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Younger Age at Crisis Following Parental Death in Male Children and Adolescents is Associated with Higher Risk for Dementia at Old Age

Ramit Ravona-Springer, MD¹, Michal Schnaider Beeri, PhD², and Uri Goldbourt, PhD³

¹Sheba Medical Center, Israel

²Department of Psychiatry, Mount Sinai School of Medicine, New York

^{1,3}Division of Epidemiology, and Neufeld Cardiac Research Institute, Sackler Faculty of Medicine, Tel Aviv University, Israel

Abstract

Aims—To examine the association of midlife report of crisis following parental death (CFPD) during childhood and adolescence, with dementia at old age.

Methods—In 1965, 9362 male participants of the Israel Ischemic Heart disease (IIHD) study were asked whether they have experienced CFPD (paternal or maternal) during the following ages: 0–6, 7–12, 13–18 or >18 years. Dementia was assessed over three decades later in 1889 survivors of the original cohort, 1,652 of whom were assessed for CFPD in 1965.

Results—Controlling for age, the estimated odds for dementia relative to individuals who reported crisis following paternal parental death (CFPR-P) at the age of 18 and above, were 3.06 (95%CI 1.42–6.61), 2.15 (95% CI 0.87–5.31) and 2.35 (95%CI 1.05–5.28) for those who reported CFPD-P at the ages of 0–6, 7–12 and 13–18 respectively. Odds for dementia were 0.60 (95% CI 0.32–1.11) for participants who reported CFPD-P at ages of 18 and above, compared to participants who did not report such a crisis. Similar results were obtained for the association of crisis reported following maternal parental death (CFPD-M) at different age groups and dementia.

Conclusions—CFPD during childhood is associated with increased risk for dementia in males who survived until old age.

Keywords

crisis; parental death; childhood; dementia

Introduction

Increasing evidence demonstrates that exposure to certain factors across lifespan (including early childhood and intrauterine phases) is associated with increased risk for dementia ^{1, 2}. Among these are psychological factors such as proneness to stress and depression ^{3, 4}. The association of these factors with dementia may be affected by subjects' age at time of

Corresponding author: Ramit Ravona-Springer, Memory Clinic, Sheba Medical Center, Ramat Gan, 52621, Israel. Telephone Number: 972-54-2550676, Fax number: 972-3-5346628, ramitrs@hotmail.com, ramit.ravona@sheba.health.gov.il.

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psychological assessment⁴, proximity to the stressogenic event or by the way psychological stress is measured, i.e. proneness to stress versus exposure to objective stress.

Death of a parent during childhood is a significant stressful event, associated with morbidity^{5,6}, mortality⁷, health related behaviors⁸ and depression^{9,10} during adulthood, each associated with late life cognitive performance and with dementia^{3,11}.

The importance of a life course approach has been recognized in other chronic diseases, enabling detection of periods of vulnerability to certain risk factors¹². Since the impact of a certain risk factor¹³ as well as recommended treatments may differ according to individual's age at exposure¹⁴, preventive interventions considering a life course approach may help to identify optimal timing for intervention or modification

In this study, the relationship of age at crisis following childhood and adolescence parental loss with dementia at old age was assessed.

Methods

The IIHD project

The sample of the Israeli Ischemic Heart Disease (IIHD) Project was chosen by stratified sampling of civil servants and municipal employees aged 40 and above in 1963. Sampling procedures, mortality and follow-up have been described in detail elsewhere¹⁵. Of 11,876 approached, 10,232 (86.2%) men agreed to participate and were enrolled in 1963. A more detailed description is available at the supplemental online version of ADAD.

Diagnosis of dementia—Dementia was diagnosed in 1999/2000 using a two-step procedure as described in detail elsewhere¹⁵. A more detailed description is also available on line at the supplemental online version of ADAD.

