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Contagion models for the transmission of drug abuse among propinquity-of-rearing defined acquaintances: A Swedish national study

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ABSTRACT

Background: Can we validate a contagion model for drug abuse (DA) in Propinquity-of-Rearing Defined Acquaintances (PRDAs)?
Methods: PRDAs were defined as pairs of same-age males born 1975–1990 who grew up within 2 km of each other, one of whom (PRDA1) being first registered for DA in national registries. Using adult residential location, we predicted, using regression splines, proximity-dependent risk for DA first registration in a second PRDA (PRDA2) within 3 years of PRDA1's registration.
Results: In 181,743 PRDA pairs, the best-fit model, controlling for age and PRDA2 community risk, included 2 slopes of proximity-risk relationships in childhood and three in adulthood. Risk for DA in PRDA2 was strongly predicted by childhood proximity to PRDA1: 0 to 0.5 km – Hazard ratio (HR) per kilometer 0.52 and 0.6–2 km 0.78. HRs for PRDA2 as a function of adult proximity to PRDA1 were: 0–1 km 0.887, 1–75 km 0.996 and > 75 km 0.9997. Proximity-dependent PRDA2 risk was moderated by age, familial risk and educational attainment, attenuated by increasing PRDA1-PRDA2 age differences and stronger for older to younger versus younger to older pairs.
Conclusions: Transmission of DA risk between acquaintances growing up together was attenuated by increasing distance in adulthood. Strength of the acquaintance, indexed by childhood propinquity and age difference, modified transmission strength. The impact of adult proximity on transmission was reduced in acquaintances with higher resistance to DA due to older age, higher educational attainment or lower familial risk. Our results support the validity of DA contagion models.

1. Introduction

Transmission within social networks or "social contagion" (Christakis and Fowler, 2013) has been demonstrated for a range of human traits and disorders including obesity (Christakis and Fowler, 2007), alcohol intake (Rosenquist et al., 2010), depression (Rosenquist et al., 2011), happiness (Fowler and Christakis, 2008), and smoking (Christakis and Fowler, 2008). While models of contagion for drug abuse (DA) have been postulated (Anthony, 2006; Dishion and Dodge, 2006), we are unaware of statistical evaluations of such models in epidemiological samples. In a previous paper, we have used both geographical categories (cohabitation vs residence in small communities vs. in large metropolitan areas) (Kendler et al., 2019) to show evidence for transmission of DA in relatives (i.e. parent-offspring and sibling pairs).

The question pursued in this paper is whether in the absence of self-report data on PRDAs, which are available only in special samples (e.g. the Framingham study), is it possible, in large epidemiological samples with geo-coded data on residence in childhood, to identify "acquaintances" who in adulthood can be shown to transmit risk of DA to one another? This is an important methodological question. If the answer is positive, it opens up a range of possible investigations in large representative samples of the nature of person-to-person transmission of DA, and its potential modification by risk and protective factors.

This report has three specific goals:

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1 Define Propinquity-of-Rearing Defined Acquaintances (PRDA) as same-aged male-male pairs growing up together in close geographical proximity.
2 Determine, when one PRDA (PRDA1) has a first DA registration, whether the subsequent risk for DA onset in the second PRDA (PRDA2) is influenced by the current geographical proximity of the pair.
3 Select indices of susceptibility to DA and examine whether, as measures of "immunity," they attenuate the impact of the PRDA1-PRDA2 proximity on risk for DA onset in PRDA2. We could not meaningfully conduct such analyses in our prior samples of close relatives because they shared many of these risk indices.

2. Methods

This study utilized several Swedish population-based registers with national coverage. Records are linked using unique personal identification numbers, replaced by anonymous serial numbers to maintain confidentiality. The study was approved by the Regional Ethical Review Board of Lund University.

2.1. Sample

From the registers, we selected all male individuals born in Sweden from 1975 to 1990. For all individuals, we included yearly (1975–2015) information about place of residence. The location of each individual has exact coordinates which, for confidentiality reasons, were delivered to us truncated into 250 × 250 m squares from which we calculated distances between places of residence. Based on this information, we created all possible pairs of individuals (potential acquaintances) born the same year and residing in the same geographical area. Such individuals were highly likely, given the distribution of school districts in Sweden, to be classmates at the same school. The geographical areas (Small Areas for Market Statistics: SAMS) are defined by Statistics Sweden to represent geographically distinct communities. There are approximately 9200 SAMS throughout Sweden, with an average population of 1000. Among the potential acquaintance pairs, all biological relatives up to first cousins and step-siblings were excluded. For each acquaintance pair, we measured the distance in meters at every year during ages 0 to 15. In our analyses, we required that the pair share the same SAMS for at least 12 out of their first 15 years and that they resided in the same SAMS at age 15. We then calculated the mean number of meters between individuals in a pair called "distance in childhood."

