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## Accepted Manuscript

Increased incidence of coronary heart disease associated with "double burden" in a cohort of Italian women

Fabrizio D'Ovidio, Angelo d'Errico, Cecilia Scarinzi, Giuseppe Costa

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Increased incidence of coronary heart disease associated with "double burden" in a cohort of Italian women

## Autors' full name and affiliations:

Fabrizio D'Ovidio: Department of Neuroscience – University of Turin Angelo d'Errico: Epidemiology Department ASL TO3 – Piedmont Region Cecilia Scarinzi: Department Environmental and health – ARPA Piedmont Giuseppe Costa: Department of Clinical and Biological Sciences – University of Turin

## **Corresponding autor:**

Fabrizio D'Ovidio Via Artisti 24bis – 10124 Torino (Italy) Telephone: +39.333.8772756 E-mail: <u>fabrizio.dovidio@unito.it</u>

## 1 Increased incidence of coronary heart disease associated with "double

- 2 burden" in a cohort of Italian women
- 3
- 4

## 5 Abstract

6 Objective of this study was to assess the risk of coronary heart disease (CHD) associated with 7 the combination of employment status and child care among women of working age, also 8 examining the sex of the offspring. Only two previous studies investigated the effect of 9 double burden on CHD, observing an increased risk among employed women with high 10 domestic burden or providing child care, although the relative risks were marginally or not 11 significant.

The study population was composed of all women 25-50 years old at 2001 census, living in 12 13 Turin in families composed only by individuals or couples, with or without children 14 (N=109,358). Subjects were followed up during 2002-2010 for CHD incidence and mortality 15 through record-linkage of the cohort with the local archives of mortality and hospital 16 admissions. CHD risk was estimated by multivariate Poisson regression models. 17 Among employed women, CHD risk increased significantly by 29% for each child in the 18 household (IRR=1.29) and by 39% for each son (IRR=1.39), whereas no association with the 19 presence of children was found among non-employed women or among employed women 20 with daughters. When categorized, the presence of two or more sons significantly increased

- 21 CHD risk among employed women (IRR=2.23), compared to those without children.
- 22 The study found a significant increase in CHD risk associated with the presence of two or
- 23 more sons in the household, but not daughters, among employed women. This is a new

finding, which should be confirmed in other studies, conducted also in countries where the
 division of domestic duties between males and females is more balanced, such as the
 European Nordic countries.

4

## 5 Keywords

6 coronary heart disease, double burden, epidemiology, employment, women, children7

## 8 1. Introduction

9 During the last decades, participation of women in the labor market has greatly increased in 10 developed countries (Jaumotte, 2003). From 1977 to nowadays employment rate in Italy has 11 increased by 17%, mainly as a direct consequence of the growth among women, who passed 12 from 31.5% to 41.3% of the total employed population (ISTAT, 2013). In contrast with these radical changes in women's labor market participation, women continue to carry out most 13 14 domestic work and child care, and such an unequal division of domestic activities between women and men overburdens employed women (Gershuny, 2000; Anxo et al., 2011). From 15 the Italian Multipurpose Survey on Time Use, carried out in 2002-2003, it was found that 16 17 domestic work was entirely accomplished by Italian women in 41% of the interviewed 18 couples (Mencarini, 2012). In 2008, approximately 64% of the employed women in Italy was 19 engaged in paid and domestic work activities for more than 60 hours per week overall, and in 20 presence of children the proportion increased to 68% (ISTAT & CNEL, 2013). A recent study 21 by the Organisation for Economic Cooperation and Development (OECD) has shown that gender differences in domestic work in Italy are the highest among the 28 EU countries, with 22 23 women performing 11 hours more domestic work than men per week (OECD, 2013).

1 Furthermore, the Italian Survey on the Time Use 2002-2003 showed that support to mothers 2 provided by children differs by gender, with female children more engaged in domestic work 3 than male ones. For example, in the age group 11-17 years: 65% of daughters were engaged 4 in domestic work, against 44% of sons; also, females devoted 44 minutes per day to domestic work, whereas sons only 22 minutes (Romano, 2012). 5 6 It has been hypothesized that the double burden posed by the combination of work and 7 domestic activities on women may affect their health (Waldron, Weiss, & Hughes, 1998). 8 Different theoretical approaches exist in this research field. According to the "Role 9 Accumulation" hypothesis, multiple roles would contribute to women's better health because 10 they provide more sources of social and economic support, self-esteem and personal satisfaction (Sieber, 1974; Thoits, 1983; Waldron & Jacobs, 1989; Moen, Dempster-McClain, 11 12 & Williams, 1992; Lahelma, Arber, Kivelä, & Roos, 2002). On the opposite side, there are 13 theories predicting worse health for women sustaining multiple roles. According to the "Role 14 Strain" hypothesis (Gove, 1984; McLanahan & Adams, 1987; Ross, Mirowsky, & Goldsteen, 1990), women who combine multiple roles (wife, mother and/or worker) may experience 15 «role overload and role conflict, which contribute to increased stress and excessive demands 16 17 on time, energy and psychological resources - resulting in poorer heath» (Waldron et al., 18 1998). The "Negative Spillover" hypothesis is a more recent theory which assumes that the 19 transfer of negative feelings from work to the family environment, and vice versa, may have harmful effects on health (Grzywacz & Marks, 2000). 20 21 A Swedish (Krantz & Ostergren, 2001; Krantz, Berntsson, & Lundberg, 2005) and a Finnish 22 (Väänänen et al., 2004) cross-sectional studies have shown that women who combine child

23 care and paid work report more psychological and physical symptoms than employed women

24 without children. However, most longitudinal studies on the "double burden" have found

either no effect or a beneficial effect of these multiple roles on women's general health or
 mortality (reviewed by Waldron et al., 1998).

