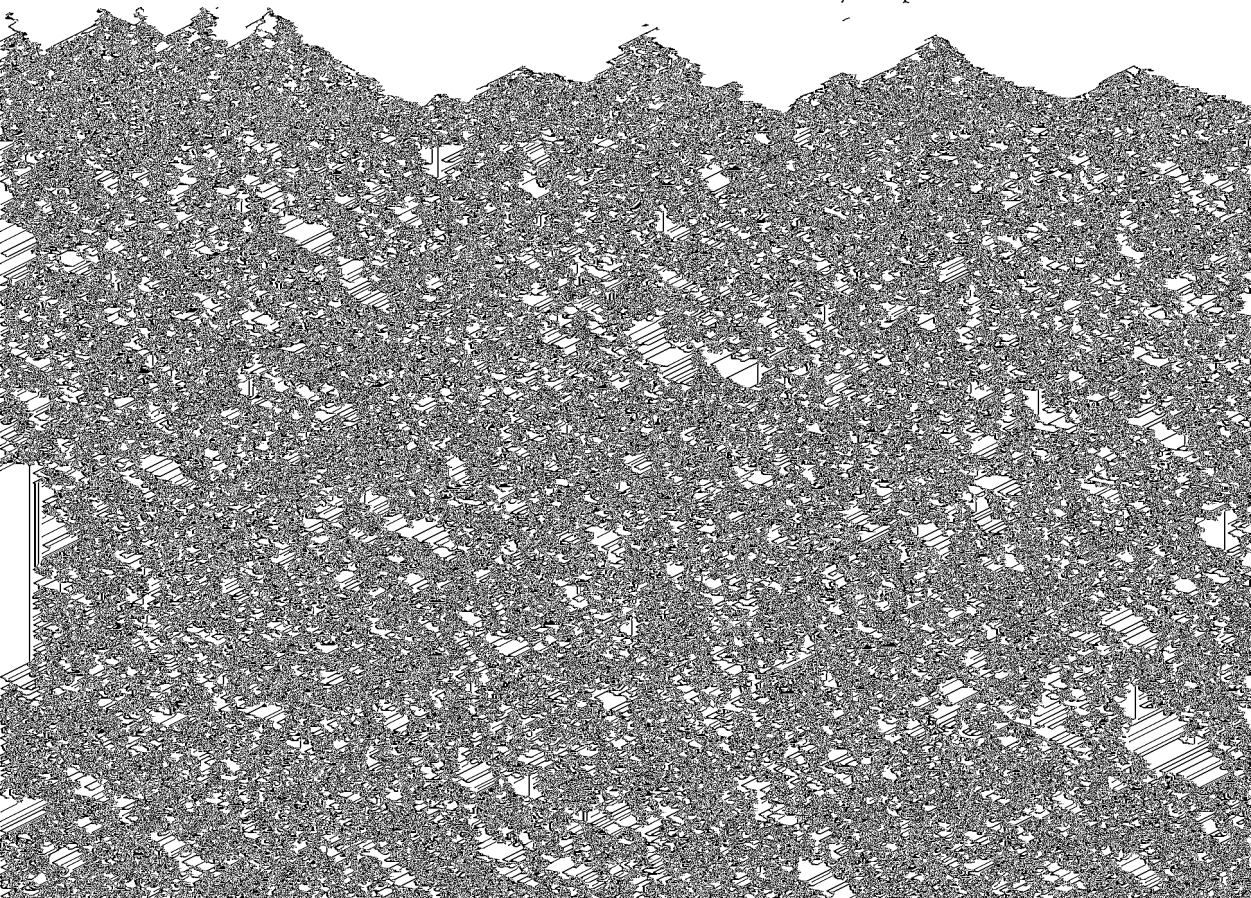


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Cardiovascular morbidity and mortality in postmenopausal women

In their forties and fifties, women have lower cardiovascular disease (CVD) rates than men of the same age (Tunstall-Pedoe et al., 1994). In their sixties, these lower rates persist but, as age increase, women catch up with men. This apparent protection from CVD has been attributed to high levels of circulating endogenous estrogens present in women rather than to chronological effect only (Bush, 1990). Thus, part of increase in CVD could be attributed to menopause. However, the effect on the cardiovascular risk (CVR) is only observed ten to fifteen years following menopause.