2.2. Key variables

Our database included dates of first registration of Drug Abuse (DA) at ages 15–60 (for details see appendix). We then selected all pairs where at least one member (whom we termed Propinquity-of-Rearing Defined Acquaintances-1 [PRDA1]) was registered for DA and measured the distance between them at the time of the first registration. This measure we call "distance in adulthood." The follow-up time for PRDA2 began the day of DA registration for PRDA1 and continued until registration for DA, death, emigration or end of follow-up (3 years after PRDA1's registration). We also included, to control for all contextual effects of PRDA2's area of residence, SAMS density, which equaled the proportion of DA in the SAMS area of individuals with ± 5 years age difference to PRDA2 with a registration of DA within a 3-year interval around the year of PRDA1's registration.

For each individual, we calculated a familial risk score (FRS) for externalizing behavior based on the morbid risk in their first, second and third-degree relatives for Drug Abuse, Criminal Behavior or Alcohol Use Disorder, disorders which, in Sweden, share a substantial proportion of their genetic and environmental risk (Kendler et al., 2016). For details, see the appendix. We also examined individual academic achievement obtained from the National School Registry as a grade point average at the end of grade nine (usually age 16). From 1988 to 1997 the score was expressed on a scale between 1 (lowest) and 5 (overall mean was 3.2). From 1998 and onwards the score was expressed on scale between 10 (lowest) and 320 (overall mean was 207). For each year and by gender, we standardized the grade score into a Z-score with mean 0 and SD 1.

To refine our definition of PRDAs, we investigated, in 294,016 potential acquaintance-pairs who both resided in the same SAMS for ≥ 12 of their first 15 years, the % DA in PRDA2 within 3 years of PRDA1's DA registration as a function of distance in childhood. Appendix table 1 depicts a monotonic relationship between proximity of the PRDAs and the risk of "transmitted" DA in adulthood. We modeled these results utilizing a range of functions (appendix table 2). The best fit model required splines at 1 and 2 km. Proximity in childhood significantly predicted later DA transmission for pairs residing within 0–1 and 1–2 km of each other but not beyond 2 km (appendix table 3). Therefore, for these analyses, we focused on PRDA pairs who lived in childhood within 2 km of each other.

2.3. Statistical methods

We then performed Cox proportional hazards models for the risk of DA in PRDA2 in the three years after PRDA1's first DA registration as a function of the distance between PRDA1 and PRDA2 in childhood and at the time of PRDA1's registration controlling for SAMS density for PRDA2 and age at registration in PRDA1. In our Cox analyses, we examined various functions to best capture the relationship between childhood and adult distance and PRDA2 risk, (e.g., linear, quadratic, logarithmic, splines) and chose the best fit model by Akaike's information criteria (AIC) (Akaike, 1987). Both individuals in certain acquaintance pairs resided at the same place of residence at age 15 as they did when PRDA1 was registered for DA. To unconfound the effects of distance in childhood and adulthood on transmission of DA, these pairs were excluded from further analysis.

For our main analyses, we used Cox proportional hazards model with time to DA in PRDA2 during follow-up, and where the predictor of primary interest was distance between PRDA1 and PRDA2 at PRDA1's first registration. We tested the proportionality assumption by including an interaction term between log of time and the distance measures. We controlled for the fact that one PRDA1 may have multiple PRDA2s with a robust sandwich estimator. In an additional acquaintanceship model, we included a separate stratum for each unique PRDA1, allowing each PRDA pair to have a separate baseline hazard function.

The next analyses first included FRS and Academic achievement as covariates and then tested them for interactions with distance in adulthood using linear probability models. Finally, we expanded our database to also include PRDA pairs that were born 1–5 years apart. In a linear probability model, we tested the interaction between distance in adulthood and age difference as well as the interaction between distance in adulthood and if PRDA1 was older/younger than PRDA2. To simplify the analyses by including only one interaction term, we modelled distance as a natural log function. All statistical analyses were performed in SAS 9.4 (SAS Institute Inc., 2012).

