suicide rate data availability)
- Available for analysis: 22 immigrant nationalities
Correspondence of COB suicide rates with immigrant suicide rates:

- $r_s = +.45$ (2-tailed $p = .03$)

- $r_s = +.48$ ($p = .04$), with controls for:
  - Average age of suicide victims,
  - Size of immigrant group,
  - National pride,
  - Quality of human conditions (QHC) index in homeland
Meta-analysis of migrant studies of suicide

- Study goal: systematic quantitative synthesis of the world literature on the association of immigrant and COB suicide rates

- Literature search strategies:
  - Essential electronic databases (PubMed, Web of Science, PsycInfo, UMI Dissertations)
  - Ref lists of retrieved studies searched
  - Cited ref search of key papers in Web of Science
Meta-analysis: Methods

- Study inclusion criteria:
  - Non-English reports eligible
  - Unpublished accounts eligible
  - Any study reporting data on suicide rates of at least \( n = 4 \) immigrant groups in a host country eligible (because: \( SE \) of Fisher \( z \)-transformed \( r \) undefined when \( n < 4 \))
  - Independent data (i.e., reports with overlap of study period not included)

- Search yielded:
  - 32 datasets suitable for inclusion (13 in journal articles, 15 in books, 4 in an unpublished dissertation)
Meta-analysis: Methods

- Summary statistics of studies:

- Literature corpus published between 1921 and 2006
- Study periods cover almost entire 20th century: midpoint yr. from early 1910s to late 1990s
- Number of immigrant groups reported in studies: 4 to 29
- Total: about 50 different immigrant nationalities
- 7 host countries: Australia, Austria, Canada, Netherlands, Sweden, UK, USA
Table 1. Summary of immigrant studies of suicide