According to the Israel Mortality Registry, 7136 men died by the beginning of the study in 1999; another 306 men died before being approached for a phone interview and 13 subjects were lost in the matching process. Detailed description about subjects assessed in 1999 is available online at as well as in previous publications¹⁵. The follow up study characterized the presence or absence of dementia in 1889 subjects: 307 were demented, 175 had cognitive impairment not sufficient to meet diagnostic criteria for dementia (cognitively impaired not demented-CIND9), and 1407 elderly were cognitively normal [No Cognitive Impairment (NCI)]. Since subjects diagnosed with CIND were not included in the analysis, the final sample for logistic regression models included 1417 subjects.

Definition of Crisis Following Parental Death (CFPD)—In 1965, participants were asked whether they had experienced a serious crisis, specifically, crisis following maternal or paternal death, in childhood, adolescence or as adults. If affirmative, they were further asked about the age range at which they had experienced the crisis, i.e.: 0–6, 7–12, 13–18 or >18 years. In the questionnaire, there was no specification as to the definition of crisis, and participants' answers were based on their subjective definition of crisis. The aim of the questionnaire was to detect CFPD rather than record age of subjects at death of parents, therefore, the group of subjects classified in 1965 as "no CFPD" included a minority of subjects whose parents were still alive as well as subjects whose parents died but they did not report crisis following their death. The number of participants who suffered parental death but did not report it as a crisis is not known. However, we assume that the number of subjects whose parents were still alive was small since the subjects' age in 1963 was 40 and above and life expectancy in Israel in 1965 was 70²⁸. Moreover, many of the subjects

immigrated to Israel after they and their families had been persecuted further increasing the odds that their parents had died by 1963–1965.

Assessment of anxiety—assessment of anxiety in 1963 is described in detail at the supplemental online version of ADAD as well as in previous publications ¹⁵.

Socioeconomic status index (SES)—assessment of SES in 1963 is described in detail at the supplemental online version of ADAD as well as in previous publications ¹⁵.

Statistical analysis—An order-directed score test of trend developed by Cuzick ¹⁶, an extension of the Wilcoxon rank-sum test, was used to examine the departure of sample results, consistent with a ‘dose-response’ association between age-at-parental death crisis report categories, and late-life dementia prevalence, from a null hypothesis of an independence of dementia rates from the above categories.

Logistic regression was used to estimate the covariate-adjusted odds ratios for dementia prevalence, associated with having been at each of three different childhood and adolescence age groups during CFPD (0–6, 7–12, 13–18), compared to the group that reported CFPD after the age of 18. Logistic regression was also used to estimate the covariate-adjusted odds ratios for dementia in subjects who reported CFPD after the age of 18 compared to subjects who did not report CFPD. Adjustment was made for age, socioeconomic status, and order of birth and country of birth.

The study was approved by the Sheba Medical Center ethics committee.

Results

In 1965, 9715 participants of the IIHD who were recruited in 1963, returned for examination. Of these, 9362 answered questions relating to CFPD. Dementia evaluation was performed in 1889 survivors of the original cohort, 1652 of whom were interviewed in midlife about CFPD. CFPD-P at each of three different childhood and adolescence age groups (0–6, 7–12, 13–18) was reported among 2252 individuals participating in the original cohort (24.0%) and among 241 survivors in 1999/2000 who were evaluated for dementia (14.6%). CFPD-M at each of three different childhood and adolescent age groups was reported in 1488 individuals participating in the original cohort (15.9%) and 169 survivors who were evaluated for dementia (10.2%) in 1999/2000. One hundred and eight (6.5%) survivors reported CFPD-P at the age of 18 or above and 71 (4.3%) reported CFPD-M at the age of 18 or above.