The WHO Monica Project is a 10-year study that monitors deaths due to coronary heart disease and acute myocardial infarction as well as coronary care and risk factors in men and women aged from 35 to 64 years in 38 defined communities from 21 countries. Data from this study are presented in



ered in only one study, comparing cardiovascular mortality with all-cause mortality (Horiuchi, 1997).

Prospective studies

The main features and results of five studies are described in tables 1.II and 1.III.

The Nurses' Health Study cohort considered 121 700 female registered nurses 30 to 55 years old ; 98 percent were white. In 1976, 116 258 of these women who were premenopausal or had a known history of menopause formed the population for the analysis of menopause and the risk of coronary heart disease (Colditz et al., 1987). A significant increase in the risk of coronary heart disease was observed among postmenopausal women with bilateral oophorectomy who had never received postmenopausal estrogen therapy. Natural menopause was not associated with a large increase in the risk of coronary heart disease. Similarly, among postmenopausal women who had undergone hysterectomy with unilateral oophorectomy, or hysterectomy without oophorectomy no material increase in the risk was observed.

The Framingham study considered a cohort of 2 873 Framingham women who were followed for 24 years. Beginning in 1948 these 2 873 women, then aged 29 through 62 years, were given a thorough cardiovascular examination. In 1978, Gordon et al. published a report based on data from the first 13 examinations. An increase in coronary heart disease incidence was found after both surgical and natural menopause, and this increase was not restricted to younger women with premature menopause. The findings suggest that the increase in coronary heart disease incidence occurs by a sudden escalation in risk at time of menopause.

A 12-year follow-up of 1 462 women initially aged 38-60 has been performed in Gothenburg, Sweden since 1968 (Lapidus et al., 1985). The 12-year incidences of the cardiovascular end-points studied are compared among women who reach menopause spontaneously at ages 40, 45 and 50. There were no statistical differences, but the risk ratios were increased for all the cardiovas-

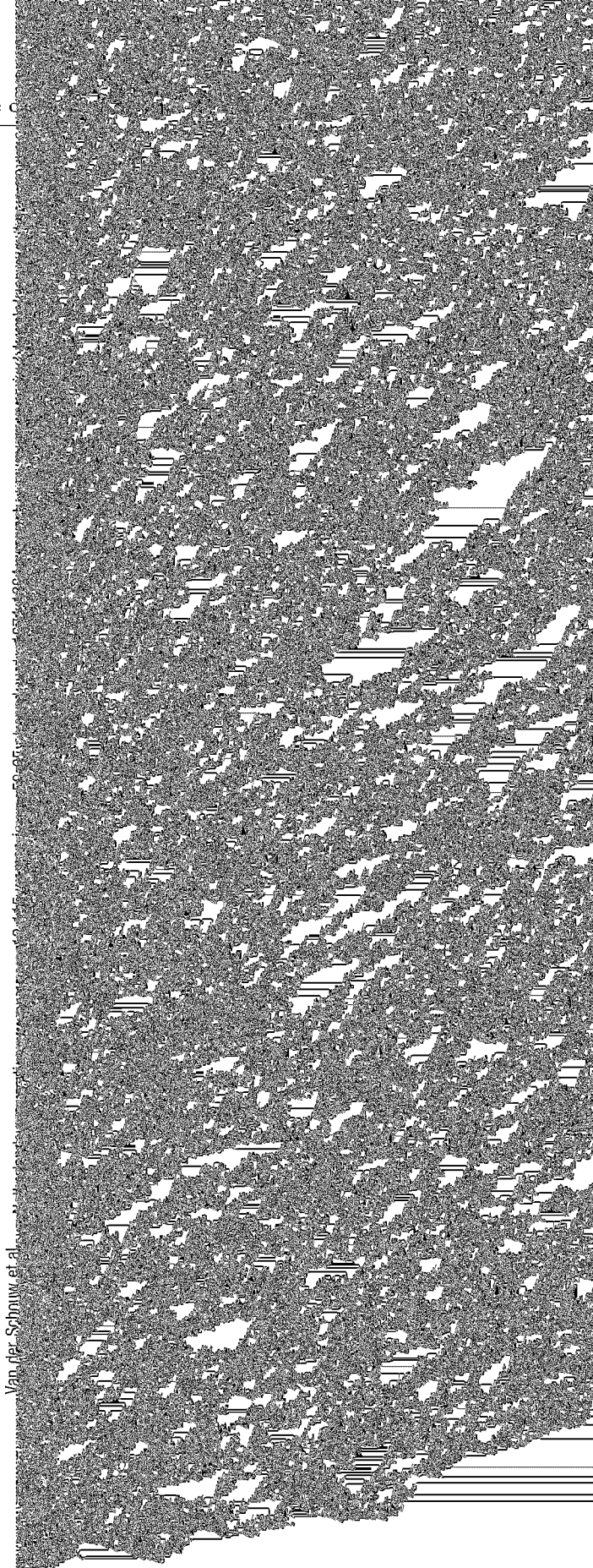
Table 1.11 : Cardiovascular morbidity or mortality in postmenopausal women