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Pub type</th>
<th>Period</th>
<th>Mid-point</th>
<th>$r_x$</th>
<th>$n$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bercz et al.</td>
<td>Australia</td>
<td>J</td>
<td>1962–1966</td>
<td>1964</td>
<td>0.809</td>
<td>14</td>
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<tr>
<td>Burville et al.</td>
<td>Australia</td>
<td>J</td>
<td>1962–1971</td>
<td>1966.5</td>
<td>0.841</td>
<td>16</td>
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<tr>
<td>Whitlock</td>
<td>Australia</td>
<td>J</td>
<td>1984–1990</td>
<td>1977</td>
<td>0.787</td>
<td>16</td>
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<tr>
<td>Hassan</td>
<td>Australia</td>
<td>B</td>
<td>1984–1990</td>
<td>1977</td>
<td>0.787</td>
<td>16</td>
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<tr>
<td>Burville</td>
<td>Australia</td>
<td>J</td>
<td>1977–1990</td>
<td>1984.5</td>
<td>0.802</td>
<td>16</td>
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<tr>
<td>Voracek et al.</td>
<td>Austria</td>
<td>U</td>
<td>1970–2006</td>
<td>1984.5</td>
<td>0.453</td>
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<tr>
<td>Kliever &amp; Ward</td>
<td>Canada</td>
<td>J</td>
<td>1964–1973</td>
<td>1966.5</td>
<td>0.619</td>
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<tr>
<td>Maier et al.</td>
<td>Canada</td>
<td>J</td>
<td>1990–1997</td>
<td>1990</td>
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<td>Mermot et al.</td>
<td>Belgium</td>
<td>B</td>
<td>1984–1990</td>
<td>1984.5</td>
<td>0.802</td>
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<tr>
<td>Raleigh &amp; Babarajin</td>
<td>England</td>
<td>J</td>
<td>1978–1985</td>
<td>1984.5</td>
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<td>Gannon et al.</td>
<td>The Netherlands</td>
<td>J</td>
<td>1996–2004</td>
<td>1997.5</td>
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<tr>
<td>Johansson et al.</td>
<td>Sweden</td>
<td>J</td>
<td>1966–1990</td>
<td>1987.5</td>
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<tr>
<td>Ferrada-Noli</td>
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<td>J</td>
<td>1965–1991</td>
<td>1989</td>
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<tr>
<td>Westman et al.</td>
<td>Sweden</td>
<td>J</td>
<td>1990–1999</td>
<td>1995.5</td>
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<tr>
<td>Freney et al.</td>
<td>USA (Pittsburgh)</td>
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<td>1911–1915</td>
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<td>Freney et al.</td>
<td>USA (Boston)</td>
<td>B</td>
<td>1911–1915, 1918–1919</td>
<td>1914.5</td>
<td>0.699</td>
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<tr>
<td>Freney et al.</td>
<td>USA (New York)</td>
<td>B</td>
<td>1911–1920</td>
<td>1915.5</td>
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<tr>
<td>Freney et al.</td>
<td>USA (Philadelphia)</td>
<td>B</td>
<td>1911–1920</td>
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<tr>
<td>Freney et al.</td>
<td>USA (Chicagow, NY)</td>
<td>B</td>
<td>1911–1920</td>
<td>1915.5</td>
<td>0.714</td>
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<tr>
<td>Freney et al.</td>
<td>USA (Chicago)</td>
<td>B</td>
<td>1912–1921</td>
<td>1916.5</td>
<td>0.679</td>
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<tr>
<td>Schmid et al.</td>
<td>USA</td>
<td>B</td>
<td>1914–1925</td>
<td>1919.5</td>
<td>0.367</td>
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<tr>
<td>Stearns</td>
<td>USA (Massachusetts)</td>
<td>J</td>
<td>1915–1920</td>
<td>1915</td>
<td>0.764</td>
<td>11</td>
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<tr>
<td>Freney et al.</td>
<td>USA</td>
<td>B</td>
<td>1915–1924</td>
<td>1920</td>
<td>0.389</td>
<td>10</td>
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<td>Freney et al.</td>
<td>USA (Chicago)</td>
<td>B</td>
<td>1919–1921</td>
<td>1920</td>
<td>0.657</td>
<td>13</td>
</tr>
<tr>
<td>Freney et al.</td>
<td>USA (St. Paul, MN)</td>
<td>B</td>
<td>1920–1924</td>
<td>1922</td>
<td>0.800</td>
<td>7</td>
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<td>Freney et al.</td>
<td>USA</td>
<td>B</td>
<td>1920–1924</td>
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<td>4</td>
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<tr>
<td>Wendling et al.</td>
<td>USA (East Bay region)</td>
<td>D</td>
<td>1930–1942</td>
<td>1937</td>
<td>0.836</td>
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<td>Wendling et al.</td>
<td>USA (San Francisco)</td>
<td>D</td>
<td>1930–1942</td>
<td>1937</td>
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<td>1930–1942</td>
<td>1937</td>
<td>0.836</td>
<td>14</td>
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<tr>
<td>Dublin et al.</td>
<td>USA</td>
<td>B</td>
<td>1959–1960</td>
<td>1959</td>
<td>0.909</td>
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<td>Kramer et al.</td>
<td>USA</td>
<td>B</td>
<td>1959–1961</td>
<td>1960</td>
<td>0.815</td>
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<td>Lester et al.</td>
<td>USA</td>
<td>J</td>
<td>1980–1981</td>
<td>1980</td>
<td>0.868</td>
<td>3</td>
</tr>
</tbody>
</table>

Country, host country, pub type, publication type (J, journal article; B, book; U, unpublished data; D, unpublished dissertation; period, study period; mid-point, mid-point (year) of study period; $r_x$, rank-order correlation coefficient for the association of immigrant and country-of-birth suicide rates; $n$, number of immigrant nationalities (countries) included in the study; T, M, F, total, male, female suicide rates (or nationalities) on which the analysis of an individual study is based.

*Study not included in the meta-analysis (complete overlap of study period with another study).
†Study not included in the meta-analysis ($r_x$ based on too few immigrant nationalities, $n < 4$).
Forest plot: Total suicide rates ($r_s = +.65$, $p < 10^{-9}$)
Forest plot: Male suicide rates ($r_s = +.69, p < 10^{-9}$)

