

Systematic Review and Meta-Analysis of Circulatory Disease from Exposure to Low-Level Ionizing Radiation and Estimated Potential Population Mortality Risks

(Little *et al.* *Environ Health Perspectives* 2012 in press)

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Meta analysis of circulatory disease

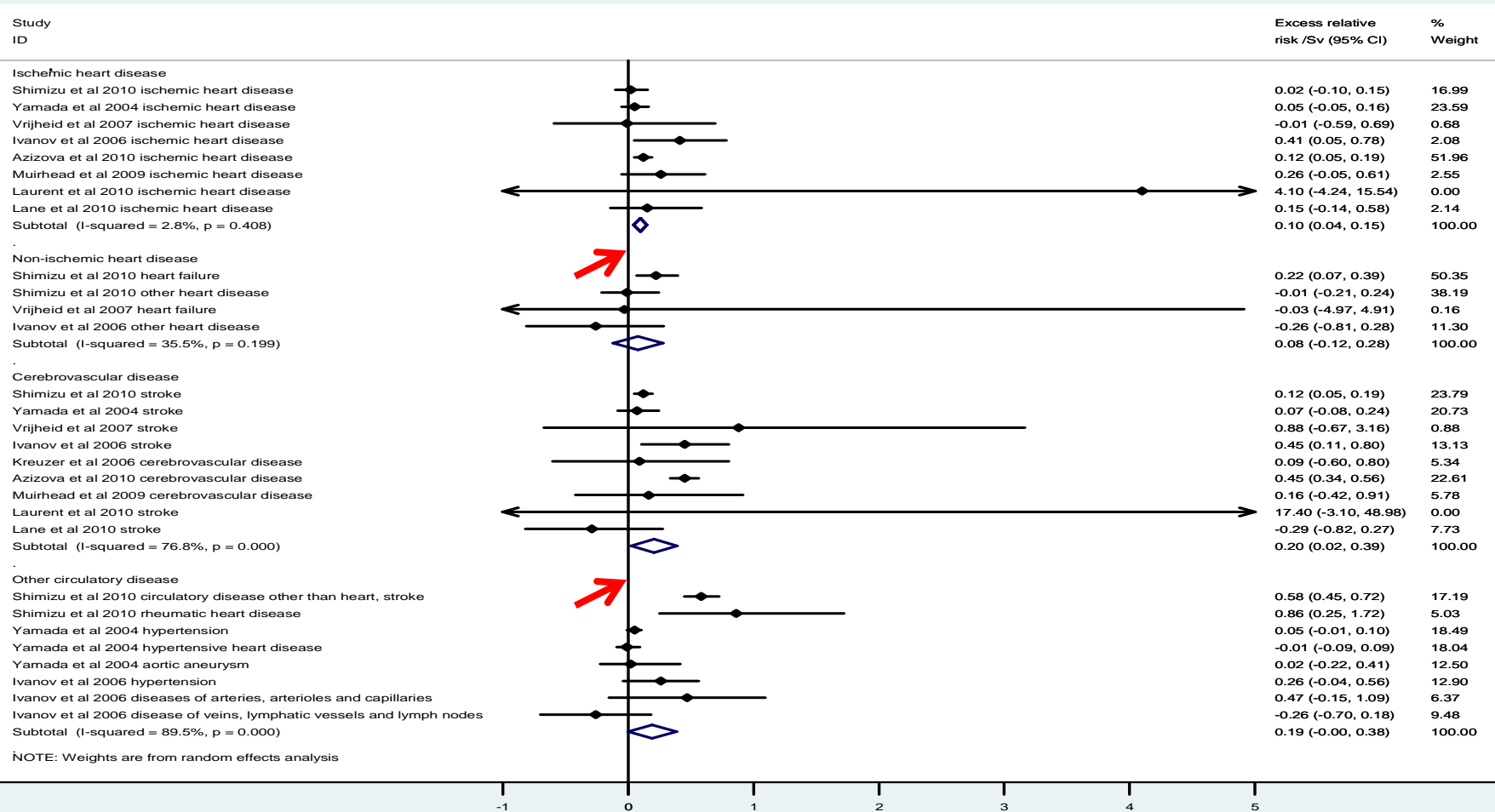
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- PubMed + ISI Thompson search using terms “radiation” + “heart” + “disease” or “radiation” + “stroke” or “radiation” + “circulatory” + “disease”, published $\geq 1/1/1990$ (search on 17/8/2011)
- Restricted to human data exposed to moderate/low whole body doses (mean < 0.5 Sv – limit suggested by radiobiology), with good quality dosimetry
- 10 studies identified
- Fixed effect + random effects analysis (random effects needed when significant heterogeneity)