3. Results

3.1. Definition of propinquity-of-rearing defined acquaintances (PRDAs)

We identified 181,743 unique PRDA pairs including 28,027 unique PRDA1s. 5809 of these had one PRDA2; 16,924 had 2–10 PRDA2s; 3980 had 11–20 PRDA2s; and 1314 had 21 or more PRDA2s. Table 1 gives basic descriptive information on these PRDA pairs. Risk for first DA registration in PRDA2s in the 3-year follow-up period was 2.1%. The average PRDA1-PRDA2 distance was much shorter when PRDA2 was affected (44.8 km) versus not affected (78.1 km). PRDA2s who developed DA were younger, had a higher familial risk, lower academic

Table 1
Descriptive Statistics on Propinquity-of-Rearing Defined Acquaintances (PRDA) from the Swedish population where at least one in the pair (PRDA1) are registered for Drug Abuse[a].

	Male –Male Pairs
N pairs	181,743
Drug Abuse % in PRDA2 (within 3 years)	2.06%
PRDA 2 affected with Drug Abuse	
Distance in adulthood from PRDA1 (Km) 25th 50th 75th percentile	1-4-18
Distance in adulthood from PRDA1 (Km) - mean	44.8 (116)
Distance in childhood from PRDA1 (Km) -mean	0.54 (0.42)
Age at Registration in PRDA1	22.4 (3.5)
SAMS Density PRDA2	3.3 (2.5)
Familial risk for PRDA2	0.80 (1.47)
Academic Achievement of PRDA2	−0.66 (1.05)
PRDA 2 not affected with Drug Abuse	
Distance in adulthood from PRDA1 (Km) 25th 50th 75th percentile	2-9-61
Distance in adulthood from PRDA1 (Km) - mean	78.1 (160)
Distance in childhood from PRDA1 (Km) -mean	0.62 (0.45)
Age at Registration in PRDA1	24.8 (4.4)
SAMS Density PRDA2	2.38 (2.1)
Familial risk for PRDA2	0.00 (0.99)
Academic Achievement of PRDA2	0.13 (0.95)

[a] Mean (SD) values when nothing else noted.

achievement, and lived in areas with a higher DA density than PRDA2s who did not develop DA.

3.2. Transmission of DA between PRDAs in adulthood

Within PRDA pairs, we jointly fitted models describing the relationship between DA transmission and geographical proximity in childhood and in adulthood. The best fit model included one spline at 0.5 km for proximity in childhood and two splines – at 1 and 75 km – for proximity in adulthood (appendix table 4). Utilizing these parameters, we examined six models predicting the HR for DA in PRDA2 in the three years after PRDA1's first registration (Table 2). Model A, including only childhood proximity data, showed stronger childhood proximity effects within 1 km than between 1 and 2 km. Model B examines only proximity effects in adulthood, e.g. within 3 years of PRDA1's first DA registration. We see strong proximity effects within one kilometer, modest effects for those living 1–75 km apart and no significant impact of distance for those residing > 75 km apart.

Model C includes both the childhood and adulthood data, and produces parameter estimates similar to those seen in models A and B. The results of model C are depicted in blue with 95% CIs in Fig. 1. Compared to an PRDA2 living within 1 km of PRDA1 at the time of his DA registration, the risk for a DA registration in PRDA2 residing 5, 10, 25, 50, 100 and 150 km away equals 0.87 (0.76; 1.01); 0.86 (0.75; 0.99); 0.81 (0.71; 0.93); 0.74 (0.64; 0.86); 0.67 (0.57; 0.79); 0.66 (0.56; 0.77), respectively.

Models A–C utilized PRDA pairs. Model D examines acquaintanceships which control for many background factors as we examine risk for DA in the multiple PRDAs of PRDA1 resulting from their relative proximity in childhood and adulthood. Because of smaller sample sizes, especially of PRDA pairs living very nearby in childhood, the CIs increase substantially especially for the distances in childhood and between 0 and 1 km in adulthood. The observed effects are no longer significant for these parameters. However, in the acquaintanceships, we see an effect of proximity on DA transmission in adulthood between 1 and 75 km and > 75 km that is very similar to that seen in our PRDA pair analyses. Fig. 1 compares results from models C and D.

3.3. Moderation of transmission by three susceptibility factors

Contagion models typically contain indices of susceptibility (or

Table 2
Results from Cox Proportional Hazards models on pairs of Propinquity-of-Rearing Defined Acquaintances from the Swedish population where at least one in the pair are registered for Drug Abuse. Numbers are Hazard Ratios and 95% CIs.