Description of study participants with CFPD data

Socio-demographic characteristics—Report of CFPD-M at any age was associated with lower midlife socioeconomic status. Of those who did not report CFPD-M, 22.9% were in the lowest socioeconomic status group in midlife compared to 35.8%, 32.0%, 30.6% and 23.6% in those who reported CFPD-M at the age groups of 0–6, 7–12, 13–17 and >18 respectively), and subjects who reported CFPD-M were also less likely to be in high socioeconomic groups in midlife compared to those who did not report CFPD-M ($\chi^2=36.89$, $DF=12$, $P<0.0005$)(table 1). Similar results were obtained when CFPD-P was examined ($\chi^2=42.49$, $DF=12$, $P<0.0005$).

Relatively fewer subjects who reported CFPD-P at age 18 and above were born in Middle East (Arab countries, Turkey and Iran) or North Africa (table 2). Subjects who reported CFPD at the age of 0–6 included a higher percentage of last born children (tables 1–2).

Midlife cardiovascular characteristics—As presented in table 3, men who reported CFPD (maternal or paternal) at different age groups did not differ in midlife cardiovascular profile from men who did not report CFPD. There were some differences in midlife diabetes rates, but no consistency was observed in the relationship between diabetes rates and CFPD at different ages (table 3).

Midlife anxiety—Anxiety rates in midlife, 27 years or longer after parental death did not differ between groups. An anxiety score of 3 (highest) was recorded in 4.3% of those who did not report CFPD-P, 4.2%, 4.1% and 4.8% in those who reported CFPD-P at ages 0–6, 7–12 and 13–18 respectively. This anxiety score was recorded in 4.2% of those who did not report CFPD-M, 5.1%, 4.2% and 3.7% in those who reported CFPD-M at ages 0–6, 7–12 and 13–18 respectively.

Survival in 1999/2000 by CFPD group—Death rates per 100,000 years by 1999/2000 were 521 among participants who did not report CFPD-P and 513, 548, 538 and 525 among those who reported CFPD-P at ages 0–6, 7–12, 13–18 and ≥ 18 respectively. Death rates per 100,000 years by 1999 were 522 among participants who did not report CFPD-M and 533, 536, 523 and 524 among those who reported CFPD-M at ages 0–6, 7–12–13–18 and $\geq$ respectively. Thus, death rates by 1999 per 10,000 person years did not differ between groups according to age at reported CFPD (maternal or paternal).

Associations of parental death at different age groups with dementia at old age

Relationships of age at CFPD-P with dementia: dementia prevalence rates in subjects who survived by 1999/2000 were 17.3% for those who did not report CFPD-P and 29.8%, 21.4%, 20.9% and 11.1% respectively for subjects who suffered CFPD-P at the ages of 0–6, 7–12, 13–18 and > 18 . Controlling for age, the odds for dementia, relative to individuals who reported crisis following paternal death at ages above 18 years, were 3.06 (95% CI 1.42–6.61), 2.15 (95% CI 0.87–5.31) and 2.35 (95% CI 1.05–5.28) for those who reported CFPD-P at the ages 0–6, 7–12 and 13–18 years (table 4). Non parametric trend test yielded $z = -3.22$ ($p = 0.001$). Adding order of birth, SES and country of birth to the logistic regression did not change results materially (table 4). Age adjusted odds ratio for dementia were 0.60 (95% CI=0.32–1.11) for those who reported CFPD-P at the age of 18 and above compared to all the participants who reported no such crisis at any age.

Relationship of age at crisis, following maternal death, with dementia: dementia prevalence rates in subjects who survived by 1999 were 17.4% for those who did not suffer CFPD-M and 27.1%, 29.3%, 23.2% and 9.9% respectively for subjects who suffered CFPD-M at the ages of 0–6, 7–12, 13–18 and > 18 years. Controlling for age, the odds for dementia relative to individuals who reported crisis following maternal death at the age of 18 and above were 3.56 (95% CI 1.25–9.02), 3.96 (95% CI 1.38–11.33) and 2.65 (95% CI 0.99–7.08) for those who reported CFPD-M at the ages of 0–6, 7–12 and 13–18 (table 4). Trend test yielded $z = -3.22$ ($p = 0.001$). Adjusting for order of birth, SES and country of birth did not change results materially (table 4). Similar to the results for paternal death, age adjusted odds for dementia were 0.52 (95% CI=0.24–1.15) for those who reported CFPD-M at ages above 18 relative compared to all the participants who reported no such crisis at any age.

