



## REVIEW

# Dietary exposure to emulsifiers and detergents and the prevalence of cardiovascular disease

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## Introduction: the remarkable rise and fall in mortality from cardiovascular disease during the 20th century

10 Since the late 1960s there have been dramatic falls in mortality from cardiovascular disease, across western and northern Europe and north America. In the UK, age-standardized death rates from cardiovascular disease declined by 74% from 1969 to 2013<sup>1</sup> and in the US the age-standardized death rate for coronary heart disease had fallen by 76% from its peak in 1968 to 2010.<sup>2</sup> Death from cardiovascular disease, particularly coronary heart disease, is to a large extent a 20th century phenomenon—doubling between 1920 and 1960, then declining rapidly from the late 1960s (Figure 1a). This point was made very effectively by Grimes in his QJM review where he also suggested that appearance and later disappearance of a biological environmental factor might be responsible.<sup>3</sup>

25 Reduction in established risk factors such as smoking (down in the US from 42% of adults in 1965 to 18% by 2013), cholesterol and blood pressure has been estimated to account for between 44 and 76% of the decline in cardiovascular mortality and treatments to account for 23–47%.<sup>4</sup> Different factors may have been more important over different time periods. For example, a Finnish study of 34 525 people followed during 1972–2012 showed that changes in smoking prevalence, serum cholesterol and systolic blood pressure accounted for nearly all observed reduction in coronary heart disease mortality during the first 10 years of the study but only about two-thirds of the continuing reduction in mortality during the last 10 years.<sup>5</sup> Some of this more recent reduction in mortality will have resulted from advances in secondary prevention and treatment but this leaves

substantial room for impact from other environmental factors acting either independently or via changes in serum cholesterol or blood pressure. One such factor is the reduction in particulate air pollution that followed the introduction of the Clean Air Act in the UK in 1956 and similar legislation in other western countries. Another factor considered here is the possible role of dietary exposure to emulsifiers and washing detergents. This could plausibly explain two odd features of the epidemiology of cardiovascular disease—the “French paradox”—the relative immunity of the French to coronary disease despite high smoking rates (Figure 1b) and the increased risk in areas with a soft drinking water supply. A “crazy hypothesis” which follows is that the decline in atheromatous disease over the past 50 years might be related in part to increasingly widespread use of dish-washing machines that will rinse away detergent.

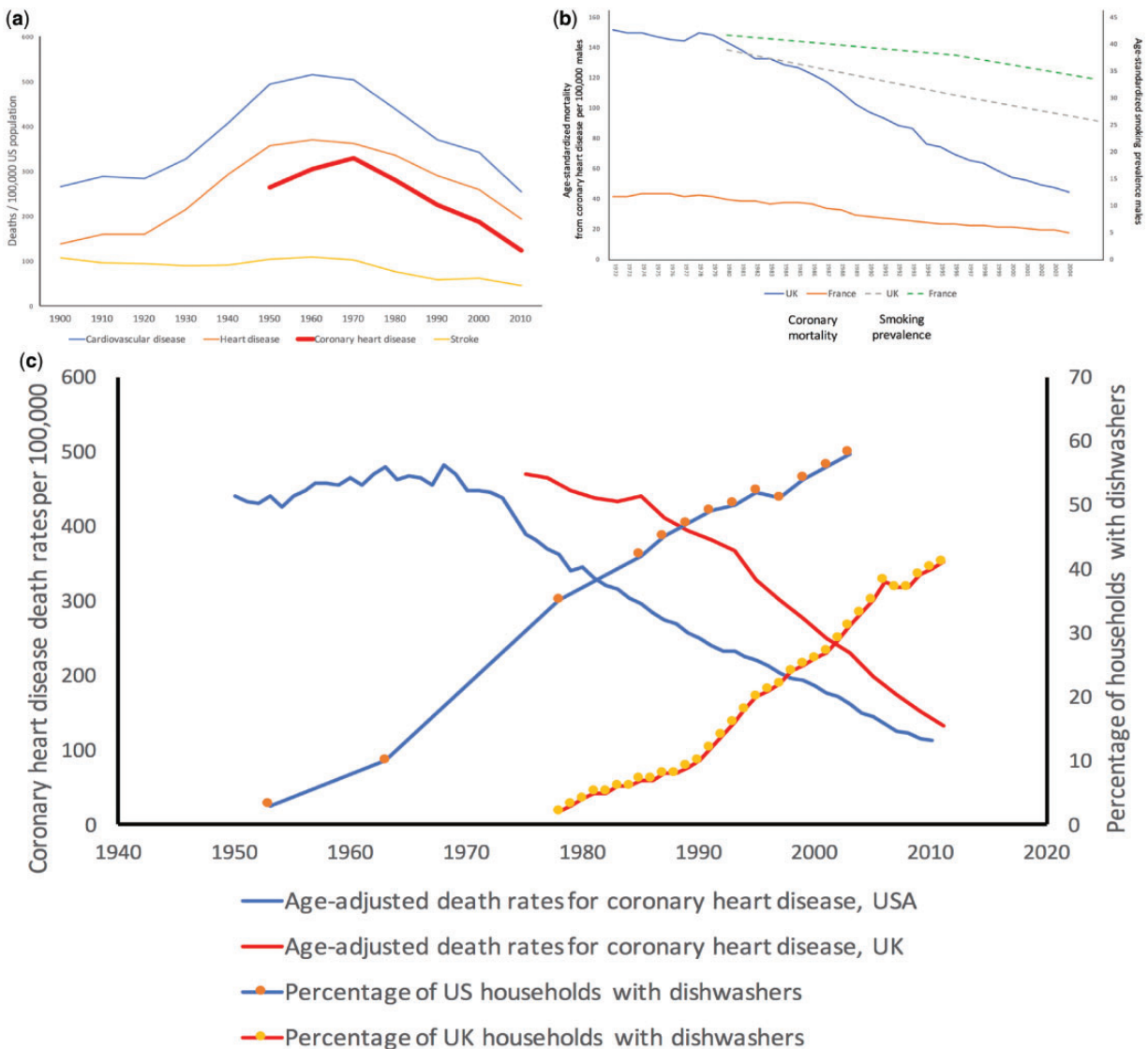
## Dietary ingestion of emulsifiers and detergents and their impacts on barrier function of the intestinal epithelium

