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

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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

Background

- 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* = 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 conspiciously 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)

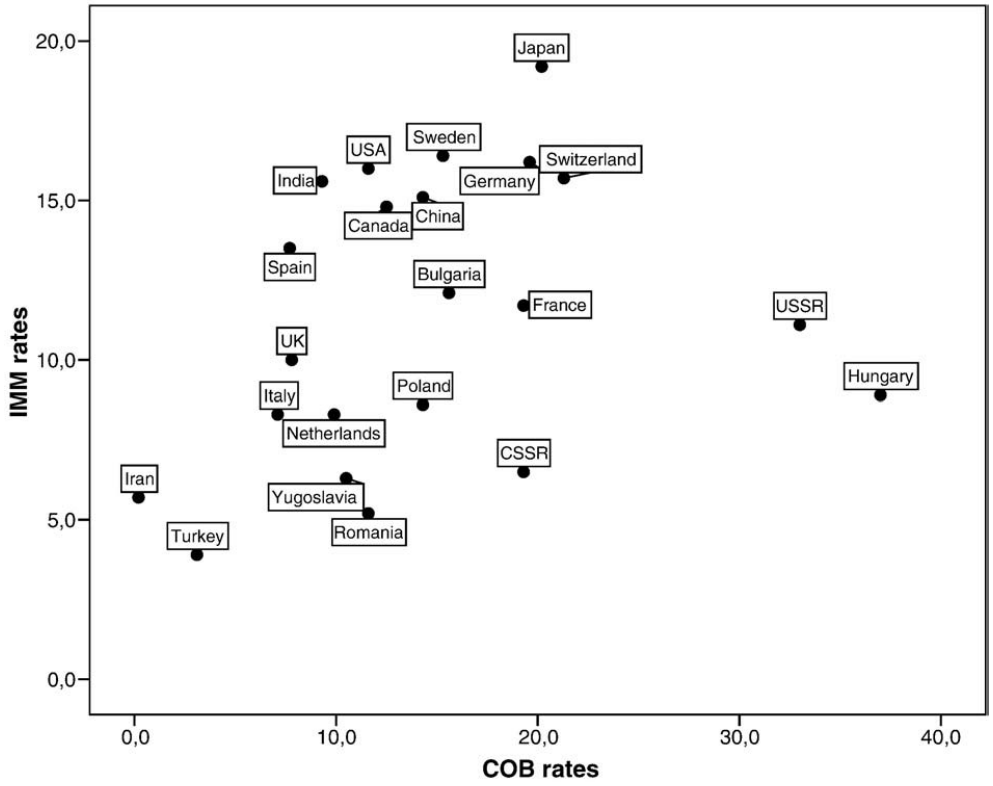
- Logic (and above interpretation) of migrant study design brought to suicidology by Ferrada-Noli (1997) and Sher (1999)