Discussion

The present study demonstrated that reported CFPD during childhood and adolescence is associated with higher risk for dementia at old age compared to report of such crisis at ages of 18 and above as well as no report of such crisis. Odds ratio for dementia were highest for those who reported CFPD-P at the age of 0–6 and for those who reported CFPD-M at the

age of 7–12 and decreased thereafter with increasing age of crisis. In subjects who reported CFPD at ages above 18, risk for dementia at old age among survivors was reduced compared to subjects whose parents died but did not report such a crisis or those whose parents were still alive in 1965. Considering participants' ages, life expectancy at the time (70 years) and deaths in wars, pogroms and the Holocaust, the majority of subjects must have lost their parents by the time of the study.

Exposure to trauma and parental loss at young age have been reported occasionally to affect morbidity later in life^{5, 6} and mortality⁷. Higher rates of cardiovascular morbidity, smoking rates and type II diabetes, all risk factors for dementia¹¹ were found in individuals who were exposed as children to traumatic experiences, even 60 years after their occurrence^{8, 17}. Parental death in children and adolescents may also be associated with decreased family income, marked distress, depressive symptoms, social withdrawal and academic difficulties, of significance long after parental death^{9, 10, 18}. Low education, low income in early life and short stature^{19, 20} have been associated with late life dementia. In our study reported CFPD at different ages and absence of CFPD were not associated with midlife cardiovascular profile, diabetes rates or smoking status, whereas early CFPD were associated with lower socioeconomic status in midlife. Survivors' dementia remained associated with reported CFPD in multivariate analysis. Depression, a possible mediator between early life CFPD and late life cognition, was not measured; however, anxiety (measured as tendency to experience tension, fear and/or sleeping problems) which is closely associated with depression²¹ was measured. Groups of subjects stratified by age at reported CFPD did not differ in anxiety score.

The tendency for increasing risk for dementia with decreasing age at CFPD may be, at least partially, explained by the fact that in parentally bereaved children and adolescents, child's age is significantly correlated with mental health outcomes, younger age being associated with increased mental health problems²². A child that loses a parent may have less developed internal coping mechanisms as well as overwhelmed and thus non efficient familial support system. Adults who lose their parents may be less overwhelmed and more resilient to such a trauma.

The association found in our study of decreased dementia prevalence in survivors who reported CFPD at ages of above 18, may be explained by the possibility that in adults, tendency to report such a crisis is an indicator of more effective coping skills, such that enable help seeking behavior, appreciation of life, strengthening of emotional bonds and growth from traumatic events²³.

Report of crisis following parental death at different ages was not associated with decreased survival by 1999/2000, the time of dementia assessment; reducing the likelihood of survival bias effect. Additionally, baseline variables related to high risk of mortality, mainly smoking, diabetes and hypertension did not differ between groups of subjects stratified according to age at reported CFPD for the entire IIHD cohort, nor in those who survived until follow up in 1999/2000.

Consistent with our findings, death of father at early life was associated with increased risk for dementia in later life in the Cache County Study²⁴ in which paternal death prior to the age of 5 was associated with a 3 fold increased risk for dementia (OR = 3.0; 95% CI: 1.1–8.4). This risk ratio was similar to the dementia prevalence ratio found in survivors of our study. In contrast, maternal death at an early age was not associated with dementia. The discrepant results may result from report of parental death, rather than reported CFPD, with dementia, in Cache. The life period in which subjects were interviewed regarding parental death differed between studies (midlife in our study versus old age in the Cache County

Study) In the Cache County Study, subjects whose parents died after the age of 19 were grouped with subjects who still reported parents living as adults, and thus comparisons to the decreased risk associated with reported crisis due to parental loss at an age > 18 found in our study is not possible. Also, circumstances of parent's deaths were perhaps not as violent in Cache County as they were in Jewish migrants to Israel from countries undergoing great turmoil.

