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Article

Age at Separation of Twin Pairs in the FinnTwin12 Study

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Abstract

Living in the same household exposes family members to shared environments and may be reflected in estimates of shared environment in twin analyses. The age at the separation of cotwins in a twin pair marks the end of such shared exposure, and the age of separation is commonly self-reported in studies. The objective of the study was to summarize the age at separation from residential records and use it to validate with self-reported separation status and age at the third and fourth wave of data collection in the FinnTwin12 cohort. Age at separation was generated from the address information, linking it to the Finnish Population information system since birth. Descriptive statistics by sex and zygosity are presented. The mean age at separation from residential records was 20.36 years old. Women separated earlier than men and dizygotic pairs earlier than monozygotic pairs. We also calculated the sensitivity and specificity with the self-reported separation status at waves 3 and 4, and interrater reliability with the self-reported separation age at wave 4. Age at separation from residential records had a relatively poor agreement with the self-report. This work enables us to use a more precise and objective measure for the shared environment in future twin studies.

Keywords: Twin; residential record; age at separation

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The twin study design is a powerful method to estimate the genetic and environmental effects on multifactorial traits and complex noncommunicable diseases (van Dongen et al., 2012). Usually, the environmental effect is encompassed by shared (symbolized as c^2) and nonshared (symbolized as e^2) components in the statistical genetic model (Knopik et al., 2017). Shared environment describes the environmental influence that occurs to make twins more similar when they live together, regardless of the genetic effect. It could be sibling level, or, broadly, family-level effects (Burt, 2014). Many studies have found that variance in liability among various traits, illnesses, or diseases could be explained by the shared environment such as intelligence (Matteson et al., 2013), educational attainment (Silventoinen et al., 2020), schizophrenia (Sullivan et al., 2003) and autism (Hallmayer et al., 2011), and for other traits as well as reviewed by Boomsma et al. (2002) and Polderman et al. (2015).

At the same time, the assumption for the equal environment should be noted for twin studies; that is, that monozygotic and dizygotic twins share environmental influences on the trait being studied to an equal extent. Violation of the assumption may bias other variance components like heritability (Harrop et al., 2013). Therefore, instead of ‘significant environmental variance’, accurate measure of the shared environment is critical for the twin model, which improves both statistical and conceptual power to deliver high-quality results (Caspi et al., 2000). Various measures of the

family environment have been proposed. A previous study from the Twins’ Early Development Study in the UK has used socioeconomic status, assumed to be purely environmental, as a family-wide environmental measure, and illustrated that it explained 20% of behavior problems’ variance (Caspi et al., 2000). Another UK twin study demonstrated that the variances of measured domestic violence on children’s externalizing and internalizing problems were 2% and 5%, respectively, and researchers suggested that this measure could avoid the latent ‘black box’ for environment effect to some extent. However, this does not exclude the possibility that genetic influences exist on these ‘environmental’ effects.

One obvious measure of the shared environment is the duration of time that twins live in their parental home. After leaving home, they might live together, but twins generally move apart and become more independent, acquire an occupation, and over time may establish their own families. Thus, the time spent in the parental home is a measure of shared environment, which can be taken into account in twin analyses.

Age at separation can be objectively obtained by identification from residential records, but generally this information is collected through interviews and questionnaires. The use of actual residential history records could estimate the role of shared environment more extensively and precisely (Chen et al., 2015; Pedersen et al., 1991). In this study, we aimed to summarize the age at separation overall and by sex and zygosity based on the FinnTwin12 cohort. Then, we used the age at separation from residential records as the gold standard to validate the self-reported separation status in the third and fourth waves of data collection.