- 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

Austrian migrant study of suicide: Results



- 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

Meta-analysis: Study details

Table 1. Summary of immigrant studies of suicide

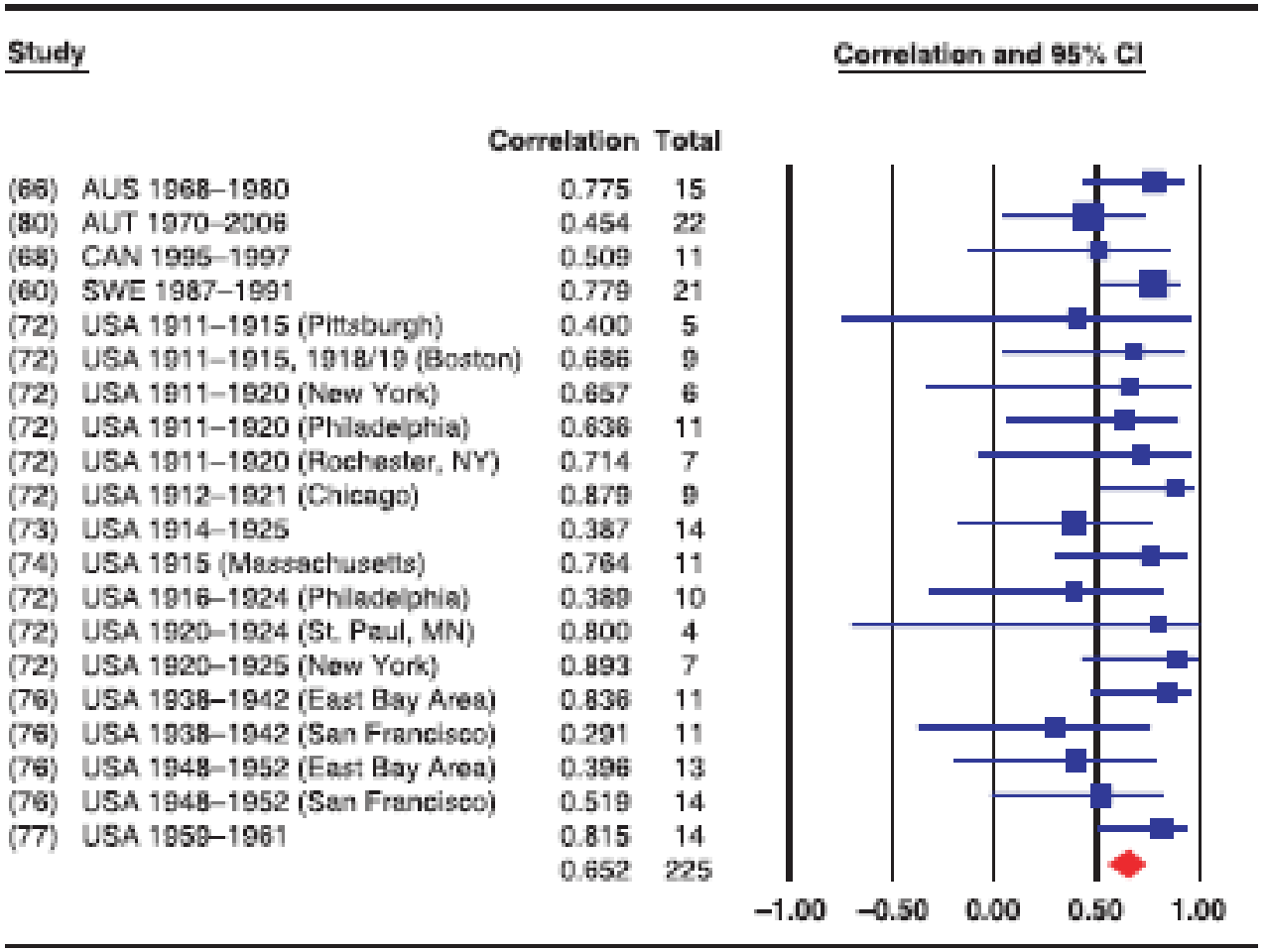
Study	Country	Pub type	Period	Mid-point	r_s			n		
					T	M	F	T	M	F
Burvill et al. (58)*	Australia	J	1962–1966	1964		0.809	0.741		14	14
Burvill et al. (64)	Australia	J	1962–1971	1966.5		0.841	0.832		16	16
Whitlock (65)*	Australia	J	1965–1967	1966		0.787	0.791		16	16
Hassan (66)	Australia	B	1968–1980	1974	0.775	0.742	0.611	15	13	13
Burvill (67)	Australia	J	1979–1990	1984.5		0.802	0.709		11	11
Voracek et al. (80)	Austria	U	1970–2006	1988	0.453			22		
Kliewer & Ward (59)	Canada	J	1969–1973	1971		0.519	0.505		29	29
Malenfant (68)	Canada	J	1995–1997	1996	0.509			11		
Marmot et al. (69)	England	B	1970–1972	1971		0.566	0.699		15	15
Raleigh & Balarajan (61)	England	J	1979–1983	1981		0.907	0.604		15	15
Garssen et al. (79)	The Netherlands	J	1996–2004	2000		0.392	0.516		22	22
Johansson et al. (70)	Sweden	J	1986–1989	1987.5		0.214	0.286		8	8
Ferrada-Noli (60)	Sweden	J	1987–1991	1989	0.779			21		
Westman et al. (71)	Sweden	J	1994–1999	1996.5		0.750	0.786		7	7
Frerey (72)	USA (Pittsburgh)	B	1911–1915	1913	0.400			5		
Frerey (72)	USA (Boston)	B	1911–1915, 1918–1919	1914.6	0.686			9		
Frerey (72)	USA (New York)	B	1911–1920	1915.5	0.657			6		
Frerey (72)	USA (Philadelphia)	B	1911–1920	1915.5	0.636			11		
Frerey (72)	USA (Rochester, NY)	B	1911–1920	1915.5	0.714			7		
Frerey (72)	USA (Chicago)	B	1912–1921	1916.5	0.879			9		
Schmid (73)	USA	B	1914–1925	1919.5	0.387			14		
Stearns (74)	USA (Massachusetts)	J	1915	1915	0.764			11		
Frerey (72)	USA (Philadelphia)	B	1916–1924	1920	0.389			10		
Cavan (75)*	USA (Chicago)	B	1919–1921	1920	0.687			13		
Frerey (72)	USA (St Paul, MN)	B	1920–1924	1922	0.800			4		
Frerey (72)	USA (New York)	B	1920–1925	1922.5	0.893			7		
Wendling (76)	USA (East Bay region)	D	1936–1942	1940	0.836			11		
Wendling (76)	USA (San Francisco)	D	1936–1942	1940	0.291			11		
Wendling (76)	USA (East Bay region)	D	1948–1952	1950	0.396			13		
Wendling (76)	USA (San Francisco)	D	1948–1952	1950	0.519			14		
Dublin (57)*	USA	B	1959	1959	0.909	0.952	0.559	12	10	10
Kramer et al. (77)	USA	B	1959–1961	1960	0.815	0.881	0.676	14	12	12
Lester (78)†	USA	J	1980	1980	0.866	1.000	1.000	3	3	3