Authors	Population study design	N	Age range	Study period	Morbidity or mortality
Coidtitz et al. (1987)	US women prospective (Nurses Health Study : NHS) CHD : non fatal MI, death due to CHD	121 700	30-55 in 1976 menopause: cessation of menses permanently	1976 to 1982	RR of CHD adjusted for age NatMp vs preMp: 1.2 (0.8-1.8) bilateral oophorectomy vs preMp : 2.2 (1.2-4.2)
Gordon et al. (1978)	Framingham prospective CHD : angina , coronary insufficiency, MI, death due to CHD	2 873	29- 62 in 1948 menopausal experience : 2-year interval	1948 to 1972	in age range 40 to 54 : RR of CHD adjusted for age NatMp vs preMp : 2.7 (p<0.001) Surgical vs preMp : 2.7 (p<0.01)
Witteaman et al. (1989)	Netherlands cross-sectional atherosclerosis diagnosed by radiographic detection of calcified deposits in abdominal aorta	676	45-55		RR adjusted for NatMp vs preMp: 3.4 (1.2-9.7) Bilateral oophorectomy vs preMp : 5.5 (1.9-15.8)

Table 1.III : Age at menopause and cardiovascular morbidity and mortality

Authors	Population	N	Age range	Study period	Morbidity
Bengtsson (1973)	Sweden case-control	control : 578 angina pectoris : 29 MI: 57	50 and 54	1968-1969	women with MI : menopause earlier than controls (p<0.05)

Van der Schouw et al.