The main limitation of this study, as described previously, is the lack of information on the incidence of dementia in the subjects from the original IIHD study reported dead before the follow up study was conducted. Another limitation pertains to the fact that only males were included in the current study. Additionally, only CIND subjects who were identified in the second phase of cognitive assessment were excluded, and there is a possibility that some CIND subjects received a TICS-m score above the 27 cutoff score, thus being classified as cognitively normal. Although the number of subjects participating in the sensitivity sample was relatively small, this sample was randomly selected from the group of subjects whose TICS was 28–29, i.e. subjects at the highest risk of being erroneously classified as cognitively normal. Indeed assessment of these subjects by a clinician at their residence demonstrated the TICS cutoff point (>27) to be highly sensitive, even to CIND. Another limitation was at home assessment of dementia based on subject and informant's report (DQ) combined with the MMSE, rather than on a broad neuropsychological battery. In this regard, it is important to emphasize that that assessment of cognitive status was directly made by a physician with expertise in dementia which enhances the certainty of the assessment.

Lack of data regarding the numbers and midlife health and psychological characteristics of most of the study subjects, who suffered parental death but did not report crisis following this loss, limits our ability to interpret the results as related to the crisis following parental loss per se compared to loss of the parent.

The strengths of our study are the relatively large sample size, longitudinal design and evaluation of CFPD at midlife, when answers regarding childhood experiences are not expected to be affected by the dementing process. In addition, an abundance of data regarding midlife demographic, psychological, social and biomedical data, all of which may affect late life cognitive status, was available to us. These variables have been controlled for when analyzing the association of age of subject at parental death and dementia risk.

Our findings support the potential contribution of early life events to late-life dementia risk. Future studies should assess possible physiological and environmental mechanisms for this association.

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Appendix

The IIHD project

The sample of the Israeli Ischemic Heart Disease (IIHD) Project was chosen by stratified sampling of civil servants and municipal employees aged 40 and above in 1963. Sampling procedures, mortality and follow-up have been described in detail elsewhere¹⁵. Of 11,876 approached, 10,232 (86.2%) men agreed to participate and were enrolled in 1963. Subsequent analyses excluded 173 men who were born outside the six pre-defined geographical areas. Among the remaining 10,059 men, 9715 returned to the second examination cycle in 1965 and 9368 and consented to reply to questions regarding CFPD.

Diagnosis of dementia

Dementia was diagnosed in 1999/2000 using a two-step procedure as described in detail elsewhere¹⁶. All identified living participants from the original cohort who consented to participate in the new assessment, were administered a 20 minute phone interview, including a sociodemographic questionnaire and the Hebrew version of the Modified Telephone Interview for Cognitive Status (TICS-m)¹⁷.

The TICS-m is based on the Mini Mental State Exam (MMSE)¹⁸. The scores of the TICS-m were highly correlated with the MMSE scores in clinical studies¹⁹. Using a threshold score of 27 out of 50 TICS-m points, the sensitivity of this test was above 99% (CI 95% 91%–100%) and the specificity was 86% (CI 95% 85%–87%) for dementia against the gold standard clinical diagnosis¹⁷. The second step was a face to face interview for all subjects with a TICS-m score of 27 or lower. The aim of the second phase of the study was to ascertain the diagnosis of dementia among subjects who were identified by the TICS-m as possibly cognitively impaired. The subjects were assessed at their residences by a physician (a neurologist or psychiatrist with expertise and extensive experience in the diagnosis of dementia). Physicians were blind to the TICS-m score. The clinical assessment included the Dementia Questionnaire (DQ)^{20, 21}, MMSE¹⁸, Global Deterioration Scale (GDS)²² and the Hachinski Ischemic Scale (HIS)²³.