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_s, 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.

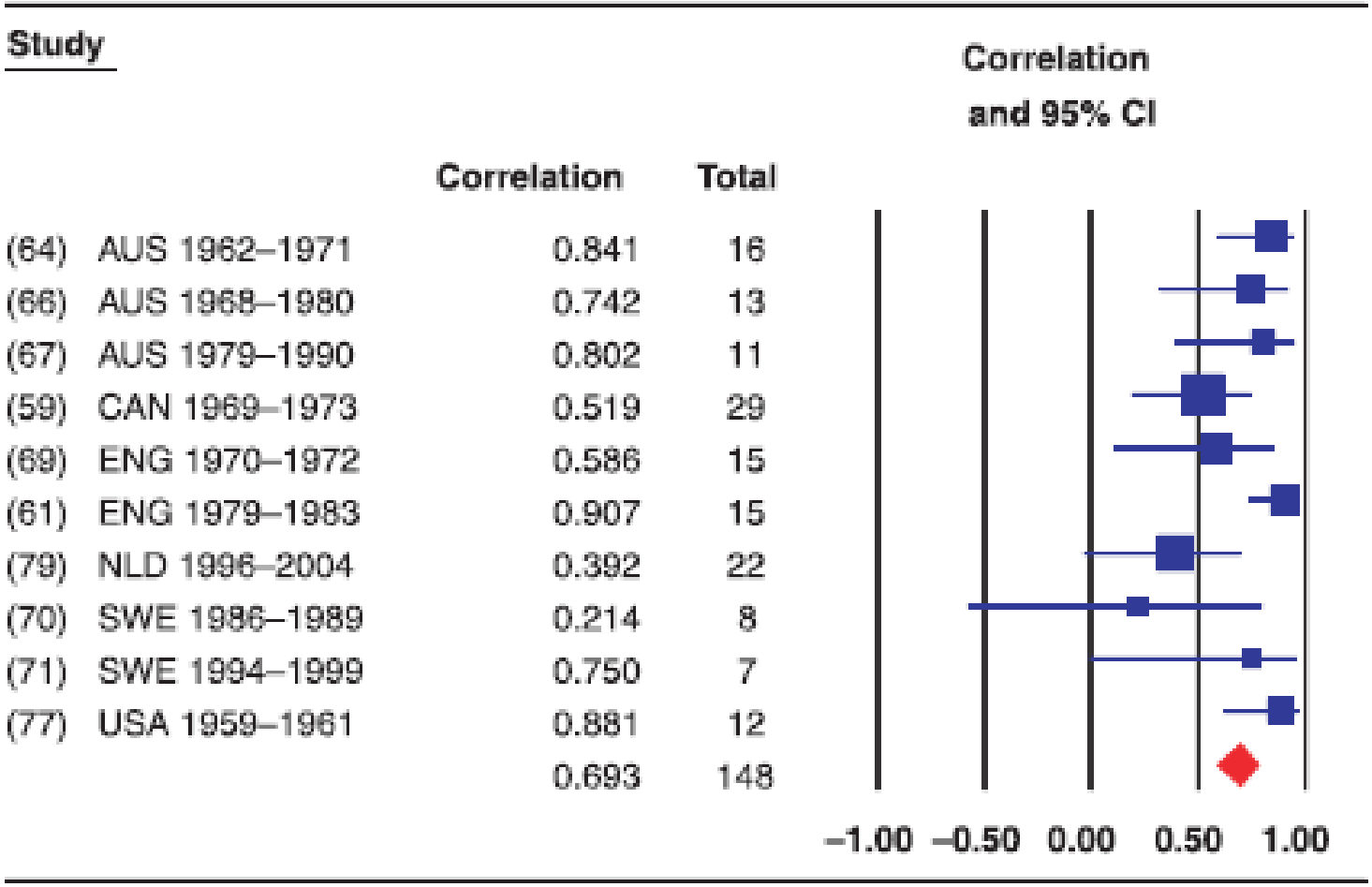
*Study not included in the meta-analysis (complete overlap of study period with another study).