3 In contrast, the only two studies investigating specifically the effect of double burden on 4 cardiovascular health observed an increased risk among employed women with high domestic 5 burden or providing child care (Havnes & Feinleib, 1980; Lee, Colditz, Berkman, & Kawachi, 2003). The first one is a prospective cohort study conducted by Haynes & Feinleib (1980) 6 7 within the Framingham Heart Study, which found a CHD risk among employed women with 8 children almost double than that of employed women without children. The second one, also a 9 prospective study, was performed by Lee et al. (2003) within the Nurses' Health Study and 10 showed that nurses caring for non-ill children 21 hours or more per week (and caring for nonill grandchildren 9 hours or more per week) had a CHD risk 50% higher than nurses not 11 caregiving. In support of these results, Brisson et al. (1999) observed a significantly higher 12 13 systolic (SBP) and diastolic blood pressure (DBP) in white-collar women reporting large family responsibilities, but only in presence of exposure to high «job strain», defined 14 according to the demand-control model (Karasek, 1979). 15

16 Considering the scarcity of evidence on the effect of the double burden posed by paid work 17 and child care on the risk of CHD in women, main purpose of this study was to examine this 18 relationship in a large Italian urban population, using number of children in the household as a 19 proxy measure of child care. This study took into account also the sex of the offspring, in the 20 light of the observed differences in terms of participation in domestic activities between sons 21 and daughters in Italy (Romano, 2012).

## 1 **2. Materials and Methods**

### 2 **2.1. Data collection.**

3 The study population was composed of all women 25-50 years old at 2001 census, resident in 4 Turin and living alone or in nuclear families (with their partners), with or without children 5 (n=109,358). Women living with people other than the partner or the children were excluded 6 because of the uncertainty on their child care support in the household. For example, grandparents, uncles or aunts could be a burden or a resource for women in performing 7 domestic work and child care, depending on their personal choices or their health status. 8 9 Baseline information on demographics, marital status, family typology, presence and number of children in the household, employment status and educational level was drawn from 2001 10 11 census data. Records from census data were linked, by means of a shared unique identification number, with those of the Municipality Registry and through this, with the local 12 archives of mortality (registry of all residents' deaths since 1970) and of hospital admissions 13 14 (which include records of all residents in Piedmont admitted to a hospital in Italy since the 1980s, with a satisfactory level of completeness since 1996). As a significant proportion of 15 16 individuals affected by acute coronary disease usually die before hospital admission, the 17 outcome of the study was represented by a binary variable, where subjects affected by CHD 18 were identified through either first hospitalization or death from CHD during the observation 19 period 2002-2010, as done in other studies using secondary data (Silventoinen, Pankow, 20 Jousilahti, Hu, & Tuomilehto, 2005; Netterstrøm, Kristensenb, & Sjølc, 2006). Women who 21 underwent hospitalization for CHD from 1996 to the start of follow-up (January 1<sup>st</sup> 2002) 22 were excluded from the study (n=94). During the follow-up period, eventual dates of 23 emigration out of Turin or death were reconstructed. Each subject contributed to person-years from January 1<sup>st</sup> 2002 until emigration, death, first hospital admission for CHD or end of 24 follow-up (December 31<sup>st</sup> 2010). 25

CHD admissions and deaths were identified in the corresponding archives through the
 presence of ICD-IX codes 410-414 in the field of main diagnosis: acute myocardial infarction
 (n=170), other acute and subacute forms of coronary heart disease (n=71), previous infarction
 (n=1), angina pectoris (n=79) and other forms of chronic ischemic heart disease (n=27).

5

## 6 2.2. Analysis

7 CHD risk was estimated by multivariate Poisson regression models, stratified by employment 8 status (employed or non-employed) and adjusted for age (5-year groups), marital status 9 (married or cohabiting; unmarried; previously married, including separated, divorced and 10 widowed) and education level (primary, secondary, higher and graduate education). The 11 analysis was stratified by employment status, after checking by test for interaction that the 12 risk of CHD associated with having children in the household was significantly different 13 between employed and non-employed women (test for interaction: p=0.03). The relationship 14 between CHD incidence and child care was assessed by operationalizing the workload linked 15 to child care in different ways: 1) number of children in the household (continuous), overall 16 and by sex; 2) combinations of number and sex of children in the household (one son, one daughter, one son and one daughter,  $\geq 2$  sons,  $\geq 2$  daughters,  $\geq 2$  sons and  $\geq 2$  daughters); 17 18 3) cumulative age of children in the household, computed as the sum of the age of all children 19 at 2001 census, also distinguished by sex, as a proxy indicator of cumulative dose of child 20 care. In multivariate Poisson regression models, all risk estimates for a given sex of the 21 children (e.g. male) were also adjusted for the presence (or number) of children of the opposite sex. 22

The association between CHD risk and cumulative age of the children was examined treating the latter either as a continuous or a categorical variable (up to 14 years, 15-29 years, 30 years or more). Furthermore, given that the effects of the double burden are expected to be stronger

in women who work long hours, a test for interaction between presence of children in the
household and number of working hours per week on CHD risk was also performed.

3

## 4 **3. Results**

## 5 **3.1. Descriptive statistics**

6 In Table 1 are presented descriptive statistics of the study population (age, place of birth,

7 marital status and education level, by employment status and presence of children in the

8 household), as well as CHD incidence in the different groups. At start of follow-up almost 4

9 out of 5 women were employed (78% of total population) and 60% of these had at least one

10 child. The whole population of employed women used to work on average 34.7 hours per

11 week, with those with children working less hours than those without children (33.5 vs. 36.4

12 hours per week, respectively).