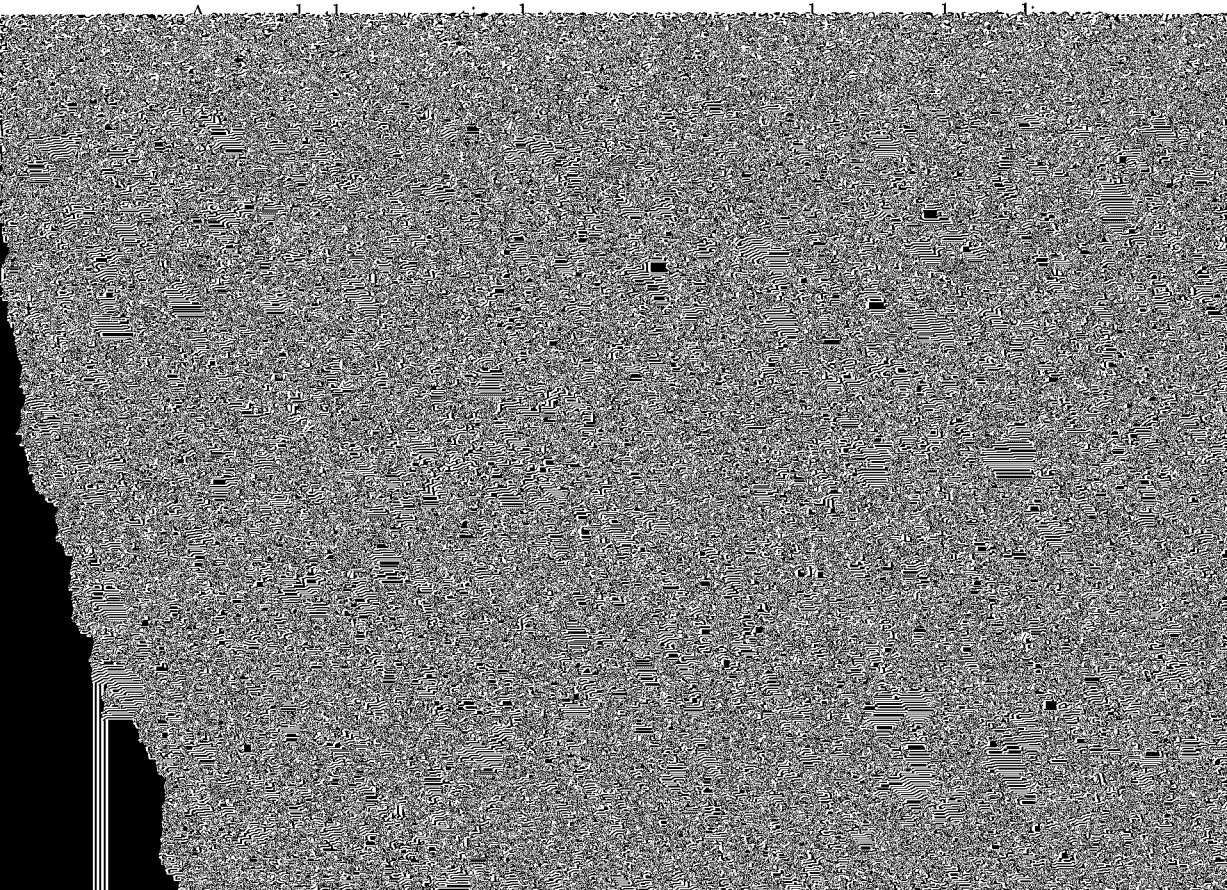


The study by Horiuchi (1997) tested the hypothesis of a postmenopausal

hospitalization for MI was known. Of the 279 MI cases, 44 % were postmenopausal at the time of MI compared with 33 % of 5 580 matched control subjects. Among women who became menopausal because of bilateral oophorectomy, the estimated relative risk of MI increased with decreasing age at menopause, and women who underwent bilateral oophorectomy before age 35 were estimated to have a risk of hospitalisation for MI approximately 7.2 times (95 % CI, 4.5 to 11.4) that of premenopausal women. Hysterectomy with preservation of at least one ovary was associated with a small increase in the risk of MI.

Bengtsson et al. (1973) retrospectively studied age at menopause in the Swedish female population from Göteborg, suffering from ischaemic heart diseases (IHD - 29 with angina pectoris and 57 with myocardial infarction) or presenting ECG changes suggesting IHD (23 women). Significantly more women with IHD were postmenopausal at 45-50 years than in the general population (578 control women). This study suggests an association between premature menopause and ischaemic heart diseases. However, all the women aged 47 or less were still menstruating at the time of their infarct, suggesting that menopause is not strictly necessary for the development of early myocardial infarction.

Critical analysis



ity acceleration, the consequences of CV diseases accounting for more than 50 % of the sex difference in the acceleration of all-cause mortality.

To ascertain the influence of age at menopause (early menopause) on CHD, all published studies have been considered, although the report of Van der Schouw et al. (1996) appears to be the most reliable. Barrett-Connor's review (Barrett-Connor and Bush, 1991) indicates that a number of results concerning the association of early menopause with the risk of heart disease are inconsistent and often not statistically significant. However, the prospective

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