†Study not included in the meta-analysis (r_s based on too few immigrant nationalities, $n < 4$).

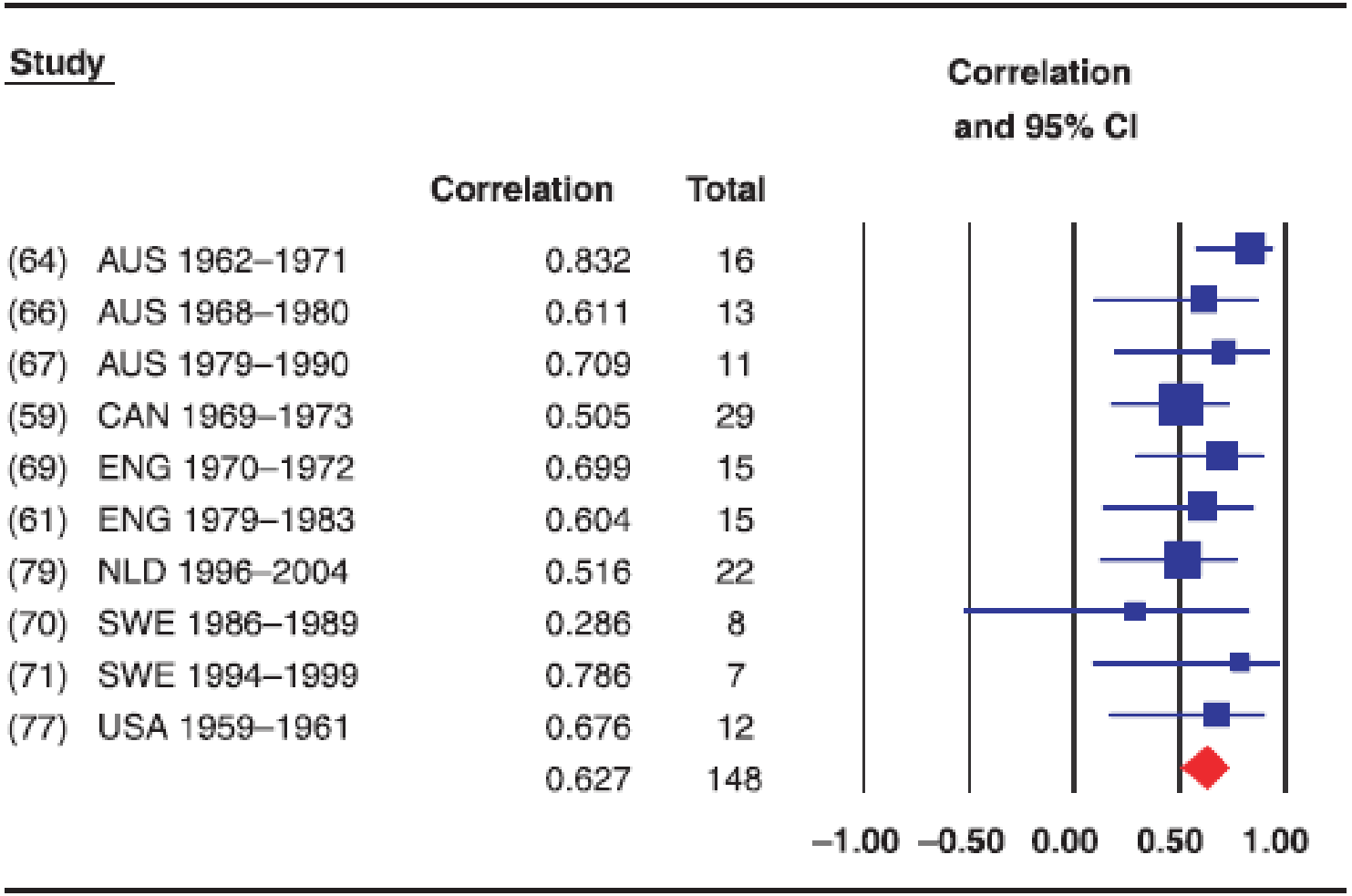
Forest plot: Total suicide rates (r_s = +.65, $p < 10^{-9}$)