13 With regard to the outcome variable, about 3 out of 1,000 women had undergone

14 hospitalization (n=348) or had died (n=16) from CHD during the period 2002-2010, for a total

15 of 364 women affected by CHD during the follow-up.

16 As expected, a positive trend in CHD incidence with increasing age was observed, with a

17 strong increase in the age group 45-50 years at baseline ( $\chi^2 p \le 0.001$ ), consistently with the

18 findings of other studies (Rosengren, Thelle, Köster, & Rosén, 2003).

19 About three quarters of the women were married or cohabiting (75%), 13% previously

20 married (widowed, divorced or separated) and 12% unmarried, with strong differences related

21 to employment status ( $\chi^2 p \le 0.001$ ) and presence of children in the household ( $\chi^2 p \le 0.001$ ).

22 Regarding education, more than half of women had a diploma (39%) or a university degree

23 (19%). The educational level was markedly higher among employed women ( $\chi^2 p \le 0.001$ ) and

among those without children ( $\chi^2 p \le 0.001$ ). CHD incidence decreased with increasing level

of education and was five times higher in the lowest educational level, compared to the
 highest one. The only exception was the category of non-employed women with a university
 degree, whose high incidence (88.4 per 100,000) was however estimated on only two CHD
 cases.

**TABLE 1.** Frequency distribution of age, place of birth, marital status and education, by employment status, presence or not of children in the household, and CHD incidence per 100,000 person-years.

		Employed	l women			Non-emple	oyed women	R .	,	T - 4 - 1
	witho	out children	with	n children	witho	out children	with	children		Total
	Ν	Annual CHD incidence	Ν	Annual CHD incidence	Ν	Annual CHD incidence	N	Annual CHD incidence	Ν	Annual CHD incidence
AGE						Ċ		I		
25-29 years	7,016	3.8	2,420	5.4	493	27.2	1,504	17.3	11,433	6.9
row %	61.4		21.2		4.3	$\sim$	13.2		100.0	
col %	20.6		4.7		13.4		7.4		10.5	
<b>30-34</b> years	9,217	4.1	8,343	5.9	617	21.0	3,095	16.0	21,272	7.0
row %	43.3		39.2		2.9		14.5		100.0	
col %	27.1		16.2		16.8		15.3		19.5	
35-39 years	6,756	1.8	13,297	15.2	545	23.0	4,323	24.9	24,921	13.5
row %	27.1		53.4		2.2		17.3		100.0	
col %	19.9		25.8		14.8		21.4		22.8	
40-44 years	4,973	31.2	13,550	37.8	564	21.7	4,743	66.9	23,830	41.9
row %	20.9		56.9		2.4		19.9		100.0	
col~%	14.6		26.3		15.3		23.5		21.8	
45-50 years	6,028	90.9	13,879	102.2	1,467	108.7	6,528	93.5	27,902	98.1
row %	21.6		49.7	$\bigcirc$	5.3		23.4		100.0	
col %	17.7		27.0		39.8		32.3		25.5	
PLACE OF BIRT	H			¥	1					
Italy	31,388	24.5	48,599	43.7	3,161	59.5	18,005	61.1	101,153	41.5
row %	31.0		48.0		3.1		17.8		100.0	

col %	92.3		94.4		85.8		89.2		92.5	
Abroad	2,602	14.6	2,890	37.4	525	48.5	2,188	11.1	8,205	23.9
row %	31.7		35.2		6.4		26.7	6	100.0	
col %	7.7		5.6		14.2		10.8		7.5	
MARITAL STAT	US							/		
married	18,039	22.6	43,525	40.5	3,244	46.3	19,302	54.0	84,110	40.1
row %	21.4		51.7		3.9		22.9		100.0	
col %	53.1		84.5		88.0		95.9		76.9	
previously married	4,296	29.1	6,492	66.2	260	197.7	758	78.6	11,806	56.6
row %	36.4		55.0		2.2		6.4		100.0	
col %	12.6		12.6		7.1	$\mathbf{x}$	3.8		10.8	
unmarried	11,655	23.5	1,472	24.8	182	70.8	133	190.6	13,442	25.9
row %	86.7		11.0		1.4		1.0		100.0	
col %	34.3		2.9		4.9	Y	0.7		12.3	
EDUCATION										
no school or elementary school	935	9.1	2,924	149.1	694	125.5	4,144	100.3	8,697	117.9
row %				R	/					
col %	10.8		33.6	8.0	8.0		47.6		100.0	
middle school	2.8		5.7	18.8	18.8		20.5		8.0	
row %	7,767	35.5	17,800	45.7	1,671	44.9	9,759	50.6	36,997	44.9
	21.0		48.1		4.5		26.4		100.0	
col %	22.9		34.6		45.3		48.3		33.8	
high school	15,704	20.6	21,092	33.2	1,036	24.6	5,005	38.3	42,837	29.1
row %	36.7		49.2		2.4		11.7		100.0	
col %	46.2		41.0		28.1		24.8		39.2	