For persons with suspected dementia, the DQ assesses, through informants, the symptoms, course, and feature of the dementia, permitting a diagnostic classification for the presence and likely type of dementia. The DQ has previously demonstrated good inter-informant and inter-rater agreement in AD probands and normal elderly control populations for detecting the presence or absence of dementia and also, among identified cases of dementia, the type of dementia^{21, 24}. Compared with a clinical assessment of dementia, the DQ was found to have excellent sensitivity (100%; 95% CI 73%–100%) and very good specificity (90%; 95% CI 63%–100%)^{25, 26}. In this study, informants were people, usually first degree relatives who had contact with the participants of at least 10 hours per week.

Dementia was diagnosed using the DSM-IV criteria. Subjects were classified as Cognitively Impaired no Dementia (CIND) if both subject and informant reported a memory problem but they had normal activities of daily living and were not demented. CIND was diagnosed at the second phase of the study, by a physician who assessed the subjects in their residence. It

is possible that some of the subjects classified as NCI during the first phase of the study (using the TICS) would have met our criteria for CIND, however, it should be noted that the TICS has demonstrated excellent sensitivity in our ¹⁶as well as in other ²⁷ samples.

A second physician, blind to the diagnosis assigned by the physician who did the face-to-face interview, examined the data gathered from each patient and assigned an independent diagnosis. Disagreement was solved by a third physician. In five cases, the patient was approached again for this purpose.

According to the Israel Mortality Registry, 7136 men died by the beginning of the study in 1999; another 306 men died before being approached for a phone interview and 13 subjects were lost in the matching process. Detailed description about subjects assessed in 1999 is available online at [as well as at \(\)](#) The remaining 2604 subjects qualified for a telephone interview, and 2038 had phone contact. The telephone screening identified 799 potentially demented subjects for a home interview. Of these, 149 could not be examined. Of the remaining 1239 subjects who were not identified as potentially demented by the TICS-m (i.e. TICS score ≥ 28), 51 subjects whose TICS score was 28 or 29, and thus with the highest risk of being erroneously classified as cognitively normal, were randomly selected and examined at home for a sensitivity study of the phone interview instruments. From the sensitivity sample examined at home, 50 were cognitively intact and one cognitively impaired but not demented. The remaining 1188 subjects were classified as non-demented. The follow up study characterized the presence or absence of dementia in 1889 subjects: 307 were demented, 175 had cognitive impairment not sufficient to meet diagnostic criteria for dementia (cognitively impaired not demented-CIND9), and 1407 elderly were cognitively normal [No Cognitive Impairment (NCI)]. Since subjects diagnosed with CIND were not included in the analysis, the final sample for logistic regression models included 1417 subjects.

Assessment of anxiety

In 1963 (age > 40) subjects were questioned regarding existence of anxiety symptoms: "Do you consider yourself a tense person?", "Do you suffer from anxiety (fear) for no evident reason?" "Do you suffer from sleep problems?" Each question could be answered "yes" or "no". A total score for anxiety was either "0", "1", "2" or "3", reflecting the number of questions answered positively.

Socioeconomic status index (SES)

This index was based on formal education and type of employment at the time of examination. Formal education included nine levels, ranging from "no formal education" to "completed university education". Employment included five levels ranging from "laborer" to professional. The SES scale ranged from "1": very low SES (three lowest education levels and the lowest employment levels) to "5": very high SES (three highest education levels as well as two highest employment level) ²⁹.