55 Synthetic food emulsifiers were introduced in the 1930s and include polysorbates, derived from polyethoxylated sorbitan and oleic acid and used in baking, spreads, ice creams and confectionery. They were thought to be harmless, based on short-term studies in healthy humans and animals. Our research group and others have however shown that relevant concentrations of polysorbate-80 plausibly present in the intestines of humans on a western diet cause a marked increase in bacterial translocation across the human intestinal epithelium in short-term culture.<sup>6</sup> A subsequent study showed that ingestion of

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**Figure 1.** (a) Death rates (not age-adjusted) from cardiovascular disease in the United States showing a marked rise and fall during the 20th century (data from <sup>20</sup>). (b) “The French paradox”. Age-standardized mortality from coronary heart disease has substantially been greater in UK than France despite higher smoking prevalence in France (data from Allender et al.<sup>12</sup> and Ng et al.<sup>21</sup>). (c) Death rates from coronary heart disease have come down in the USA and UK (data from <sup>1,2</sup>); percentage of households with dishwashers has gone up. (data from <sup>22-24</sup>). Is this an irrelevant coincidence or has 20th century man been inadvertently suffering from detergent poisoning?

polysorbate-80 by mice induced gut inflammation and metabolic syndrome.<sup>7</sup> These effects are associated with changes in the gut microbiota and the bacterial translocation occurs across (not between) epithelial cells that would normally be a very effective barrier to bacteria.

The commonest dietary emulsifier is lecithin—a variable mixture of phosphatidyl choline, phosphatidyl ethanolamine and phosphatidyl inositol—present in egg yolk where it acts as the emulsifier for mayonnaise, but also ubiquitous in animal and plant cell walls. The impact of dietary lecithin on bacterial translocation has yet to be rigorously studied but a high intake of dietary lecithin has been incriminated as a risk factor in coronary artery disease although emphasis has been placed on the pro-atherogenic effects of the choline metabolite tri-methylamine-N-oxide, serum concentrations of which correlate strongly with risk for subsequent cardiovascular events.<sup>8</sup>

Further studies on other permitted food emulsifiers are awaited.

The impact of washing detergents on the intestine has mainly been reported following case reports of accidental one-off ingestion which may cause acute damage to the upper intestine and airways. Very little study has been made of effects of longer-term lower dose exposure. One study performed in dogs over 50 years ago showed extensive atheroma and marked hypercholesterolaemia after 2–3 weeks of a drastic protocol of intravenous Triton (non-ionic detergent) 250 mg/kg infused every fourth day.<sup>9</sup> A more physiological study in rats showed that ingestion over several weeks of drinking water containing a 1% solution of a common dishwashing detergent caused marked and irreversible duodenal villous atrophy.<sup>10</sup>

A role for ingested emulsifiers and detergents in coronary disease pathogenesis could be mediated either by bacterial

translocation, which has been shown to occur in patients with cardiovascular disease,<sup>11</sup> and consequent inflammation or possibly by a direct action of emulsifiers/detergents entering the circulation.

