Salt reduction lowers cardiovascular risk: meta-analysis of outcome trials

A recent Cochrane Review by Rod Taylor and colleagues, published simultaneously in The Cochrane Library¹ and the American Journal of Hypertension², stated in the plain language summary that "Cutting down on the amount of salt has no clear benefits in terms of likelihood of dying or experiencing cardiovascular disease". The Cochrane Library's own press release headline included this statement: "Cutting down on salt does not reduce your chance of dying". Both of these statements are incorrect.

The study reported in the paper by Taylor and colleagues is a meta-analysis of randomised trials with follow-up for at least 6 months on the effect of reducing dietary salt on total mortality and cardiovascular mortality and events. There were seven trials with 6250 participants (665 deaths). One of these trials in heart failure, in our view, should not have been included because the participants were severely salt and water depleted due to aggressive diuretic therapy (frusemide 250–500 mg twice daily, and spironolactone 25 mg per day) as well as captopril 75–150 mg per day and fluid restriction to 1000 mL per day. While on these treatments, participants were randomly assigned to a reduced salt intake or their usual salt intake. In view of the fact that the dose of diuretics was not adjusted downwards, a lower salt

intake is likely to worsen the salt and water depletion and therefore, unsurprisingly, resulted in worse outcomes.

In the remaining six trials, there is a reduction in all clinical outcomes (all-cause mortality, cardiovascular mortality and events) (table), although none of these are statistically significant. This trend of consistent reductions in all clinical outcomes seems to have been overlooked by Taylor and colleagues.1 The non-significant findings are most likely the result of a lack of statistical power, particularly as Taylor and colleagues analysed the trials for hypertensives and normotensives separately. We have reanalysed the data by combining data for hypertensives and normotensives together. Our results show that there is now a significant reduction in cardiovascular events by 20% (p<0.05) (figure) and a non-significant reduction in all-cause mortality (5-7%), despite the small reduction in salt intake of 2.0-2.3 g per day. The results of our reanalysis, contrary to the claims by Taylor and colleagues, support current public health recommendations to reduce salt intake in the whole population.

Taylor and colleagues call for further large longterm randomised trials of salt reduction on clinical outcomes.^{1,2} According to their own calculations, at least 2500 cardiovascular events need to be obtained to

	Trials in normotensives (n=3)*	Trials in hypertensives (n=3)*	
Reduction in salt intake at end of trial (g per day [95% CI]); duration 6-36 months	2·0 (1·1 to 2·9)	2·3 (1·8 to 2·8)	
Fall in blood pressure at end of trial (mm Hg [95%CI]); duration 18-36 months			
Systolic	1·11 (-0·11 to 2·34)	4·14 (2·43 to 5·84)	
Diastolic	0·80 (0·23 to 1·37)	3·74 (-0·93 to 8·41)	
Difference in all-cause mortality at longest follow-up (95%CI); duration 7 months to 12.7 years	10% reduction (RR 0·90, 0·58 to 1·40)	4% reduction (RR 0.96, 0.83 to 1.11)	
Difference in cardiovascular events at longest follow-up (95%CI); duration 7 months to $11\cdot5$ years	29% reduction (RR 0·71, 0·42 to 1·20)	16% reduction (RR 0.84, 0.57 to 1.23)	
Difference in CVD mortality at longest follow-up (95%CI); duration 7 months to 6 years		31% reduction (RR 0·69, 0·45 to 1·05)	
RR=relative risk; CVD=cardiovascular disease. * Not all measurements were	e made in all trials.		
Table: Change in salt intake, blood pressure, and clinical outcom in heart failure)	nes with results from the meta-analysis b	y Taylor and colleagues¹ (excluding the trial	

Study*	Reduced-salt		Control		Relative risk of CVD events (95% CI)	Relative risk (95% CI)
	Events	Total	Events	Total		
TOHPI	17	321	32	311		0.51 (0.29-0.91)
TOHP II	71	938	80	935	-	0.88 (0.65-1.20)
Morgan	6	34	5	33		1.16 (0.39-3.45)
TONE	36	322	46	331	- ■	0.80 (0.53-1.21)
Total	130	1615	163	1610	•	0.80 (0.64-0.99)
					0.1 1 10	
					Favours reduced-salt Favours control	

Figure: Relative risk of cardiovascular disease (CVD) events in our meta-analysis of outcome trials of salt reduction at longest follow-up combining hypertensive and normotensive individuals

Duration of follow-up ranged from 7 months to 11-5 years. We used fixed effect model with normotensives and hypertensives combined. Heterogeneity χ^2 =3-20, df=3 (p=0-36); l^2 =6%. Test for overall effect Z=2-02 (p=0-04). TOHP I=Trial of Hypertension Prevention, phase 1. TOHP II=Trial of Hypertension Prevention, phase 2. TONE=Trial of Nonpharmacologic Interventions in Elderly. *Data for individual trials taken from Taylor and colleagues' meta-analysis.¹

detect a 10% reduction (at 80% power and 5% significance level).² This would require randomisation of about 28 000 participants to a low or high salt intake and then maintenance of the two separate diets for at least 5 years. Such a trial is impractical because of logistical and financial constraints, and the ethical issues of putting a group of people on a high salt diet for so many years.

In our view, Taylor and colleagues' Cochrane review and the accompanying press release reflect poorly on the reputation of The Cochrane Library and the authors. The press release and the paper have seriously misled the press and thereby the public—for example, in the UK the *Daily Express* front page headline read "Now salt is safe to eat—Health fascists proved wrong after lecturing us all for years" and there were similar headlines throughout the world.

The totality of evidence, including epidemiological studies, animal studies, randomised trials, and now

outcome studies all show the substantial benefits in reducing the average intake of salt.⁶⁻⁹ Most countries have adopted policies to reduce salt intake by persuading the food industry to reformulate food with less salt, as is occurring successfully in the UK,¹⁰ and also by encouraging people to use less salt in their own cooking and at the table. WHO has recommended salt reduction as one of the top three priority actions to tackle the global non-communicable disease crisis.¹¹ A reduction in population salt intake will have major beneficial effects on health along with major cost savings in all countries around the world.^{6,12,13}

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