Table 1

Socio-demographic variables in midlife according to age during CFPD*

Age at CFPD*	Age (sd)	SES [^]					Order of birth			
		1 [^]	2	3	4	5 [^]	Total	First born	Middle born	Last born
Age at CFPD-P*	No crisis	1,554 (22.0)	1,647 (23.4)	2,307 (32.6)	798 (11.2)	766 (10.8)	7,072 (100)	2,059 (29.1)	3,673 (51.9)	1,340 (19.0)
	0-6	239 (36.4)	154 (23.4)	174 (26.4)	53 (8.0)	38 (5.8)	658 (100)	156 (23.7)	211 (31.9)	294 (44.4)
	7-12	160 (34.6)	109 (23.4)	127 (27.4)	29 (6.4)	38 (8.2)	463 (100)	114 (24.7)	219 (47.5)	128 (27.8)
	13-18	177 (31.3)	140 (24.7)	165 (29.2)	46 (8.1)	38 (6.7)	566 (100)	119 (20.9)	283 (49.8)	165 (29.3)
	> 18	109 (20.1)	135 (25.0)	201 (37.1)	54 (10.0)	42 (7.8)	541 (100)	143 (26.5)	276 (51.2)	120 (22.3)
	Total	2,239 (24.1)	2,185 (23.5)	2,974 (32.0)	980 (10.5)	922 (9.9)	9,300 (100)	2,591 (27.8)	4,662 (50.0)	2,047 (22.2)
Age at CFPD-M*	No crisis	1,794 (22.9)	1,839 (23.5)	2,529 (32.3)	849 (10.8)	817 (10.5)	7,828 (100)	2,271 (29.0)	3,949 (50.5)	1,607 (20.5)
	0-6	125 (35.8)	80 (22.9)	101 (28.9)	26 (7.5)	17 (4.9)	349 (100)	81 (23.2)	155 (44.4)	113 (32.4)
	7-12	100 (33.0)	82 (27.0)	90 (29.8)	15 (4.9)	17 (5.3)	304 (100)	64 (21.0)	163 (53.5)	77 (25.5)
	13-18	114 (30.6)	83 (22.3)	97 (26.1)	41 (11.0)	37 (10.0)	372 (100)	73 (19.4)	174 (46.4)	128 (34.2)
	> 18	106 (23.6)	101 (22.5)	158 (35.2)	49 (10.9)	35 (7.8)	449 (100)	102 (22.9)	221 (49.5)	123 (27.6)
	Total	2,239 (24.0)	2,185 (23.5)	2,975 (32.0)	980 (10.5)	923 (10.0)	9,302 (100)	2,591 (100)	4,662 (100)	2,048 (100)

* CFPD= Crisis Following Parental Death, CFPD-P= Crisis Following Parental Death- Paternal, CFPD-M= Crisis Following Parental Death-Maternal.

[^] SES= Socio Economic Status; 1= lowest SES, 5= highest SES

Table 2

Country of origin according to age during CFPD*

	Age at CFPD*	Country of origin						Total
		Israel	East Europe	Central Europe	Balkan	Middle East	North Africa	
Age at CFPD-P*	No crisis	938 (13.8)	1,425 (20.0)	1,038 (14.6)	1,306 (18.4)	1,525 (21.4)	833 (11.8)	7,110 (100)
	0–6	121 (18.2)	91 (13.7)	52 (7.8)	84 (12.6)	241 (36.2)	77 (11.5)	666 (100)
	7–12	63 (13.5)	70 (15.0)	43 (9.3)	64 (13.8)	160 (34.4)	65 (14.0)	465 (100)
	13–18	74 (12.9)	102 (17.8)	69 (12.0)	83 (14.5)	156 (27.3)	88 (15.5)	572 (100)
	≥18	79 (14.5)	100 (18.4)	90 (16.6)	97 (17.8)	112 (20.8)	65 (11.9)	543 (100)
	Total	1,320 (14.1)	1,788 (19.1)	1,292 (13.8)	1,634 (17.5)	2,194 (3.5)	1,128 (12.0)	9,356 (100)
Age at CFPD-M*	No crisis	1,108 (14.1)	1,494 (18.9)	1,101 (14.0)	1,395 (17.7)	1,851 (23.5)	925 (11.8)	7,874 (100)
	0–6	65 (18.4)	48 (13.6)	28 (8.0)	50 (14.2)	110 (31.3)	51 (14.5)	352 (100)
	7–12	37 (12.1)	58 (18.9)	27 (8.8)	42 (13.6)	97 (31.6)	46 (15.0)	307 (100)
	13–18	45 (12.0)	96 (25.5)	51 (13.5)	54 (14.3)	77 (20.5)	53 (14.2)	376 (100)
	≥18	66 (14.7)	92 (20.5)	85 (19.0)	92 (20.5)	59 (13.2)	55 (12.1)	449 (100)
	Total	1,321 (14.1)	1,788 (19.1)	1,292 (13.8)	1,633 (17.4)	2,194 (23.5)	1,130 (12.1)	9,358 (100)