## 5 Washing detergents, rinsing habits and dishwashers as possible explanations for the French paradox and the increased risk of coronary disease in soft water areas

Southern European countries, most notably France, have had around one-third the peak mortality rate from cardiovascular disease compared with northern or western European countries or the US, despite having a higher smoking prevalence.<sup>12</sup> Some of this lowered mortality has been attributed to the “Mediterranean” diet. However, the recent European Prospective Investigation of Cancer (EPIC)-Norfolk study of 23 902 individuals followed for an average of 12.2 years reported a rather modest effect of a Mediterranean diet with a hazard ratio for cardiovascular mortality of 0.91 (95% CI 0.87–0.96) per one standard deviation.<sup>13</sup>

When dishes are washed by hand using liquid detergents failure to rinse is probably quite a common practice in the UK. I first became aware of this when a head of foam appeared on fruit cordial diluted in glasses that had been washed and left to dry by a household visitor who did not rinse. In a case-control study of diet and colon cancer conducted about 15 years ago in the Merseyside region we included some additional questions on dish rinsing practice and found that about one in three of 512 healthy middle-aged controls (median age 67) made no attempt to rinse.<sup>14</sup> It is very difficult to obtain quantitative published information about dish rinsing practices in France but internet anecdotes suggest that they are less likely to leave unrinsed detergent to dry on the dishes, although there is some suggestion that it is the British habit of non-rinsing that is the exception compared with many other countries.<sup>15</sup> Detergents are more difficult to rinse off in soft rather than hard water so increased detergent ingestion could also feasibly explain the association between increased coronary risk and soft drinking water that has been noted particularly in the UK.<sup>16</sup> This association has been postulated previously, before the marked fall in cardiovascular mortality became apparent.<sup>17</sup>

Soap powders were introduced in the 1860s and rapidly came into standard use for dishwashing becoming increasingly used until the 1940s when synthetic liquid detergents were introduced, taking over the market by around 1960. If the hypothesis linking emulsifier and detergent ingestion with coronary disease is correct, then some of the reduction in coronary mortality since the late 1960s might be due to increased use of dishwashing machines which rinse automatically. The uptake of dishwashers into US and UK households has occurred particularly since the late 1960s (Figure 1c). This is of course no proof of causality and a similar figure might be drawn showing an increase in fast food outlets, which would not be expected to reduce coronary risk—although fast food tends to be eaten off disposable, hence non-soapy, dishes. This also highlights the puzzling disconnect between the simultaneous fall in cardiovascular mortality and rise in prevalence of obesity. The hypothesis that dishwashers protect against coronary disease is dented by the low cardiovascular mortality rates in Japan where dishwashing machines are uncommon but perhaps effective rinsing of hand washed dishes is more prevalent there—moreover intake of dietary fat is much lower in Japan as is intake of food emulsifiers<sup>18</sup> so perhaps it may be a combination of emulsifier or detergent ingestion and dietary fat that is harmful.

## Interactions between emulsifiers/detergents and bacteria in the intestine and implications for other conditions

Experimental studies suggest an important interaction between emulsifiers and the gut bacteria.<sup>6,7,19</sup> The intestinal site where this interaction occurs could also be very important and could be affected by the rates at which different emulsifiers or detergents degrade or are otherwise removed during their passage through the intestine. Conjugated bile acids, which are of course naturally occurring detergents present in all of us, maybe cause few problems since they undergo highly efficient re-absorption which starts at least 100 cm proximal to the ileo-caecal valve so that relatively little conjugated bile acid may reach the more numerous bacteria present just upstream of the ileo-caecal valve. We have previously suggested that emulsifiers that survive passage through to the terminal ileum could contribute to Crohn’s disease pathogenesis<sup>18</sup> and recent studies have also shown that dietary emulsifiers, including polysorbate-80, can promote experimental colitis-induced colorectal cancer.<sup>20</sup> There is a problem though—in recent decades Crohn’s disease incidence has been rising in most countries while coronary mortality has been falling. There is also a disconnection between the marked rise in incidence of obesity and metabolic syndrome and the fall in coronary disease. This might mean that the emulsifier hypothesis is only correct for coronary disease or Crohn’s disease but not both. An alternative explanation might be that food emulsifiers may act differently to the more powerful washing detergents. It is plausible that food emulsifiers could increase bacterial translocation in the terminal ileum, promoting classical ileal/ileo-colonic Crohn’s disease and metabolic syndrome, while more powerful detergents could act on the proximal intestine and induce atheroma via different mechanisms. There is certainly sufficient experimental evidence to justify further study.

## Conclusion

The potential harm caused by human ingestion of emulsifiers and detergents has largely been overlooked until recently. Further studies are needed to assess its impact on bacterial translocation, gut microbiota and biomarkers relevant to “20th century” diseases including cardiovascular disease. Meanwhile it seems sensible to rinse the dishes.

*Conflict of interest:* None declared.

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