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Method

Study Population

The study participants were from the FinnTwin12 cohort, and we included all twins who had replied to at least one of the questionnaires sent to them in adolescence (age 11–12, 14, 17). The third follow-up was in young adulthood. The retention rate in the three follow-ups ranged from 66% to 92%. It is a prospective twin study starting from 1994–1999 (wave 1) when the twins were 11–12 years old and currently finishing the fourth wave in young adulthood. Besides, maternal, paternal, and teachers' questionnaires on multiple aspects, such as behavioral and emotional development, substance use behavior, and so on, were also obtained. The FinnTwin12 cohort consisted of two stages: epidemiological and intensive study. The intensive study was a random-sampling subset of the epidemiological study, which collected more detailed information on genotype and phenotype. An overview of the study has been published recently (Rose et al., 2019). In wave 3 at age 17, the twins were asked about how much time they spent with their cotwins. One response alternative was that they lived apart, which was used to classify the pairs as living apart or together. In wave 4, two separate questionnaires were administered and age at separation was reported only by those twins who had not taken part in the intensive assessments at age 14 (see Rose et al., 2019, for details on the participants). The date of return of the questionnaires was recorded at both waves.

Measure

The variable of interest, age at separation, was extracted from the residential records. This was obtained by linking the twin personal identification numbers to their residential history in the Finnish Population information system for all the addresses at which they had resided since birth (1983–1987). The address data consisted of North and Eastern coordinates by EUREF-FIN, which is a planar coordinate system with the unit of the meter (Uikkanen, 2021), and the ages at which they had moved into and out of each address. The age at separation was the first age that one of the cotwins moved into a new address that was different from their cotwin who remained in the old address. Alternatively, it was when both twins moved to new and separate addresses. The age at separation was consistent within the pair.

Additionally, we also obtained twins' residential distance from each other after the separation, which was calculated by the equation: $Distance = \sqrt{(x_1 - x_2)^2 + (y_1 - y_2)^2}$, using the coordinates after the separation. We also computed the age that the other cotwin moved to a new different address. The relationship between age at separation and other variables is presented in Figure 1.

Demographic information included sex (male, female), zygosity (dizygotic, monozygotic) and the birth year. Zygosity and sex were combined into five categories: male monozygotic (MMZ), female monozygotic (FMZ), male dizygotic (MDZ), female dizygotic (FDZ) and opposite-sex dizygotic (OSDZ). The analysis of variance test was used to evaluate whether there was a difference in age at separation between demographic groups. *P* values were reported.

Validation

First, we generated a two-way table to assess the sensitivity and specificity of age at separation from residential records and self-report at waves 3 and 4. The 'gold standard' was a binary variable as to whether the ages when twins who filled out the survey at

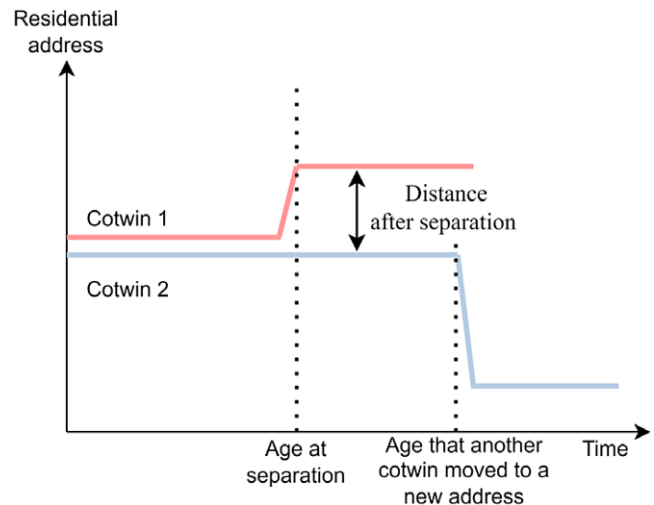


Fig. 1. Age at separation and other variables in the study.

waves 3 or 4 were older than the age at separation from residential records (yes, separated) or not (no, not separated). The comparable test was the self-reported separation status (yes, no) in each wave.

Second, interrater reliability was used to assess the consistency between age at separation from residential records and from self-report at wave 4. The overall scatter plot between those two was generated. According to the differential information pattern, the twins were divided into different groups (Figure 2). Then, after rounding up the age at separation from residential records to no decimal, we calculated the percent agreement, Cohen's kappa coefficient and Gwet's AC₁ in each group as the interrater reliability assessment. Gwet's AC₁ is an alternative and stable interrater agreement assessment to avoid the paradoxes of Cohen's kappa (Gwet, 2008; Wongpakaran et al., 2013). In the assessment, we excluded the twins whose age at separation in residential records was older than the age they filled out in the wave 4 survey, which meant they had separated after wave 4 or have not separated yet.