raduation	9,584	12.8	9,673	29.1	285	88.4	1,285	18.4	20,827	21.9
row %	46.0		46.4		1.4		6.2		100.0	
col %	28.2		18.8		7.7		6.4	<u>C</u>	19.0	
otal	33,990	23.7	51,489	43.3	3,686	57.9	20,193	55.8	109,358	40.2
row %	31.1		47.1		3.4		18.5	1	100.0	
col %	100.0		100.0		100.0		100.0		100.0	
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2 Frequency distribution of number and gender of children in the household by employment 3 status is presented in table 2: 17.5% of women had 1 son, 16% 1 daughter, 14% 1 son and 1 4 daughter, 9.8% 2 or more sons, 8% 2 or more daughters and 0.2% (227 women) 2 or more 5 sons and 2 or more daughters. Age-adjusted CHD incidence was higher among non-employed 6 than among employed ones, overall and in most exposure categories. In particular, among 7 women with two or more sons in the household, a very high CHD incidence was observed 8 among those employed (79.8), which was almost the double of the incidence of the non-9 employed (55.5). An exceptionally high CHD incidence was also observed among employed 10 women with two or more sons and two or more daughters (261.4), although computed on a 11 very small population (n=88), with only two exposed cases.

12

**TABLE 2.** Frequency distribution of the combinations of children in the household by employment status, CHD events, CHD incidence per 100,000 person-years and Incidence Rate Ratio (IRR) of CHD adjusted for age<sup>a</sup>.

				employed wom	en			R I	non-employed we	omen	
		Ν	CHD events	Annual CHD incidence	<b>IRR</b> <sup>a</sup>	95% CI <sup>a</sup>	N	CHD events	Annual CHD incidence	<b>IRR</b> <sup>a</sup>	<b>95% CI</b> <sup>a</sup>
without children		33,866	64	23.4	1		3,666	17	58.3	1	
	col %	39.6	25.3			. (	15.4	15.3			
1 son		14,638	47	38.3	1.11	0.76-1.62	4,585	22	58.2	0.99	0.52-1.86
	col %	17.1	18.6				19.2	19.8			
1 daughter		13,576	42	36.9	1.15	0.77-1.70	3,909	19	58.2	1.05	0.55-2.02
	col %	15.9	16.6				16.4	17.1			
1 son and 1 daughter		10,554	31	34.6	1.01	0.65-1.55	4,796	25	62.3	1.12	0.60-2.09
	col %	12.3	12.3				20.1	22.5			
>= 2 sons		6,939	47	79.8	2.24	1.53-3.28	3,864	18	55.5	0.96	0.49-1.86
	col %	8.1	18.6				16.2	16.2			
>= 2 daughters		5,818	20	40.5	1.21	0.73-2.01	2,920	10	40.7	0.76	0.35-1.67
	col %	6.8	7.9				12.2	9.0			
>= 2 sons and >= 2 daughters		88	2	261.4	7.77	1.90-31.78	139	0	-	-	-
	col %	0.1	0.8				0.6	0.0			
Total		85,479	253	35.7	0.79	0.63-0.99	23,879	111	56.1	1	-
	col %	100.0	100.0				100.0	100.0			
<sup>a</sup> age in five years classes.											

1

#### 2 **3.2.** Presence of children in the household and CHD risk among women

The risk of CHD among employed women was similar to that of non-employed women, after controlling for age, education and marital status (IRR=0.98, 95% CI=0.76-1.24). In the overall population, the presence of children increased the risk of CHD significantly by 18% for each child (IRR=1.18, 95% CI=1.04-1.33), although the risk was significantly different between employed (IRR=1.29, 95% CI=1.11-1.49) and non-employed women (IRR=0.96, 95% CI=0.78-1.19).

9 Distinguishing number of children by sex (Table 2, model II), in the whole population CHD 10 risk increased significantly by 24% for each son (IRR=1.24, 95% CI=1.07-1.43), whereas the 11 increase in risk was smaller and non-significant for daughters in the household (IRR=1.11, 12 95% CI=0.95-1.30 for each daughter). The CHD risk associated with sons was significantly 13 modified by employment status (test for interaction: p=0.02), with a significant increase 14 among employed women (IRR=1.39, 95% CI=1.17-1.66) and a risk below unity for nonemployed ones (IRR=0.96, 95% CI=0.74-1.23). Also examining the effect on CHD risk for 15 16 the combination of number and sex of children, a significant interaction was found between 17 employment and having two or more sons in the household (p=0.03); the associated risk was 18 in fact significantly increased among employed women (IRR=2.23, 95% CI=1.48-3.36), but 19 close to unity among non-employed ones (IRR=0.99, 95% CI=0.50-1.96) (Table 2, model III). 20 In contrast, no significant association was found in either group for having one child, 21 independently of the sex, or two children of opposite sex, or two or more daughters. However, 22 a very high risk was found for women with two or more sons and two or more daughters, 23 although based on only two exposed cases (IRR=8.29, 95% CI=2.01-34.23). 24 With respect to marital status, only among previously married women the interaction between

25 employment and presence (yes/no) of children in the household (p=0.02) was statistically

1 significant (among married women: p=0.94; among unmarried women: p=0.27). However, the 2 risk of CHD associated with having two or more sons was, among employed married women, 3 only slightly lower than that estimated among employed women as a whole (IRR=1.93, 95% 4 CI=1.21-3.10). The risk was markedly higher among previously married women (IRR=5.11, 5 95% CI=2.01-12.96; 9 exposed cases), whereas no exposed cases were present among 6 unmarried women. In the whole population, a significantly increased risk was observed 7 among women exposed to a cumulative age of sons >=30 years (IRR=1.66, 95% CI=1.16-8 2.36), but again with a striking difference between employed (IRR= 2.28, 95% CI=1.50-3.46) 9 and non-employed women (IRR=0.87, 95% CI=0.45-1.70) (test for interaction: p=0.004). In contrast, no significant excess risk was present in any category of cumulative exposure to 10 11 daughters' care, independently of employment status. Regarding working hours, no significant interaction was found among employed women 12 13 between working hours and number of children in the household (p=0.48), independently of their gender (sons: p=0.47; daughters: p=0.06). Similarly, the interaction between working 14 15 hours and the different combinations of children by gender (model III) was not statistically significant (p=0.27). 16