Nature of Sample	Model A PRDA Pair	Model B PRDA Pair	Model C PRDA Pair	Model D Acquaintance-ship	Model E PRDA Pair	Model F PRDA Pair
Distance in childhood between acquaintances: 0-0.5 Km	0.50 (0.41, 0.63)		0.52 (0.42, 0.65)	0.84 (0.64; 1.10)	0.61 (0.49, 0.76)	0.57 (0.45; 0.71)
Distance in childhood between acquaintances: 0.6-2 Km	0.76 (0.68; 0.85)		0.78 (0.69; 0.88)	1.13 (0.80; 1.62)	0.83 (0.74; 0.94)	0.79 (0.71; 0.89)
Age of PRDA1 and PRDA2 at PRDA1's first DA registration	0.87 (0.86; 0.88)	0.89 (0.88; 0.89)	0.88 (0.87; 0.89)	–	0.88 (0.87; 0.89)	0.88 (0.87; 0.89)
SAMS Density for PRDA2 at year of Drug Abuse registration in PRDA1	1.13 (1.11; 1.14)	1.13 (1.12; 1.15)	1.13 (1.12; 1.15)	1.09 (1.07; 1.11)	1.10 (1.09; 1.12)	1.11 (1.10; 1.13)
Distance between PRDA2 and PRDA1 at Drug Abuse registration in PRDA1 (0-1 km)		0.8500 (0.7355; 0.9824)	0.8870 (0.7677; 1.0248)	0.9599 (0.7997; 1.1523)	0.9637 (0.8349; 1.1124)	1.0109 (0.8708; 1.1735)
Distance between PRDA2 and PRDA1 at Drug Abuse registration in PRDA1 (1.1 – 75 km)		0.9959 (0.9943; 0.9975)	0.9964 (0.9947; 0.9980)	0.9963 (0.9940; 0.9986)	0.9974 (0.9958; 0.9991)	0.9980 (0.9964; 0.9997)
Distance between PRDA2 and PRDA1 at Drug Abuse registration in PRDA1 (75.1 – km)		0.9997 (0.9993; 1.0001)	0.9997 (0.9993; 1.0000)	0.9993 (0.9987; 0.9998)	0.9997 (0.9993; 1.0001)	0.9999 (0.9995; 1.000)
Log of Familial Risk Score in PRDA2					3.63 (3.40; 3.87)	
Low Academic Achievement in PRDA2 (n = 176,681)						1.92 (1.87; 1.97)

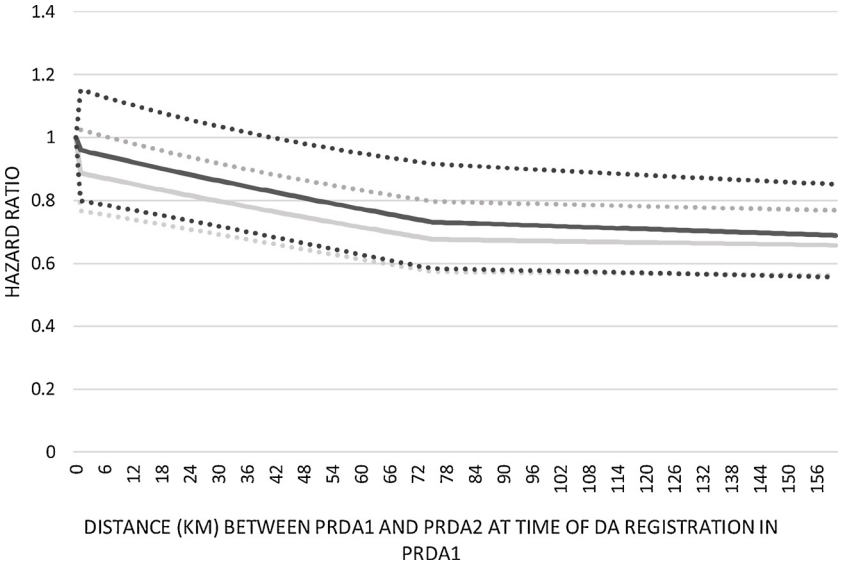

Fig. 1. The association between distance between PRDA 1 and PRDA 2 at the time of PRDA1's First Registration for Drug Abuse and the Hazard Ratio for a First Registration for Drug Abuse in PRDA2. The solid light grey (blue) line represents the results of Model C for PRDA pairs in Table 2 with Two Regression Splines at 1.0 and 75.0 km. The dotted light grey (blue) lines represent the 95% Confidence Intervals around these estimates. The solid dark grey (red) line represents the results of Model D for PRDAships in Table 2 with the same Regression Splines. The dotted dark grey (red) lines represent the 95% Confidence Intervals around these estimates. PRDA = Propinquity-of-Rearing Defined Acquaintance. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

"immunity"), of exposed individuals. We here explore three: age, familial risk and academic achievement.