Results

Study Participants

Besides 33 twin pairs never separated by the end of follow-up in December 2020, a total of 2475 twin pairs (4950 twins) had valid information on age at separation. The mean age at separation was 20.36 years (*SD* 2.79), with a median of 19.94 years. Figure 3 shows the distribution, and the data fit the normal distribution via visual assessment. The descriptive characteristics and age at separation are shown in Table 1. There was little difference in the number of males and females included. The dizygotic twins formed the majority (67.7%). However, we did not know the zygosity of 148 twin pairs (296 twins). By the combination of sex and zygosity, there were 15.6% MMZ, 16.7% FMZ, 18.4% MDZ, 15.8% FDZ and 33.6% OSDZ of twins. Sex, zygosity and their combination contributed to the significant difference of age at separation within different groups. The deciles of age at separation by sex and zygosity are presented in Table 2. FDZ had the smallest quantiles of age at separation at 5th and 10th, which were also lower than overall quantile. MMZ twins had the largest 75th, 90th and 95th quantile of age at separation.

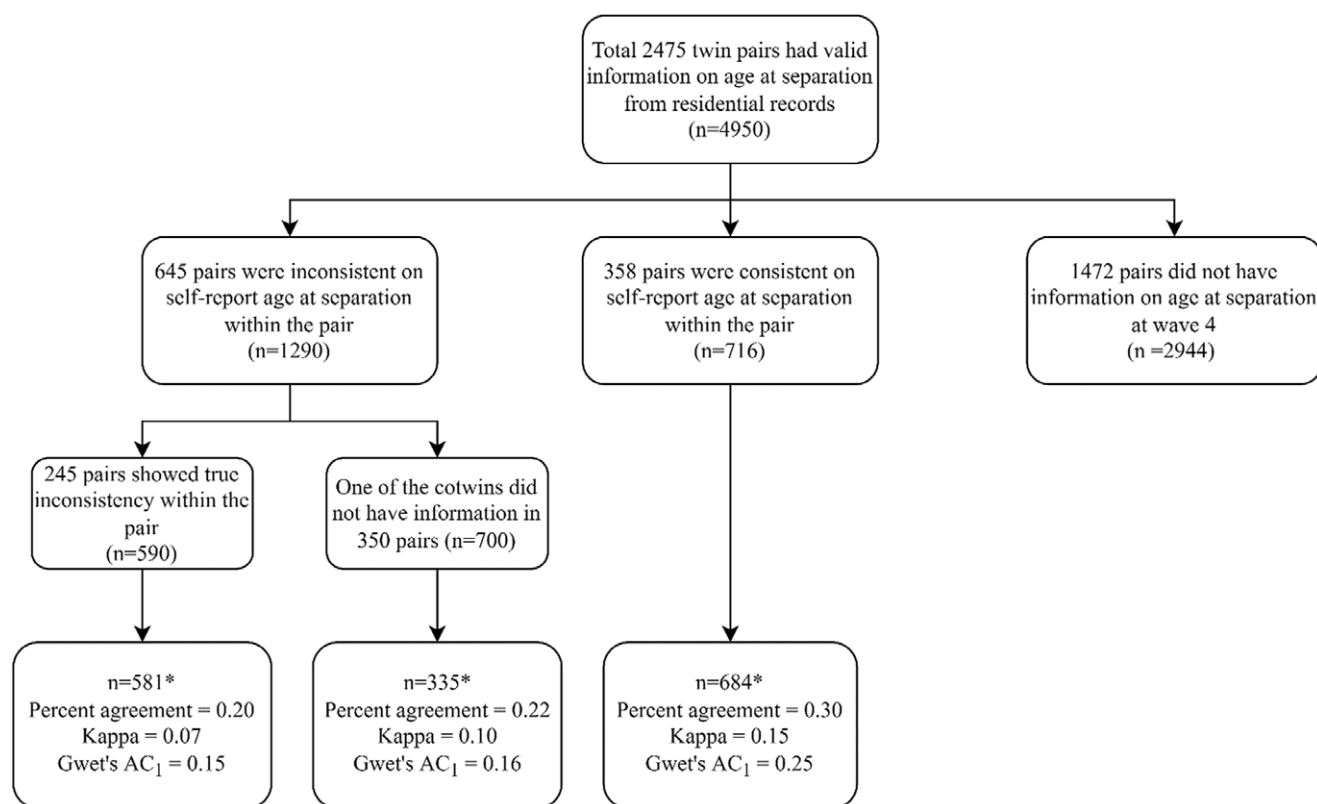


Fig. 2. Flowchart of interrater reliability assessment.

Note: *Lost twins in the interrater reliability assessment because the age at separation from residential records was larger than the age at wave 4.

Twins did not have information on self-reported age at separation at wave 4 due to several reasons: (1) they were not provided this question as they were part of the intensively assessed twins study set; (2) they did not answer this question on wave 4's survey; (3) they were lost to follow-up in wave 4.

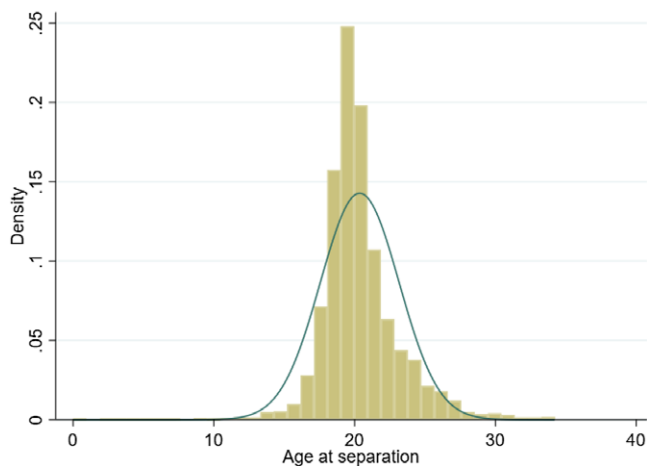