Overall findings from meta-analysis

(Little *et al. Environ Health Perspectives* 2012 in press)

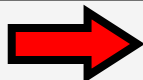
Significant excess risk in two out of four circulatory disease groups (ischemic heart, stroke), significant excess risk overall



Meta-analysis of moderate/low dose circulatory disease: excess relative risk coefficients

(Little *et al. Environ Health Perspectives* 2012 in press)

Circulatory disease subtype	Studies Included	Fixed-effect ERR / Sv (+95% CI)	Random-effect ERR / Sv (+95% CI)	Heterogeneity <i>p</i>
Ischemic heart disease	Yamada <i>et al.</i> , Ivanov <i>et al.</i> , Vrijheid <i>et al.</i> , Muirhead <i>et al.</i> , Azizova <i>et al.</i> , Shimizu <i>et al.</i> , Laurent <i>et al.</i> , Lane <i>et al.</i>	0.10 (0.05 to 0.15)	0.10 (0.04 to 0.15)	0.408
Non-ischemic heart disease	Ivanov <i>et al.</i> , Vrijheid <i>et al.</i> , Shimizu <i>et al.</i>	0.12 (-0.01 to 0.25)	0.08 (-0.12 to 0.28)	0.199
Cerebrovascular disease	Yamada <i>et al.</i> , Ivanov <i>et al.</i> , Kreuzer <i>et al.</i> , Vrijheid <i>et al.</i> , Azizova <i>et al.</i> , Muirhead <i>et al.</i> , Shimizu <i>et al.</i> , Laurent <i>et al.</i> , Lane <i>et al.</i>	0.20 (0.14 to 0.25)	0.21 (0.02 to 0.39)	<0.001
Circulatory disease apart from heart disease and stroke	Yamada <i>et al.</i> , Ivanov <i>et al.</i> , Shimizu <i>et al.</i>	0.10 (0.05 to 0.14)	0.19 (-0.00 to 0.38)	<0.001



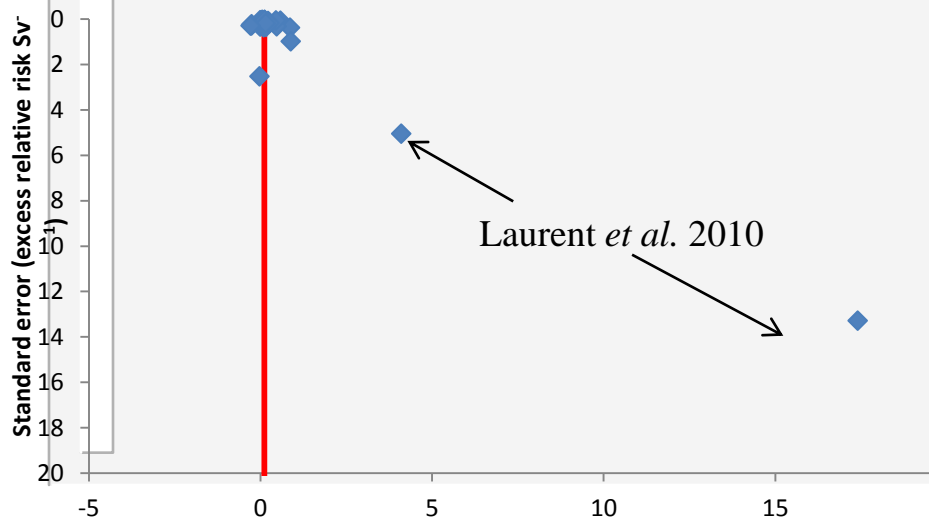
Random effects model suggests significant excess risk for all endpoints except non-ischaeamic heart and other circulatory
Excluding Laurent *et al.* makes almost no difference

Problems with meta-analysis: publication bias?