Table 3

Baseline cardiovascular characteristics according to age during CFPD*

Age at CFPD*	Systolic BP* (mmHg) (sd)	Diastolic BP* (mmHg) (sd)	Cholesterol (mg/dl) (sd)	Height (cm) (sd)	Weight (Kg) (sd)	BMI (Kg/m ²) (sd)	% diabetes	% ever smoked
Age at CFPD-P*	None	86 (12)	209 (40)	167.3 (6.6)	72.0 (10.6)	25.7 (3.3)	4.3	68
	0–6	86 (12)	207 (39)	165.8 (6.6)	69.7 (11.2)	25.3 (3.6)	4.1	68
	7–12	136 (21)	207 (39)	166.4 (6.7)	70.5 (10.7)	25.4 (3.3)	7.3	67
	13–18	136 (20)	209 (40)	167.0 (6.7)	71.8 (11.2)	25.7 (3.3)	5.8	72
	>18	134 (18)	209 (39)	167.1 (6.4)	72.3 (10.0)	25.8 (3.1)	5.7	69
Age at CFPD-M*	None	135 (20)	209 (40)	167.3 (6.6)	72.0 (10.7)	25.7 (3.3)	4.5	68
	0–6	135 (20)	205 (39)	166.0 (6.5)	70.1 (11.2)	25.4 (3.6)	3.7	70
	7–12	136 (21)	207 (43)	165.1 (6.9)	69.5 (10.9)	25.5 (3.5)	4.6	67
	13–18	135 (20)	211 (40)	166.6 (7.0)	71.0 (11.3)	25.5 (3.4)	6.1	67
	>18	133 (18)	210 (41)	166.8 (6.5)	72.1 (10.1)	25.9 (3.2)	5.8	71

* BP= Blood pressure

The association of age during CFPD* (at age groups younger than 18 compared to CFPD* at age ≥18**) and dementia at old age

Table 4

	Age at CFPD	n	OR for dementia adjusted for age (95% CI)	OR for dementia adjusted for age and birth order (95% CI)	OR for dementia adjusted for age, birth order, country of birth and SES) (95% CI)
Age at CFP-DP*	0-6	94	3.06 (1.42-6.61)	3.04 (1.41-6.56)	3.02 (1.35-6.73)
	7-12	56	2.15 (0.87-5.31)	2.17 (0.88-5.36)	2.58 (1.00-6.58)
	13-18	91	2.35 (1.05-5.28)	2.32 (1.03-5.22)	2.30 (0.99-5.36)
Age at CFP-DM*	0-6	59	3.56 (1.25-9.02)	3.41 (1.26-9.21)	3.52 (1.23-0.01)
	7-12	41	3.96 (1.38-11.33)	4.48 (1.53-3.09)	4.22 (1.36-13.1)
	13-18	69	2.65 (0.99-7.08)	2.53 (0.95-6.8)	2.61 (0.93-7.40)

** number of subjects who reported crisis following parental death after the age of 18 was 108 following paternal death and 71 following maternal death