Fig. 3. Distribution of age at separation from residential records.

The overall mean of residential distance between cotwins in the pair after the separation was 63.43 km (SD 111.79), excluding 67 twin pairs ($n = 134$) in which at least one cotwin did not have the address information. There were 99 individual twins who did not move at all after the separation from cotwins and presumably continued to live at their parental home. For the rest, the mean age of twins ($n = 2376$) whose cotwins had already left, moving to another new address, was 22.02 years old (SD 3.34). There were 1122 twins who had moved to a different location within one year

after separation (only 72 of 1122 twins moved at the same time along with cotwins); 512 twins moved between one to two years, and the remaining twins moved at least after three years.

Validation

At both waves, we lost information on separation status for some twins (Table 3). At wave 3, 4054 twins answered the question of whether they were apart from their cotwins; overall, only 6.5% reported living apart from their cotwins. The percentages of twins who answered yes and separated before wave 3 (residential records) and who answered no and separated after wave 3 (residential records) were 2.9% and 88.8%, respectively; therefore, the sensitivity was 0.37 and the specificity was 0.96. At wave 4, the valid responses on the question of separation reduced to 1780, and the overall proportion of twins living apart from their cotwins increased to 95.3%. There were 92.1% of twins separated before they took the wave 4 survey (residential records) and confirmed in the survey. Another 2.5% of twins did not separate at wave 4 (residential records) and answered no on the separation question, so the sensitivity was 0.98 and the specificity was 0.44.