TABLE 3. Incidence Rate Ratio (IRR) of CHD associated with children in the household (also distinguished by gender) (models I-III) and with sons' and daughters' cumulated age (model IV) – Poisson regression models stratified by employment status and adjusted for age<sup>a</sup>, education<sup>b</sup> place of birth<sup>c</sup> and marital status<sup>d</sup>.

		emplo	yed women		non-em	ployed wor	men
		N (CHD events)	IRR	95% CI	N (CHD events)	IRR	95% CI
Model I	number of children <sup>e</sup>	51,613 (189)	1.29	1.11-1.49	20,213 (94)	0.96	0.78-1.19
Model II	number of sons <sup>e</sup>	33,082 (133)	1.39	1.17-1.66	14,091 (65)	0.96	0.74-1.23
model II	number of daughters <sup>e</sup>	31,012 (107)	1.16	0.95-1.42	12,536 (57)	0.97	0.73-1.27
	without children	33,866 (64)	1	$\overline{\langle}$	3,666 (17)	1	
	1 son	14,638 (47)	1.11	0.75-1.66	4,585 (22)	1.03	0.54-1.96
	1 daughter	13,576 (42)	1.17	0.78-1.76	3,909 (19)	1.13	0.58-2.19
Model III	1 son and 1 daughter	10,554 (31)	1.03	0.65-1.63	4,796 (25)	1.19	0.63-2.24
	>= 2 sons	6,939 (47)	2.23	1.48-3.36	3,864 (18)	0.99	0.50-1.96
	>= 2 daughters	5,818 (20)	1.27	0.75-2.15	2,920 (10)	0.81	0.37-1.80
	>= 2 sons and >= 2 daughters	88 (2)	8.29	2.01-34.23	139 (0)	-	-
	cumulated age of sons (0-14 years) <sup>e</sup>	19,138 (24)	0.74	0.47-1.17	6,724 (18)	1.02	0.57-1.83
	cumulated age of sons (15-29 years) <sup>e</sup>	11,303 (73)	1.41	1.03-1.91	5,447 (35)	1	0.64-1.59
Model IV	cumulated age of sons (over 30 years) <sup>e</sup>	2,641 (33)	2.28	1.50-3.46	1,920 (12)	0.87	0.45-1.70
Model IV	cumulated age of daughters (0-14 years) <sup>e</sup>	18,855 (41)	1.37	0.95-1.98	6,462 (13)	0.69	0.36-1.30
	cumulated age of daughters (15-29 years) <sup>e</sup>	10,239 (55)	1.07	0.77-1.48	4,898 (34)	1.13	0.72-1.76
	cumulated age of daughters (over 30 years) <sup>e</sup>	1,918 (11)	1.14	0.61-2.15	1,176 (10)	1.29	0.63-2.60

<sup>a</sup> age in five years classes.

<sup>b</sup> education in 4 classes: no school or elementary school, middle school, high school and graduation.
<sup>c</sup> place of birth in 2 classes: Italy and abroad.
<sup>d</sup> marital status in 3 classes: unmarried, married and previously married (separated, divorced and widowed).

<sup>e</sup> continuous variable

## 2 4. Discussion

1

3 The present study showed a significant relationship between CHD risk and the double burden posed by combining paid work and child care among women in Turin. While among non-4 5 employed women the presence of children did not increase the risk of CHD, among those 6 employed the risk increased by 29% for each child. This association between such an 7 overburden and incidence of CHD is consistent with the only two studies on the subject in the 8 literature (Haynes & Feinleib, 1980; Lee et al., 2003). In both studies, in fact, intensive child 9 care was associated with an increased CHD risk among employed women, although the risk 10 estimates were marginally or not statistically significant.

11 With respect to the studies cited above, the most original aspect of our research was that the 12 risk of CHD was assessed according to the sex of the offspring; the results showed that only the presence of two or more sons in the household increased the risk of developing CHD. 13 14 Parity has been found associated with an increased risk of CHD or cardiovascular diseases 15 (CVD) in several studies, although the two main articles reviewing the available evidence on 16 the subject got to opposite conclusions (Ness, Schotland, Flegal, & Shofer, 1994; De Kleijn, 17 Van der Schouw, & Van der Graaf, 1999). However, the results of more recent studies would 18 indicate that CHD risk is actually higher among women with children than among nulliparous 19 (Lawlor et al., 2003; Catov et al., 2008; Parikh et al., 2010). From a biological point of view, 20 the finding of an increased CHD risk limited to women with male children could, in theory, 21 be explained by higher intrauterine growth (Hindmarsh, Geary, Rodeck, Kingdom, & Cole, 22 2002) and greater weight of male foetuses compared to female ones (Maršál et al., 1996) which would involve higher energy expenditure during sons' than daughter's pregnancies 23

