

WRC WATER RESEARCH CENTRE

90/11

TRACE ELEMENTS IN WATER AND CARDIOVASCULAR DISEASE -
EPIDEMIOLOGY

(H4156 CXD)

Final Report to the Department of the Environment 1981-1984

Project Leader: R F Lacey

Author: P Powell

June 1984

766-M

RESTRICTION: This report has the following restricted
distribution:

External: DOE Nominated Officer - 16 Copies
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Internal: Director, appropriate Assistant
Director and Manager, plus 4 copies
to Directorate Scientific Staff.

DOE CONTRACT REFERENCE: PECD 7/7/08

CONTRACT DURATION: APRIL 1981 - MARCH 1985

WRC ENVIRONMENT

MEDMENHAM LABORATORY: Henley Road,
Medmenham P. O. Box 16 Marlow Bucks SL7 2HD

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SUMMARY

This contract relates to investigations of the trace inorganic constituents in tap-water, undertaken between April 1981 and March 1984. The project had two objectives:

- To investigate the relationship between the chemical composition of drinking water, the prevalence of CVD risk factors measured in man and the incidence of cardiovascular disease.
- To develop a reliable, practicable and economical method of assessing the mean intake of metals derived from plumbing systems by typical inhabitants of a particular house or water supply zone. This objective embraces several metals, but particular emphasis has been given to lead.

This report is concerned solely with progress under the first of these objectives. Work on the second objective will continue beyond March 1984, for one year to end in March 1985, and so it is being covered by separate reports.

The contract period has seen the publication of a number of epidemiological papers based mainly on information generated by the earlier stage of the contract. New information has, however, been presented on the relationship between blood-lead and water-lead.

Collaboration with the Royal Free Hospital has continued. WRC has provided the water data for Phase II of the Regional Heart Study, and offered interpretive advice on it to the research team at the Royal Free Hospital. An initial examination of this data on a town-by-town basis suggests that, even allowing for personal risk factors such as smoking and blood pressure, water quality still 'explains' some of the regional variation in cardiovascular disease. The initiative for further statistical analysis rests mainly with the team from the Royal Free Hospital.

The practical implications of research to date have been widely publicised, as have the results of the 'changes' work.

The overall outcome of the epidemiological research assisted by this contract has been to confirm the existence of a water-related factor, independent of socio-economic or geographical influences on CVD. Estimates of the strength of this factor have, however, been smaller than suggested by some of the earlier studies. It has not been possible to identify a specific water constituent as responsible, and there is little hope of doing so by epidemiological research.

While there remains further scope for epidemiological work to demonstrate whether the water factor, that appears to operate at the community level, is actually effective in terms of risk to the individual, the initiation of new studies of the type needed for this is probably not possible for WRC. Work by the Royal Free Hospital on Phases II and III of the Regional Heart Study is however not yet complete and will be continuing.

PREFACE

On the 1st April 1977, the Department of the Environment placed a contract (Ref. DGR/480/656) with the Water Research Centre to investigate the trace inorganic constituents of tap-water and the possibility that the quality of drinking water may be a risk factor for cardiovascular disease (CVD). This original contract ended on 31st March 1981, but was immediately renewed for a further period of three years to end on 31st March 1984 (Ref. PECD 7/7/08).

This report is concerned solely with progress with the investigations of CVD, and constitutes a final contract report for the period April 1981 to March 1984 for those parts of the contract relating to CVD.

The contract has been renewed for one year from 1st April 1984 to end 31st March 1985, to allow work to investigate the inorganic constituents of tap-water (particularly lead) to be completed. This aspect of the April 1981 to March 1984 contract, together with the studies undertaken during the extension (April 1984 to March 1985), will be the subject of further reports.

CONTENTS

Page

SUMMARY

1.	<u>INTRODUCTION</u>	1
2.	<u>THE REGIONAL HEART STUDY</u>	1
2.1	WRC COLLABORATION	1
2.2	PHASE I	2
2.3	PHASE II	3
2.4	LEAD	5
3.	<u>PRACTICAL IMPLICATIONS</u>	5
4.	<u>ADDITIONAL STUDIES</u>	6
4.1	NEW FIELD STUDIES	6
4.2	'CHANGES'	7
5.	<u>OUTCOME OF THIS CONTRACT</u>	7
6.	<u>GENERAL CONCLUSIONS AND FUTURE PROSPECTS</u>	8
	<u>REFERENCES</u>	10

1. INTRODUCTION

This project, under the renewed contract from April 1981 had two objectives:

- (1) To investigate the relationship between the chemical composition of drinking water, the prevalence of CVD risk factors measured in man and the incidence of cardiovascular disease.
- (2) To develop a reliable, practicable and economical method of assessing the mean intake of metals derived from plumbing systems by typical inhabitants of a particular house or water supply zone. This objective embraces several metals, but particular emphasis will be given to lead.