Figure 4 presents a scatterplot with the overlaid linear prediction for age at separation between residential records and self-report at wave 4. The coefficient of the linear prediction was .53 with .35 R^2 by the regression model. For various reasons, 1472 twin pairs did not have information on self-reported age at separation at wave 4. In 358 twin pairs (716 twins), they were consistent on self-reported age at separation within the pair. For them, the kappa

Table 1. Characteristics of the study population

Characteristics	Twin individual	Age at separation (year)		<i>p</i> value of age at separation	Distance after separation (km) ^b	
	<i>n</i> (%)	Mean (<i>SD</i>)	Median		Mean (<i>SD</i>)	Median
Overall	4950	20.36 (2.79)	19.94		63.43 (111.79)	11.53
Sex				<.001		
Male	2499 (50.5)	20.73 (3.04)	20.35		58.65 (106.28)	10.48
Female	2451 (49.5)	19.99 (2.47)	19.6		68.28 (116.84)	12.93
Zygosity^a				<.001		
Monozygotic	1502 (32.3)	20.67 (3.19)	20.11		63.44 (117.23)	9.46
Dizygotic	3152 (67.7)	20.16 (2.54)	19.83		63.96 (110.35)	12.51
Year of birth				.6		
1983	1108 (22.4)	20.43 (2.81)	19.9		70.64 (116.72)	12.4
1984	998 (20.2)	20.35 (2.91)	19.88		60.92 (108.24)	11.7
1985	1014 (20.5)	20.40 (2.54)	20		55.59 (103.77)	10.46
1986	932 (19.9)	20.24 (2.66)	19.95		62.03 (117.12)	12.55
1987	898 (19.1)	20.37 (3.04)	19.94		67.70(112.08)	10.97
Sex and zygosity combination^a				<.001		
MMZ	724 (15.6)	21.09 (3.65)	20.72		54.52 (102.88)	8.6
FMZ	778 (16.7)	20.28 (2.65)	19.61		71.70 (128.62)	10.28
MDZ	854 (18.4)	21.07 (2.77)	20.61		59.59 (108.73)	10.43
FDZ	736 (15.8)	19.85 (2.30)	19.56		69.69 (111.01)	18.29
OSDZ	1562 (33.6)	19.81 (2.39)	19.59		63.62 (110.88)	12.63

Note: ^a296 twin individuals with unknown zygosity were excluded; ^bAt least one cotwin in the pair did not have address information among 67 twin pairs (*n* = 134). MMZ, male monozygotic; FMZ, female monozygotic; MDZ, male dizygotic; FDZ, female dizygotic; OSDZ, opposite-sex dizygotic.

Table 2. Deciles of age at separation by sex and zygosity

Characteristics ^a	Quantile						
	5th	10th	25th	50th	75th	90th	95th
Overall	16.96	17.89	18.90	19.92	21.36	23.87	25.28
Sex and zygosity combination^a							
MMZ	17.31	18.36	19.40	20.72	22.29	25.73	27.46
FMZ	16.85	17.65	18.87	19.61	21.50	23.99	25.10
MDZ	17.74	18.45	19.46	20.61	22.02	24.85	26.22
FDZ	16.67	17.62	18.70	19.56	20.60	22.81	24.15
OSDZ	16.72	17.69	18.69	19.59	20.67	22.65	23.87

Note: ^a296 twin individuals with unknown zygosity were excluded. MMZ, male monozygotic; FMZ, female monozygotic; MDZ, male dizygotic; FDZ, female dizygotic; OSDZ, opposite-sex dizygotic.

coefficients of age at separation between from residential records and from self-report were .15 and the Gwet's AC₁ was .25 (*n* = 684). Among 645 twin pairs who showed inconsistency within the pair on self-reported age at separation, 245 twin pairs showed true inconsistency and the mean difference of the self-reported age at separation between cotwins within the pair was 1.44 years (*SD* 0.92). In the remaining 350 twin pairs, one of the cotwins in the pair did not have information on self-reported age at separation. Their interrater reliability assessments' results were also reported (Figure 4).