Young age of PRDA2 at PRDA1's first DA registration has a strong main effect on the probability of DA transmission (Table 2). We see significant positive interactions between PRDA2's age and our three adult transmission parameters (slopes of proximity effects at 0–1, 1–75 and > 75 km with respective p values of < 0.0001, < 0.0001 and 0.0002). These results are depicted in Fig. 2a where the y-axis represents the % of DA onset in PRDA2 within three years of PRDA1's DA registration and the x-axis is PRDA1-PRDA2 proximity. The five lines reflect 5th, 25th, 50th, 75th, and 95th percentile of age of PRDA2 at PRDA1 registration. The effect of proximity on risk is relatively strong when PRDA2 is 19, 22 and 24 but begins then to diminish and nearly disappears by age 33.

Model E in Table 2 indicates a robust main effect of familial risk for externalizing disorders on the probability of DA transmission. Significant positive interactions were seen between PRDA2's familial risk and two of our three adult transmission parameters (p values of < 0.0001, < 0.0001 and 0.056, respectively). These results are seen in Fig. 2b where five lines reflect 0th, 50th, 75th, 95th, and 99th percentile of familial risk. (We report the 0th percentile because the FRS distribution is zero inflated where zero indicates no relatives with externalizing syndromes.) Strong and moderate proximity effects are seen for those at very high (95th and 99th percentile) and moderately high familial risk (75th percentile). However, for those whose familial risk are in the lower half of the population, no appreciable impact of PRDA1-PRDA2 proximity on DA risk is observed.

Model F in Table 2 indicates a robust main effect of educational attainment on risk for DA transmission. Significant interactions are seen with PRDA2's educational attainment and all three of our adult transmission parameters (p values of < 0.0001, < 0.0001 and 0.0014, respectively). These results are depicted in Fig. 2c where the four lines reflect the mean educational attainment, 1 SD below and above the mean and 2 SDs below. Relatively strong proximity effects are seen in those who are 1 and 2 SDs below the mean of educational attainment. However, for those whose academic achievement are at or above the mean, proximity effects were absent.

3.4. Effect of age differences on transmission of drug abuse in PRDA pairs

Prior analyses examined PRDAs born in the same calendar (and likely same school) year. To gain further insight into factors modifying DA transmission, we fitted a single model of PRDA pairs with age differences of 0–5 years (Fig. 3, Appendix table 5). We see an orderly reduction in mean risk for DA registration in PRDA2 as a function of age differences between PRDA1 and PRDA2. Finally, in this sample, older PRDA1s transmitted risk for DA to younger PRDA2s considerably more strongly (Beta-coefficient = 1.51 (1.32; 1.69) appendix table 6, figure 1) than younger PRDA1s transmitted to older PRDA2s.

4. Discussion

We sought to clarify whether a contagion model for DA transmission could be applied to PRDAs defined by registry and geographical information in Sweden. In all our analyses, we controlled for a key potential confound – that proximity effects arise because PRDAs residing closer together in adulthood are more correlated in their exposure to psychosocial risks for DA. We did so by accounting for the density of DA in similarly aged individuals in the small community in which PRDA2 resided at the time of PRDA1's registration, thereby controlling for community level influences on DA.

We emphasize six major findings. First, even within our empirically defined small 2-km radius, proximity of the rearing residence in childhood strongly predicted transmission of DA in adulthood in our PRDA pairs. Compared to living next-door, the HR for DA transmission was 0.72 and 0.50 for PRDAs living 0.5 and 2.0 km away. These findings suggest that what we might call "acquaintanceship strength," indexed by childhood geographical proximity, plays a strong role in the transmission of DA risk in adulthood. That is, among PRDAs, the magnitude of DA contagion effects is related to the strength of the acquaintanceship.

Second, in adulthood, the impact of proximity on DA transmission was not linear. Rather, our best-fit model suggested 3 functions: a relatively strong effect operating over very short distances (< 1 km), a moderate effect acting over intermediate distances (1–75 km) and little to no effect operating over long distances (> 75 km).