<table>
<thead>
<tr>
<th>Study</th>
<th>Correlation</th>
<th>Total</th>
</tr>
</thead>
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<tr>
<td>AUS 1962–1971</td>
<td>0.841</td>
<td>16</td>
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<td>AUS 1968–1980</td>
<td>0.742</td>
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<td>AUS 1979–1990</td>
<td>0.802</td>
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<tr>
<td>CAN 1969–1973</td>
<td>0.519</td>
<td>29</td>
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<tr>
<td>ENG 1970–1972</td>
<td>0.586</td>
<td>15</td>
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<td>ENG 1979–1983</td>
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<td>NLD 1996–2004</td>
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<td>SWE 1986–1989</td>
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<tr>
<td>SWE 1994–1999</td>
<td>0.750</td>
<td>7</td>
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<tr>
<td>USA 1959–1961</td>
<td>0.881</td>
<td>12</td>
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<tr>
<td></td>
<td>0.693</td>
<td>148</td>
</tr>
</tbody>
</table>
Forest plot: Female suicide rates ($r_s = +.63$, $p < 10^{-9}$)
Evaluation of meta-analytic findings

- Fixed-effect model of meta-analysis: justified (cross-study effect heterogeneity neither substantial nor significant)

- Subgroup analysis: no effect heterogeneity across publication types

- Sensitivity analysis: no study influential for overall effect (still highly significant when removing one study at a time from the model)

- Cumulative meta-analysis: effect already significant from earliest studies onwards, and stable later on

- Publication bias tests: no signs thereof

- Effect robustness (Fail-safe N): 100s of additional („missed“) studies with zero effect (never observed) necessary to bring observed overall effect to insignificance (very unlikely; so effect is robust)
Regression (individual datapoints pooled across all studies) of immigrant suicide rates simultaneously on COB suicide rates, dummy-coded host countries, and study period midpoint yr.

- Regression models throughout significant
- only significant predictor: COB rates
- nil effects of host country and study period
Limitations of available evidence (many...)

- Migrant study findings are only suggestive, not conclusive.

- Specifically, migrant studies cannot narrow down the kinds of genetic factors they indicate.

- The effect is entirely ecologic (i.a., a group-level finding).

- The effect (correlational) says nothing about increases (on the absolute level) in suicide risk among immigrant groups.

- As with other observational designs in epidemiology, many variables beyond investigational control and thus potential confounders (here: time of residence, demographic composition, suicide methods, etc.).
Limitations of available evidence (many...)

- Nationality is a fallible person variable – blurs ethnic and population genetic boundaries

- Migrants are self-selected group, demographically biased, not representative of home country population

- Existing literature covers classic major immigration countries (Australia, Canada, UK, USA), but no evidence for important further ones (Denmark, Germany, Israel, New Zealand, etc.)

- By geographic location, some countries investigated (Australia, Canada, USA) almost exclusively host overseas immigrants, whereas others (Austria, Sweden, UK) not
Further gaps in the literature – future directions

- Variant of migrant study design: investigate patterns of suicide prevalence in repatriates (e.g., in the USA)

- Fusion of migrant and adoption study designs: investigate suicide risk of international adoptees (now feasible for some countries, e.g., Sweden)
Conclusions

- Key finding: immigrants appear to carry their (relative) risk of suicide from their homelands to the host country

- This by itself is an intriguing finding (e.g., meta-analysis already cited in a highly-cited review paper on suicide in *Lancet*, by Hawton & van Heeringen, 2009)

- Applying logic of migrant study design of genetic epidemiology, this effect (correspondence) is consistent with assumption of population differences in prevalence of genetic risk factors for suicide
Conclusions

- Effect apparently of some generality (meta-analytically based on 50 immigrant nationalities in 7 major host countries located on 3 continents, and study periods spanning entire 20th century)

- This refutes previous speculations of allegedly narrow effect (e.g., specific to certain birth cohorts or certain host country characteristics)

- Also interesting: effect unchanged, although direction of global migration significantly changed (1st-half 20th century: mainly from Europe to Anglo-American sphere; vs. 2nd-half 20th century: mainly from threshold and developing countries to European and Anglo-American countries)
Conclusions

- Interesting: effect shows up despite known sources of unreliability working against it: e.g., small immigrant groups yield unstable suicide rates, cross-national and cross-temporal quality differences in suicide ascertainment

- Further surprising: studies reporting zero or even negative correlations between immigrant and COB suicide rates are unknown (very different from similar studies of other outcomes: homicide rates, mortality from motor vehicle accidents, all other violent deaths)

- Finally, so far one study shows effect extends to 2nd-generation immigrants (Sweden: Hjern & Allebeck, 2002)
THANK YOU! – And: questions, please!