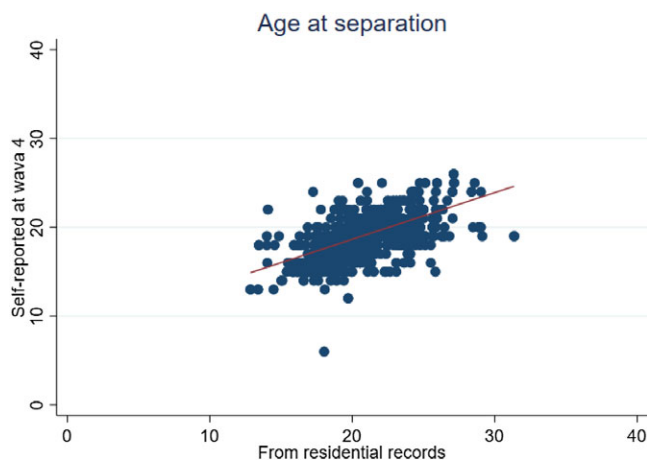
Discussion

With 2475 twin pairs born 1983–1987, the mean age at separation was 20.36 years, generated from residential records, and its distribution was approximately normal. Significant differences were observed between different sex or zygosity groups. However, through the interrater reliability assessment, the age at separation from the residential records showed relatively poor agreement with the self-report.

The purpose of identifying the age at separation is to better represent the shared environment in the twin study. Before the separation, twins usually live together at their primary home. In the 1980s, using the Swedish Twin Registry (STR), Pedersen et al. (1984) summarized age at separation in months, assessed by questionnaire among twins reared apart. They also compared the traits' correlation between twins reared apart and reared together and found that reared apart twins' correlation on height, weight and other variables was generally lower than reared together twins (Pedersen et al., 1984). Later, Chen and colleagues (2015) combined the self-reported within-pair contact frequency and age at separation as shared environment in a larger general STR sample and detected the simultaneous contribution of shared environment for traits. In addition, they suggested that twins who spent a longer time together would be more similar in traits. The self-reported age at separation in Sweden was lower than ours from residential records in Finland. Moreover, the study of twins reared apart could be regarded as a special extreme case of using age at separation to gauge the shared environment's effect as age at separation equals or is close to zero. In the Minnesota Study of Twins Reared Apart, besides the great genetic effect, rearing together

Table 3. Separation status derived from residential records and self-reported separation at waves 3 and 4

Self-report separation	Age at separation (residential records)			
	At wave 3 (twin individual $n = 4054$)		At wave 4 (twin individual $n = 1780$)	
	< age at this wave	> age at this wave	< age at this wave	> age at this wave
Yes	116 (2.9%)	144 (3.6%)	1639 (92.1%)	57 (3.2%)
No	195 (4.8%)	3599 (88.8%)	39 (2.2%)	45 (2.5%)

**Fig. 4.** Scatter plot of age at separation between from residential records and from self-report at wave 4.

only contributed slightly to familial resemblance on a few behavioral dimensions, in comparing monozygotic twins reared apart (MZA) to reared together (MZT) (Bouchard et al., 1990). While the environmental factors had the ability to mediate the normal and abnormal personality, the magnitude was smaller than genetic mediation (Markon et al., 2002). Similarly, Rose et al. (1990) used social contact as the common environment's index and modeled its effect on cotwin similarity for alcohol consumption in the Finnish twin cohort. These earlier studies indicate the need to integrate the age at separation into the twin model to comprehensively assess measures of the shared environment. However, we still need to be cautious about the possible existence of covariance between genetics and environment in the age at separation. For example, researchers suggested the mutual effect between similarity and frequency of contact of twins based on a sample of Australian twins (Posner et al., 1996). Therefore, in the future, analysis of identity by descent sharing among DZ twins, which represents the degree of the common ancestor, could help to explore this question (Nait Saada et al., 2020).

Females tended to separate at an earlier age and further apart from their cotwins than males in the study, which suggests that sex may contribute to environmental effects differentially. For regular tobacco use, Pedersen et al. (1984) indicated that rearing (shared) environmental effect accounted for 20% of the variance in males, but the twin model for females suggested a more important portion of 63% for correlated environmental (shared and unique) effect in 778 male-male and female-female twin pairs raised together and apart from the STR (Kendler et al., 2000). In the Swedish Adoption/Twin Study of Aging (SATSA), the difference in shared rearing environmental effect between males and females was also found in traits of coping

scales (problem-solving, turning to others, and avoidance; Kato & Pedersen, 2005). Based on 93 pairs of MZA and 154 pairs of MZT in SATSA, an analysis of BMI to estimate the shared rearing environment only had a satisfactory fit in the model of males, not females (Stunkard et al., 1990). The sex-specific mechanism of the shared environment should be taken into consideration in further twin studies.