Third, our findings for DA transmission in adulthood in PRDA-pairs were replicated within acquaintanceship. Confounders operating between unique PRDA pairs are unlikely to substantially bias our findings.

Fourth, a key component of most infectious disease models is variable susceptibility to disease risk due to varying "immunity." We could test these using PRDAs in ways that would have been more difficult in our studies of relatives among whom many risk factors would be highly correlated. We found strong interactions between age, familial risk and educational attainment on the proximity-effects on DA transmission. Notably, among individuals with low familial risk or high educational attainment, the effect of proximity on DA transmission disappeared (Fig. 2b and c). Valid contagion models for DA transmission will have to

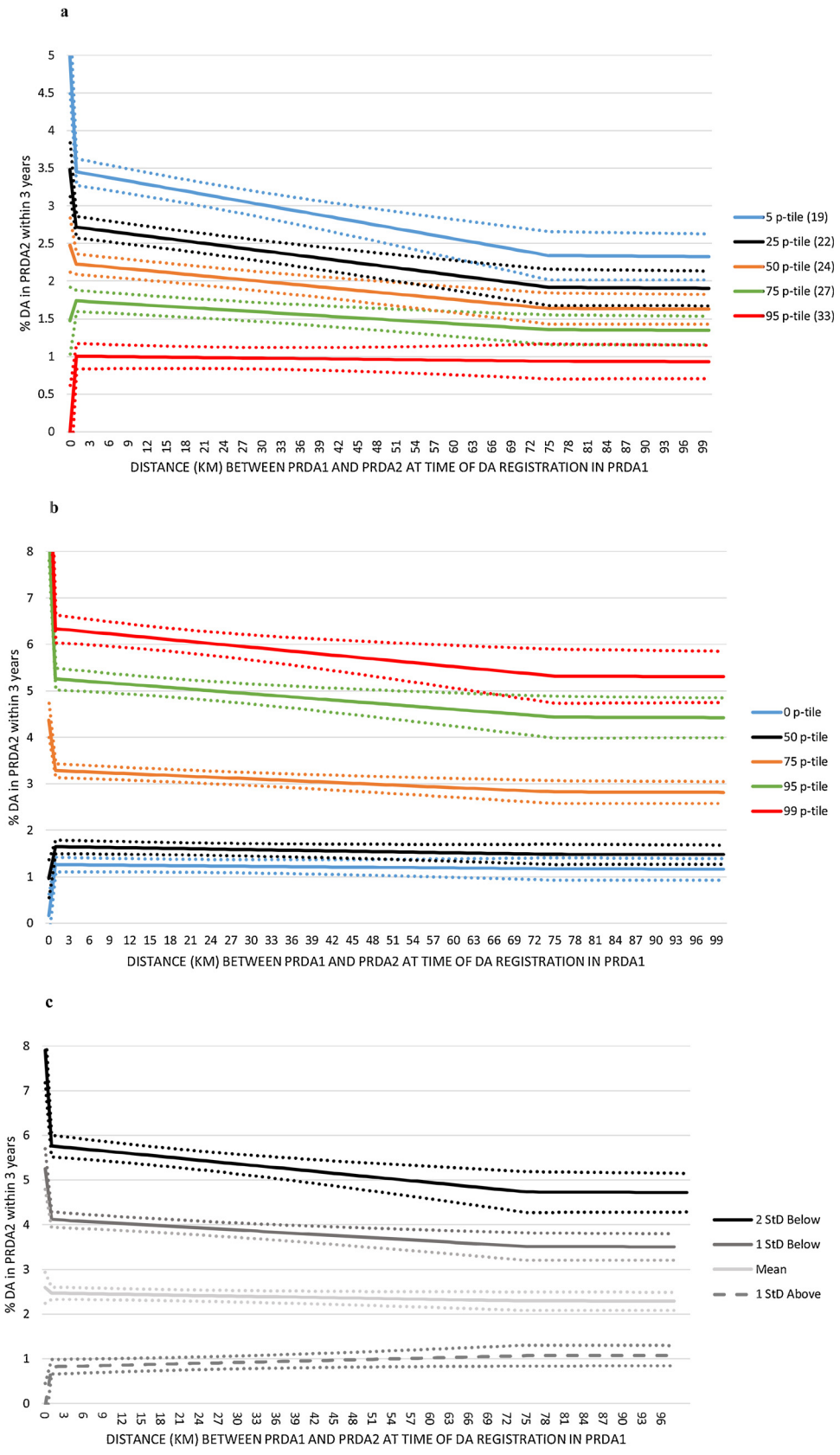

Fig. 2. (a) A Linear Probability Model including Age of PRDA2 at Drug Abuse Registration of PRDA1 (multiple colored lines), Distance between PRDA1 and PRDA2 at time of registration in PRDA1 (x-axis) and their interaction in the prediction of the risk for Drug Abuse in PRDA2 (y-axis). The model controlled for Distance in childhood, and SAMS density for PRDA2 [see methods for details] and contained splines at 1.0 and 75.0 km. Significant interactions were found between age of PRDA2 and the three slopes of risk as a function of promixity: 0–1 km - $p < 0.0001$; 1–75 km $p < 0.0001$ and > 75 km $p = 0.0002$. Depicted are the estimated curves from the 5th to the 95th by the percentile of age distribution in PRDA2 with the mean age to which that is equivalent. (b) A Linear Probability Model including PRDA2's Familial Risk Score for Externalizing Behaviors (multiple colored lines), Distance between PRDA1 and PRDA2 at time of registration in PRDA1 (x-axis) and their interaction in the prediction of the risk for Drug Abuse in PRDA2 (y-axis). The model controlled for Distance in childhood, Age of PRDA2 at Drug Abuse Registration of PRDA1 and SAMS density for PRDA2 [see methods for details] and contained