1	(Tamimi et al., 2003). However, differences observed between sexes in these parameters are
2	likely too small to exert a negative influence on women's health (Maršál et al., 1996).
3	Number of children has also been found positively associated with several risk factors for
4	CHD, such as metabolic syndrome (Catov, 2008), hypertension (Brisson et al., 1999;
5	Zimmerman & Hartley, 1982), high levels of triglycerides and low HDL cholesterol levels
6	(Catov, 2008), high BMI (Lawlor, 2003; Hardy, Lawlor, Black, Wadsworth, & Kuh, 2007),
7	increased tone of the sympathetic nervous system (Eller, Kristiansen, & Hansen, 2011) and
8	diabetes mellitus type II (Hardy et al., 2007). Therefore, these CVD risk factors have been
9	proposed as possible mediators of parity on CHD risk, but no studies, to our knowledge,
10	reported differences related to the sex of the offspring in these intermediate outcomes.
11	With regard to socio-cultural factors, the association between the presence of male children in
12	the household and the risk of developing CHD could be explained in the light of the results of
13	the Italian Survey on the Time Use 2002-2003, showing that in Italy female children are more
14	engaged in domestic work than male ones. The gap starts to be relevant in the age group 11-
15	17 years, in which the proportion of females engaged in domestic activities is almost 50%
16	higher than that of males (65% vs. 44%) and the time spent per day is about the double for
17	females than males (44 vs. 22 minutes) (Romano, 2012). Such a difference between offspring
18	gender in term of domestic activities appears consistent with the observation that CHD risk
19	was associated with cumulative exposure to sons child care only in higher class of exposure
20	(15-29 years and $>=30$ years), which suggests a chronic effect of exposure to the "double
21	burden" on CHD risk.

Another possible explanation of the different CHD risk among employed women by the sex
of their children comes from the results of Italian Health Behaviour in Shool-aged Children
(HBSC) international survey, promoted by the World Health Organization. These findings
showed some gender differences, with higher frequencies in males, with respect to the abuse

1	of alcohol and cannabis (Cavallo et al., 2013). Therefore, employed women may be
2	overburdened by the combination of working outside the household for many hours and
3	responsibilities and concerns due to the deviant behaviour of their adolescent sons.
4	Although no study investigated women's CHD risk by sex of the offspring, a few focused on
5	the relationship between children's sex and women's longevity or mortality; however, most of
6	these studies were conducted in pre-industrial or traditional developing societies, which limits
7	their generalizability to developed contemporary ones (Helle, Lummaa, & Jokela, 2002; Van
8	de Putte, Matthijs, & Vlietinck, 2004; Hurt, Ronsmans, & Quigley, 2006). Some of them
9	found an increased risk of mortality associated with the number of sons, but not of daughters
10	(Helle et al., 2002; Van de Putte et al., 2004; Hurt et al., 2006), although other studies did not
11	find significant differences in mortality by sex of the offspring (Jasienska, Nenko, &
12	Jasienski, 2006; Cesarini, Lindqvist, & Wallace, 2007).
13	These findings suggest that the association between parity and CHD risk is more likely
14	attributable to the physical and mental workload associated with child-rearing, rather than to
15	biological factors related to pregnancy. The higher risk observed among previously married
16	women, compared to married ones, would also support a causal relationship between child
17	care burden and the CHD occurrence, given the higher burden expected among these women,
18	who need to provide child care without partner's support.
19	The results of the present study, however, should be interpreted in the light of some
20	limitations in the study design and methods. First of all, it was not possible to control for
21	several potential confounders or mediators of the association between double burden and
22	CHD, such as BMI, diabetes, smoking, alcohol and physical inactivity, all CHD risk factors
23	potentially correlated with parity, since these data were not available at census. Nonetheless,
24	the state in second in CUID with more limited to second end on a solid mode whild and it

- 24 given that the increase in CHD risk was limited to employed women with male children, it
- 25 does not seem plausible that the observed association was attributable to lack of adjustment

1 for these variables, unless their prevalence was different between employed women with male 2 and female children. For example, a higher BMI among employed women with children may have confounded the relationship between number of children and CHD incidence, but only a 3 4 higher BMI among employed women with sons, compared to those with daughters, would 5 explain the specificity of the association with male offspring. To answer this question, we 6 analyzed data from the National Health Interview 2005 on physical activity, BMI, and smoking, restricting the analysis to women 25-50 years old living in Northern Italy 7 (N=7,021). In this survey, very small differences were found in average BMI ( $\chi^2$  p=0.99), or 8 in the proportion of women performing physical activity ( $\gamma^2$  p=0.88) or smoking ( $\gamma^2$  p=0.88), 9 by number or sex of the children living in the household (personal elaboration of the authors). 10 Another limitation concerns the possible misclassification of the number of children and the 11 professional status of the women enrolled, deriving from the impossibility of detecting 12 13 newborn children (and therefore also the change in the condition of mother), as well as changes in employment status during the follow-up period. Therefore, it was assumed that 14 during the follow-up the number of children remained constant and that the professional 15 status of women did not change, with the expected consequence of a non-differential 16 17 misclassification of exposure to these factors and an underestimate of the associated relative 18 risks. Similarly, lack of information on women's employment status before 2001 census could 19 have led to identify as non-employed also women who have worked just until before 2001 census, and vice versa, making uncertain the duration of combined exposure to paid work and 20 child care. 21

With regard to the employment status of women, the absence of work stress indicators in the available databases could represent a significant information bias. Recent reviews on the relationship between exposure to psychosocial factors at work and CHD incidence have confirmed the presence of a significant excess risk associated with exposure to stress defined

1 according to the two most popular models (Kivimäki, Nyberg, & Batty, 2012; Siegrist, 2010), 2 i.e. the demand-control (Karasek, 1979) and the effort-reward imbalance model (Siegrist, 3 1996). It is therefore expected that the effect of the double burden of employed women on 4 CHD risk would be theoretically higher for women exposed to stress factors at work. For 5 example, using the demand-control model, Brisson et al. (1999) observed a significant 6 increase in blood pressure only among employed women exposed to both high job strain and 7 high household workload, whereas the increase was lower and not significant among women 8 exposed to high levels of only one of these factors.