DZ twin pairs separated at a younger age and tended to live further apart from each other (larger median distance after separation) compared to MZ twin pairs. It is possibly due to more warmth, closeness and less conflict among MZ twin pairs (Segal & Knafo-Noam, 2021), so that they might have a stronger desire to live together or closer to each other. The STR study also found that the mean ages at separation of same-sex DZ and OSDZ twin pairs were smaller than the MZ twin pairs (Chen et al., 2015). In the epigenetics study based on SATSA, researchers found that MZ twin pairs shared more epigenetic mutations than DZ twin pairs in the mixed-effect model, which could be extrapolated to the different environmental influences between zygosity (Wang et al., 2019). However, based on findings from the Chinese National Twin Registry, zygosity was not correlated with the proportion of twins reared apart, so it seems that zygosity would not likely affect the shared environment (Gao et al., 2015). In our study, although the age at separation in FMZ was smaller than in MMZ, the difference between these two numbers was small.

A novel aspect that the use of accurate residential history provides is to permit computation of the distance between residences of the twins in pairs after separation. While distance itself does not tell us how much contact and interaction there is between the twins, longer distance does impose time constraints on how much personal interaction there can be. Living in the same local community is different from living several hours distant. The residential history also permits estimation of the number of moves before and after separation, and the distance moved during various periods of interest. We will study these topics in more detail in other work.

There were several possible reasons limiting achieving a better agreement of age at separation between from residential records and from self-report at wave 4. First was the recall bias from the questionnaire at wave 4. There was an average 6.64 years difference between the age the survey was filled out and self-reported age at separation at wave 4. Moreover, cotwins within the pair (245 twin pairs) answered the question of age at separation inconsistently at wave 4, although it should be the same within the pair. Second, it is possible that after the separation, they actually lived quite close together, which made them feel like they were still living together. There were 33 twin pairs who were consistent for self-reported age at separation within the pair but were inconsistent between age at separation from the self-report and resident records at wave 4, who lived within 2 km after separation. Third, we also found that some twin pairs had moved back to the same residence after separation, which may interfere with their judgment of separation. Moreover, when Finnish men are doing military service, their residential records do not change to their service location. This could create the illusion that the twin pairs were still living together from residential records.

The strength of the study is that age at separation is generated by the residential records, which came from the Finnish Population information system since birth, and thus, it is more reliable, objective and less biased compared to the traditional self-report. Second, we also obtained the residential distance after separation, which could be a better measure of the degree of

separation and twins' later interaction in later studies. We were also limited to a smaller number of twins who provided self-reported age at separation at wave 4, because those twins missing the information were not provided this question as they were in the intensively assessed twin study subset and did not answer this question, or were lost to follow-up at wave 4. We also excluded twins separated after the age they filled out the wave 4 surveys from the interrater reliability assessment. So, interrater reliability results may not have adequate power.

Conclusion

Based on the FinnTwin12 cohort, we summarized the age at separation from residential records. Females and DZ twin pairs tended to separate earlier and live further apart than males and MZ twin pairs. However, the agreement between age at separation from residential records and from self-report was relatively poor. These findings provide grounds to recommend using age at separation and related variables to measure shared environment more precisely in future twin studies.

Data

The FT12 data are not publicly available due to the restrictions of informed consent. However, the FT12 data are available through the Institute for Molecular Medicine Finland (FIMM) Data Access Committee (DAC) (fimmdac@helsinki.fi) for authorized researchers who have IRB/ethics approval and an institutionally approved study plan. To ensure the protection of privacy and compliance with national data protection legislation, a data use/transfer agreement is needed, the content and specific clauses of which will depend on the nature of the requested data.

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Conflicts of interests. All authors declare that they have no actual or potential conflict of interest.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Ethical approval for both data collection waves was provided by Indiana University's Institutional Review Board and the ethical committee of the Helsinki and Uusimaa University Hospital District.

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