splines at 1.0 and 75.0 km. Significant interactions were found between the Familial Risk score for PRDA2 and the three slopes of risk as a function of promixity: 0–1 km $p < 0.0001$; 1–75 km $p < 0.0001$ and > 75 km $p = 0.0556$. Depicted are the estimated curves from the 0th to the 99th by the percentile of Familial Risk Score in PRDA2. (c)– A Linear Probability Model including PRDA2's Academic Achievement at age 16 (multiple colored lines), Distance between PRDA1 and PRDA2 at time of registration in PRDA1 (x-axis) and their interaction in the prediction of the risk for Drug Abuse in PRDA2 (y-axis). The model controlled for Distance in childhood, Age of PRDA2 at Drug Abuse Registration of PRDA1 and SAMS density for PRDA2 [see methods for details] and contained splines at 1.0 and 75.0 km. Significant interactions were found between the Academic Achievement at age 16 for PRDA2 and the three slopes of risk as a function of promixity: 0–1 km - $p < 0.0001$; 1–75 km $p < 0.0001$ and > 75 km $p = 0.0014$. Depicted are the estimated curves from 2 stadard deviations (SDs) below the mean to one SD above the mean.

include such measures, as individuals differ widely in their relative immunity to the transmission of DA from their PRDAs.

Fifth, both the main effect of transmission of DA and its relationship with proximity attenuated with increasing age differences in PRDAs. These results, like those of geographical proximity in childhood, support the role of acquaintanceship strength in DA transmission. Given the small geographical regions involved and the Swedish policy to include in one school class everyone born in the same calendar year, most

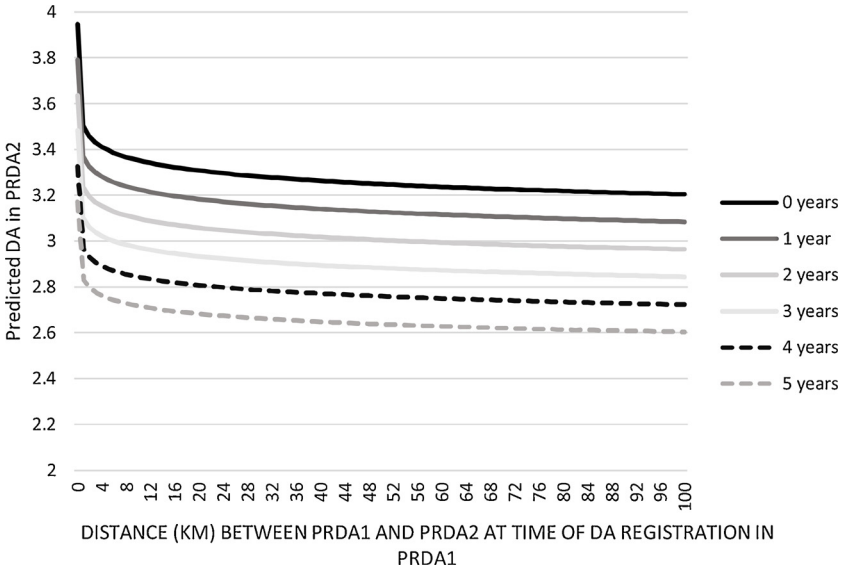

Fig. 3. linear probability model testing the interaction between distance in adulthood at the onset of Drug Abuse in PRDA1 and age difference in PRDA pairs born 1–5 years apart. To avoid the problem of comparing models with different splines, we simplified the analyses by including only one interaction term for all samples and modelled distance as a natural log function (p: 0.0185:).