9 In conclusion, this study found a significantly increased risk of CHD associated with the 10 presence of children in the household among employed women, which was limited to women 11 with two or more male children, whereas no association was present among non-employed 12 women. This is a new finding, which should be confirmed in other studies conducted also in 13 countries where the division of domestic (and specifically child care) duties between males 14 and females is more balanced, such as the European Nordic countries (Francavilla, Gianelli, Mangiavacchi, & Piccoli, 2013). In fact, the generalizability of the results of the present study 15 may be limited by the peculiarities of the Italian traditional family model, which tends to 16 overload the female gender with most of the burden of domestic responsibilities. 17 18 Our results suggest the need to foster social discussion in Italy on the distribution of 19 household duties and child care activities, which may help to go beyond the Italian 20 "traditional" family model. The repetition of similar research in countries with a more 21 gendered equitable division of the domestic work and child care, such as Nordic countries, 22 may help clarifying the mechanism through which employed women with sons are at higher 23 risk of CHD. The eventual persistence of such a strong association in these countries would 24 suggest that it may be attributable to other characteristics differentiating sons and daughters, 25 rather than the extent of their domestic work; for example, a more deviant behavior of sons

- 1 than daughters, made even more stressful and problematic for the working mothers by their
- 2 engagement for many hours per day outside the family.
- 3

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**TABLE 1.** Frequency distribution of age, place of birth, marital status and education, by employment status, presence or not of children in the household, and CHD incidence per 100,000 person-years.

		Employed	l women			Non-emple	oyed women		,	T - 4 - 1
	witho	out children	with	n children	witho	out children	with	children		Total
	Ν	Annual CHD incidence	Ν	Annual CHD incidence	Ν	Annual CHD incidence	N	Annual CHD incidence	Ν	Annual CHD incidence
AGE						Ċ		I		
25-29 years	7,016	3.8	2,420	5.4	493	27.2	1,504	17.3	11,433	6.9
row %	61.4		21.2		4.3	$\sim$	13.2		100.0	
col %	20.6		4.7		13.4		7.4		10.5	
30-34 years	9,217	4.1	8,343	5.9	617	21.0	3,095	16.0	21,272	7.0
row %	43.3		39.2		2.9		14.5		100.0	
col %	27.1		16.2		16.8		15.3		19.5	
35-39 years	6,756	1.8	13,297	15.2	545	23.0	4,323	24.9	24,921	13.5
row %	27.1		53.4		2.2		17.3		100.0	
col %	19.9		25.8		14.8		21.4		22.8	
40-44 years	4,973	31.2	13,550	37.8	564	21.7	4,743	66.9	23,830	41.9
row %	20.9		56.9		2.4		19.9		100.0	
col~%	14.6		26.3		15.3		23.5		21.8	
45-50 years	6,028	90.9	13,879	102.2	1,467	108.7	6,528	93.5	27,902	98.1
row %	21.6		49.7	$\bigcirc$	5.3		23.4		100.0	
col %	17.7		27.0		39.8		32.3		25.5	
PLACE OF BIRT	H			¥	1					
Italy	31,388	24.5	48,599	43.7	3,161	59.5	18,005	61.1	101,153	41.5
row %	31.0		48.0		3.1		17.8		100.0	

col %	92.3		94.4		85.8		89.2		92.5	
Abroad	2,602	14.6	2,890	37.4	525	48.5	2,188	11.1	8,205	23.9
row %	31.7		35.2		6.4		26.7	6	100.0	
col %	7.7		5.6		14.2		10.8		7.5	
MARITAL STAT	TUS							Y	-	
married	18,039	22.6	43,525	40.5	3,244	46.3	19,302	54.0	84,110	40.1
row %	21.4		51.7		3.9		22.9		100.0	
col %	53.1		84.5		88.0		95.9		76.9	
previously married	4,296	29.1	6,492	66.2	260	197.7	758	78.6	11,806	56.6
row %	36.4		55.0		2.2		6.4		100.0	
col %	12.6		12.6		7.1	$\mathbf{N}$	3.8		10.8	
unmarried	11,655	23.5	1,472	24.8	182	70.8	133	190.6	13,442	25.9
row %	86.7		11.0		1.4		1.0		100.0	
col %	34.3		2.9		4.9	Y	0.7		12.3	
EDUCATION										
no school or elementary school	935	9.1	2,924	149.1	694	125.5	4,144	100.3	8,697	117.9
row %	10.8		33.6	8.0	8.0		47.6		100.0	
col %	2.8		5.7	18.8	18.8		20.5		8.0	
middle school	7,767	35.5	17,800	45.7	1,671	44.9	9,759	50.6	36,997	44.9
row %	21.0		48.1	)	4.5		26.4		100.0	••••
col %	22.9		34.6		45.3		48.3		33.8	
high school	15,704	20.6	21,092	33.2	1,036	24.6	5,005	38.3	42,837	29.1
row %	36.7	20.0	49.2	55.2	2.4	21.0	11.7	50.5	100.0	<i>2</i> /,1
col %	30.7 46.2				2.4					
	40.2		41.0		28.1		24.8		39.2	

graduation	9,584	12.8	9,673	29.1	285	88.4	1,285	18.4	20,827	21.9
row %	46.0		46.4		1.4		6.2		100.0	
col %	28.2		18.8		7.7		6.4		19.0	
Total	33,990	23.7	51,489	43.3	3,686	57.9	20,193	55.8	109,358	40.2
row %	31.1		47.1		3.4		18.5		100.0	
col %	100.0		100.0		100.0		100.0		100.0	