Forest plot: Male suicide rates (r_s = +.69, $p < 10^{-9}$)



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)

Effect generalizability across space and time

Table 2. Association of immigrant and country-of-birth suicide rates: generalizability across space and time

IMM rates	Predictor	β	*t*	*P*	*r*	r_p	r_{sp}
Total	[Constant]	–	0.106	0.915	–	–	–
	COB rates	0.642	13.512	< 0.001	0.642	0.642	0.642
	Dummy AUS	−0.005	−0.089	0.929	−0.003	−0.006	−0.004
	Dummy AUT	−0.007	−0.096	0.924	−0.004	−0.006	−0.005
	Dummy CAN	−0.005	−0.079	0.937	−0.003	−0.005	−0.004
	Dummy ENG	na	na	na	na	na	na
	Dummy NLD	na	na	na	na	na	na
	Dummy SWE	0.006	0.087	0.931	0.009	0.005	0.004
	Period	0.004	0.044	0.965	0.001	0.003	0.002
Model summary: $F(6,260) = 30.438$, $\bar{r}^2 = 0.413$, $P < 0.001$							
Males	[Constant]	–	−0.156	0.799	–	–	–
	COB rates	0.683	12.585	< 0.001	0.681	0.681	0.681
	Dummy AUS	0.086	0.463	0.644	0.017	0.034	0.025
	Dummy AUT	na	na	na	na	na	na
	Dummy CAN	0.002	0.010	0.992	−0.027	0.001	0.001
	Dummy ENG	0.060	0.337	0.737	0.009	0.025	0.018
	Dummy NLD	0.076	0.179	0.858	0.013	0.013	0.010
	Dummy SWE	0.082	0.222	0.824	0.011	0.016	0.012
	Period	0.001	0.084	0.933	0.024	0.006	0.005
Model summary: $F(7,183) = 22.718$, $\bar{r}^2 = 0.465$, $P < 0.001$							
Females	[Constant]	–	−0.212	0.740	–	–	–
	COB rates	0.643	11.388	< 0.001	0.643	0.644	0.643
	Dummy AUS	0.091	0.473	0.637	0.001	0.035	0.027
	Dummy AUT	na	na	na	na	na	na
	Dummy CAN	0.118	0.525	0.600	0.012	0.039	0.030
	Dummy ENG	0.102	0.415	0.679	0.009	0.031	0.023
	Dummy NLD	0.081	0.165	0.853	0.001	0.014	0.010
	Dummy SWE	0.092	0.239	0.811	0.009	0.018	0.014
	Period	0.001	0.131	0.896	0.027	0.010	0.007
Model summary: $F(7,183) = 18.611$, $\bar{r}^2 = 0.416$, $P < 0.001$							

IMM rates, immigrant suicide rates (dependent variable in regression models); [Constant], intercept of regression models; COB rates, country-of-birth suicide rates; Dummy AUS, AUT, CAN, ENG, NLD, SWE, dummy-coded host country (USA coded with zeros on all dummy variables); na, host country not available for analysis; Period, mid-point of study period; β, standardized regression coefficient for predictor; *t*, respective *t*-statistic; *P*, respective *P*-value; *r*, r_p, r_{sp}, zero-order, partial and semipartial correlation coefficient between predictor and dependent variable; *F*, respective *F*-statistic for regression model; $\bar{r}^2$, variance explained by regression model.

- 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!