of our same-age PRDAs would have been school classmates for a large part of their childhood. A final observation, further validating our model, was that, consistent with prior analyses in siblings and cousins (Kendler et al., 2019), older PRDAs transmitted DA more strongly to younger PRDAs than vice-versa.

Sixth, important advantages accrue from being able to examine transmission of DA among PRDAs rather than only relatives. Sample sizes are much larger and the results more generalizable. Factors governing the strength of transmission (e.g. proximity of rearing in childhood versus during adulthood) and the level of "immunity" can be examined with greater acuity thereby more closely approximating a full model of contagion (Grefenstette et al., 2013). Further research possibilities include: i) the examination of the transmission of DA among networks of PRDAs, ii) the further exploration of features, such as being coworkers, which impact on adult transmission and iii) further expansions of features influencing "immunity" including prior psychiatric illness and alcohol, criminal or employment problems.

4.1. Limitations

These results should be interpreted in the context of five potential methodological limitations. First, our results apply only to the Swedish population assessed between 1975 and 2015. Electronic means of human communication have evolved dramatically across this period and may change the role of geographical proximity in transmission of DA. Second, our assessment of DA was limited to data available from Swedish registries. While such administrative data has important advantages (e.g., no refusals or reporting biases), it certainly includes false negative reports for individuals with DA. Our measures likely reflect the more severe end of DA spectrum that produces medical or legal consequences. Third, DA is an emerging phenomenon and the timing of registration is unlikely to capture precisely the onset of abuse. Indeed, the transition from use to abuse typically takes a few years, which explains why we here examined a three-year window in PRDA2 after PRDA1's DA registration (Lopez-Quintero et al., 2011; Sartor et al., 2014; Wagner and Anthony, 2002). Fourth, we have focused here only on male to male DA transmission. In accord with our prior findings in siblings and cousins (Kendler et al., In Press, 2019), preliminary analyses of PRDAs indicates that this transmission is stronger than that observed in female-female or opposite-sex PRDA pairs. Finally, our use of the term "transmission" can best be understood as a latent explanatory concept. We lack the data to clarify the precise mechanisms whereby a DA registration in PRDA1 predicts a subsequent increased risk for DA in PRDA2 the strength of which varies as a function of their geographical proximity.

4.2. Conclusion

In male-male PRDAs, where acquaintance was defined by growing up within 2 km of one another, transmission of DA risk in adulthood from the first of the pair to be affected to the second PRDA, was attenuated by increasing distances between their residences with a sharp decline in risk over the first kilometer, a slow decline from 1 to 75 km and marginal effects above 75 km. In adulthood, transmission was considerably stronger in individuals who lived very close to each other in childhood and were of the same age and likely school classmates. In PRDAs with high "immunity" to DA, indexed by older age, high educational attainment or low familial risk, proximity effects in DA transmission were substantially reduced. These results are all consistent with those predicted by a contagion model for DA.

Contributors

All mentioned authors contributed substantially to the writing and editing of the present paper. K.S. Kendler, H. Ohlsson, J. Sundquist and K. Sundquist were responsible for the acquisition, analysis, or interpretation of the data. K.S. Kendler and K. Sundquist were responsible for the study concept and design. K. Sundquist had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. K.S. Kendler was responsible for the drafting of the manuscript. Critical revision of the manuscript for important intellectual content was handled by K.S. Kendler, J. Sundquist, K. Sundquist, and H. Ohlsson. K.S. Kendler and H. Ohlsson were responsible for statistical analysis. Funding was obtained by K.S. Kendler, K. Sundquist and J. Sundquist. K. Sundquist and J. Sundquist handled administration, technical, or material support. K.S. Kendler and K. Sundquist were responsible for study supervision. All authors have approved the final manuscript.

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Conflict of interest

No conflict declared.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2019.03.027.

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