**TABLE 2.** Frequency distribution of the combinations of children in the household by employment status, CHD events, CHD incidence per 100,000 person-years and Incidence Rate Ratio (IRR) of CHD adjusted for age<sup>a</sup>.

				employed wom	en			X	non-employed w	omen	
		Ν	CHD events	Annual CHD incidence	<b>IRR</b> <sup>a</sup>	<b>95% CI</b> <sup>a</sup>	N	CHD events	Annual CHD incidence	<b>IRR</b> <sup>a</sup>	<b>95% CI</b> <sup>a</sup>
without children		33,866	64	23.4	1		3,666	17	58.3	1	
	col %	39.6	25.3				15.4	15.3			
1 son		14,638	47	38.3	1.11	0.76-1.62	4,585	22	58.2	0.99	0.52-1.86
	col %	17.1	18.6				19.2	19.8			
1 daughter		13,576	42	36.9	1.15	0.77-1.70	3,909	19	58.2	1.05	0.55-2.02
	col %	15.9	16.6				16.4	17.1			
1 son and 1 daughter		10,554	31	34.6	1.01	0.65-1.55	4,796	25	62.3	1.12	0.60-2.09
	col %	12.3	12.3				20.1	22.5			
>= 2 sons		6,939	47	79.8	2.24	1.53-3.28	3,864	18	55.5	0.96	0.49-1.86
	col %	8.1	18.6				16.2	16.2			
>= 2 daughters		5,818	20	40.5	1.21	0.73-2.01	2,920	10	40.7	0.76	0.35-1.67
	col %	6.8	7.9				12.2	9.0			
>= 2 sons and >= 2 daughters		88	2	261.4	7.77	1.90-31.78	139	0	-	-	-
	col %	0.1	0.8				0.6	0.0			
Total		85,479	253	35.7	0.79	0.63-0.99	23,879	111	56.1	1	-
	col %	100.0	100.0				100.0	100.0			
<sup>a</sup> age in five years classes.							1				

TABLE 3. Incidence Rate Ratio (IRR) of CHD associated with children in the household (also distinguished by gender) (models I-III) and with sons' and daughters' cumulated age (model IV) – Poisson regression models stratified by employment status and adjusted for age<sup>a</sup>, education<sup>b</sup> place of birth<sup>c</sup> and marital status<sup>d</sup>.

		employed women			non-employed women		
		N (CHD events)	IRR	95% CI	N (CHD events)	IRR	95% CI
Model I	number of children <sup>e</sup>	51,613 (189)	1.29	1.11-1.49	20,213 (94)	0.96	0.78-1.19
Model II	number of sons <sup>e</sup>	33,082 (133)	1.39	1.17-1.66	14,091 (65)	0.96	0.74-1.23
	number of daughters <sup>e</sup>	31,012 (107)	1.16	0.95-1.42	12,536 (57)	0.97	0.73-1.27
Model III	without children	33,866 (64)	1	~	3,666 (17)	1	
	1 son	14,638 (47)	1.11	0.75-1.66	4,585 (22)	1.03	0.54-1.96
	1 daughter	13,576 (42)	1.17	0.78-1.76	3,909 (19)	1.13	0.58-2.19
	1 son and 1 daughter	10,554 (31)	1.03	0.65-1.63	4,796 (25)	1.19	0.63-2.24
	>= 2 sons	6,939 (47)	2.23	1.48-3.36	3,864 (18)	0.99	0.50-1.96
	>= 2 daughters	5,818 (20)	1.27	0.75-2.15	2,920 (10)	0.81	0.37-1.80
	>= 2 sons and >= 2 daughters	88 (2)	8.29	2.01-34.23	139 (0)	-	-
Model IV	cumulated age of sons (0-14 years) <sup>e</sup>	19,138 (24)	0.74	0.47-1.17	6,724 (18)	1.02	0.57-1.83
	cumulated age of sons (15-29 years) <sup>e</sup>	11,303 (73)	1.41	1.03-1.91	5,447 (35)	1	0.64-1.59
	cumulated age of sons (over 30 years) <sup>e</sup>	2,641 (33)	2.28	1.50-3.46	1,920 (12)	0.87	0.45-1.70
	cumulated age of daughters (0-14 years) <sup>e</sup>	18,855 (41)	1.37	0.95-1.98	6,462 (13)	0.69	0.36-1.30
	cumulated age of daughters (15-29 years) <sup>e</sup>	10,239 (55)	1.07	0.77-1.48	4,898 (34)	1.13	0.72-1.76
	cumulated age of daughters (over 30 years) <sup>e</sup>	1,918 (11)	1.14	0.61-2.15	1,176 (10)	1.29	0.63-2.60

<sup>a</sup> age in five years classes.
 <sup>b</sup> education in 4 classes: no school or elementary school, middle school, high school and graduation.
 <sup>c</sup> place of birth in 2 classes: Italy and abroad.
 <sup>d</sup> marital status in 3 classes: unmarried, married and previously married (separated, divorced and widowed).

<sup>e</sup> continuous variable

## **HIGHLIGHTS:**

- 1) retrospective study (2002-10) on women aged 25-50 years at baseline
- 2) CHD risk increased significantly by 18% for each child, only among employed women
- 3) having two or more sons doubled CHD risk, also only among employed women
- 4) no significant increase in CHD risk was present among women with daughters
- 5) results may be due to a gendered division of domestic work among Italian adolescents

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