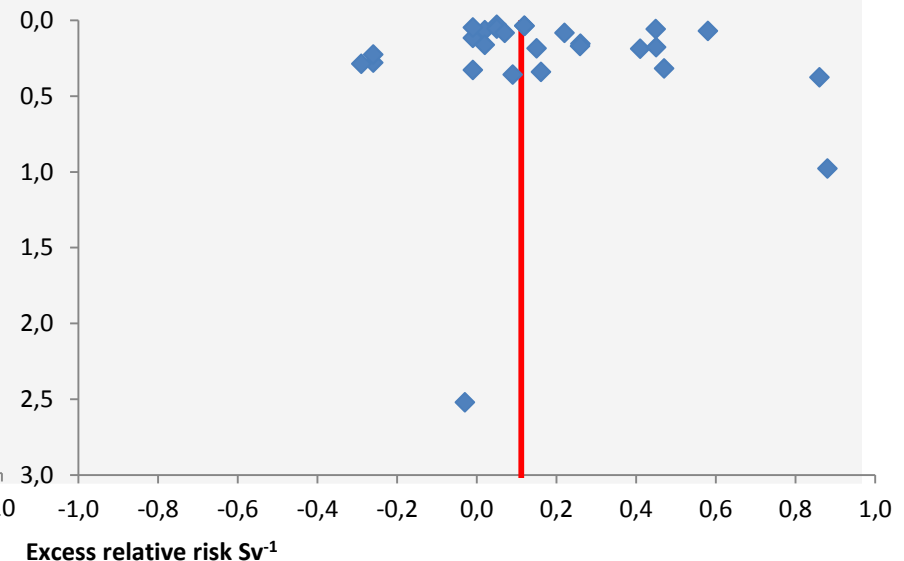
(Little *et al. Environ Health Perspectives* 2012 in press)

- Generally expect bias towards publications with significant results
- Funnel plot (mean *vs* SE) is (after excluding Laurent *et al.*) reasonably symmetric, implying little or no bias
- Formally confirmed by Egger *et al*, Duval & Tweedie tests

All data



All data excluding Laurent *et al.* 2010



Radiation-Exposure-Induced Death for Various Subtypes of Circulatory Disease, by Country

(Little *et al. Environ Health Perspectives* 2012 in press)

Country	Radiation-Exposure-Induced Death, x 10 ⁻² Sv (+95% CI) using Random Effects Model							
	Ischaemic heart disease	Other heart disease	Stroke	Other circulatory disease	All circulatory disease	UNSCEAR cancer risks All solid cancer	Leukemia excl CLL	
China	0.92 (0.41, 1.42)	0.11 (-0.16, 0.37)	4.31 (0.48, 8.14)	1.43 (-0.01, 2.86)	6.76 (2.63, 10.89)	3.95 3.89	0.27 0.42	
France	0.50 (0.22, 0.78)	0.54 (-0.85, 1.94)	0.92 (0.10, 1.74)	0.53 (0.00, 1.05)	2.50 (0.77, 4.22)	-	-	
Germany	1.71 (0.76, 2.65)	0.97 (-1.52, 3.46)	1.69 (0.19, 3.19)	1.38 (-0.01, 2.76)	5.75 (2.39, 9.10)	-	-	
Japan	0.57 (0.25, 0.88)	0.80 (-1.25, 2.85)	2.19 (0.24, 4.14)	0.45 (0.00, 0.91)	4.01 (1.13, 6.89)	4.65 4.90	0.32 0.43	
Russia	2.82 (1.26, 4.39)	0.31 (-0.49, 1.11)	4.59 (0.51, 8.66)	0.79 (0.00, 1.57)	8.51 (4.00, 13.02)	→ Circulatory disease risk comparable with cancer risk		
Spain	0.91 (0.41, 1.42)	0.82 (-1.28, 2.52)	1.91 (0.21, 3.60)	0.81 (0.00, 1.63)	4.45 (1.73, 7.17)			
Ukraine	4.14 (1.85, 6.43)	0.20 (-0.31, 0.70)	2.85 (0.31, 5.39)	0.93 (0.00, 1.85)	8.11 (4.53, 11.69)			
UK	1.70 (0.76, 2.64)	0.37 (-0.58, 1.32)	2.24 (0.25, 4.22)	0.76 (0.00, 1.53)	5.07 (2.55, 7.58)		5.15 4.40	0.38 0.43
USA	1.82 (0.81, 2.82)	0.57 (-0.89, 2.03)	1.29 (0.14, 2.44)	0.80 (0.00, 1.61)	4.48 (2.22, 6.74)		4.74 4.41	0.47 0.42

Conclusions

- ❑ Meta-analysis of moderate+low-dose data suggests significant excess risk for two out of four circulatory disease endpoints (ischaemic heart, stroke), and aggregate risk significant
- ❑ Risk factors from moderate+low-dose cohorts suggest radiation-associated population risks of circulatory disease are similar to radiation-induced cancer