These two objectives have been pursued by almost separate programmes of research. Work under the second objective is continuing beyond March 1984 to end in March 1985, and will be the subject of separate reports. This final report is therefore confined to the epidemiological objective defined in (1) above.

2. THE REGIONAL HEART STUDY

2.1 WRC COLLABORATION

The British Regional Heart Study (RHS) is an epidemiological study of cardiovascular disease in Great Britain, being undertaken by the Royal Free Hospital School of Medicine, London (RFH), and funded by the Medical Research Council. The Department of the Environment's contract covers WRC's collaboration in the RHS but the RFH is not under any contract to WRC nor to DOE.

The study is essentially in three phases:

Phase I - a retrospective study of CVD mortality and environmental and socio-economic factors in approximately 250 towns in Great Britain;

Phase II - a cross-sectional clinical survey of around 8000 middle-aged men in 25 towns, to include measurements of established and possible risk factors for CVD;

Phase III - a prospective study of morbidity and mortality in the men in Phase II of the study.

Details of the overall design of the study are given elsewhere (1,2).

2.2 PHASE I

The WRC's involvement in the first phase of the RHS was covered by a previous contract from the Department (1,2). Since then, the RFH team have made two refinements to the statistical analysis relating to this work (3,4).

The refinements were, first, weighting to allow for differences in the population sizes of the towns, and, second, allowance for 'spatial autocorrelation' to take account of the fact that adjacent towns are alike in many respects, not all of which are represented by variables in the model. Table 1 below indicates how the size of the water effect is diminished as these refinements are introduced. The 'standardised regression effect' is the percentage change in CVD mortality that is associated with a change in the variable of interest of one standard deviation, whilst holding all the other variables (temperature, rainfall, etc.) constant. In this study one standard deviation in the water hardness data was 109 mg/l.

Table 1 Standardised Regression Effects

	Water hardness up to 170 mg/l	Water hardness above 170 mg/l
Ordinary model	-7.8 (t= -5.0)	-0.8 (t= -0.6)
Weighted model	-7.7 (t= -5.0)	-1.0 (t= -0.8)
Spatial model	-5.1 (t= -3.0)	-1.0 (t= -1.8)
Weighted spatial model	-4.7 (t= -2.8)	-1.8 (t= -1.4)

Hence in the weighted spatial model, an increase of 109 mg/l in hardness (in the range up to 170 mg/l) is associated with a 4.7% decrease in CVD mortality. Although the size of the effect above 170 mg/l has increased, it is still not significantly different from zero. Neither, however, is it significantly different from the size of the effect below 170 mg/l.

These refinements slightly reduce the estimated size of the hardness effect, although the association remains significant. The previously reported non-linearity in the hardness effect is also weakened.

2.3 PHASE II

The second phase of the RHS involved the clinical examination of around 8000 men in 24 towns. The WRC has collaborated in the water aspects of this study and, in particular, with the sampling of the tap-water at the homes of a sub-set of about 1100 men. A general description of this phase of the Regional Heart Study is given elsewhere (5).

The field work for this phase was completed in 1980, before the start of this period of contract. However, a problem concerning the analysis of the water samples in the two hardest

water towns, Hartlepool and Lowestoft, persisted into the present contract. This problem was eventually overcome, and a complete set of water quality data transferred to the RFH. The data included estimates of each individual's intake from drinking water for each of the trace elements. These estimates were obtained by combining data for the concentration of trace elements in tap-water with the quantity of water consumed by each individual. A number of corrections were also incorporated into the data, allowing for the dilution of the samples by preservative, for example. These corrections do not seriously affect the summary results previously reported to the Department (6).

An additional report has been prepared (WRC External Report 706-M) which summarises the range of trace element levels found in the tap-water samples, on a source-by-source basis. It also considers the effect of piping materials on the levels of some of the trace element, and examines possible inter-relationships between the various water quality parameters measured. Report 706-M updates and extends the previous analysis(6). The report has been circulated to the collaborating water authorities, together with a request for information as to whether the supplies to the RHS towns have changed significantly since our original visit. This has been done to fulfill the requirements of the contract. It is intended to keep this question under review as long as Phase III of the RHS continues, even though the Department's contractual interest has ended. The Department has given permission for Report 706-M to be made more widely available as a WRC Technical Report.

Integration of the water quality data with the personal data on each individual should enable progress to be made under the objective (1) above. The personal details available include outcome variables such as the presence or otherwise of heart disease, and risk factors such as smoking and drinking habits, and socio-economic classification. However, Phase II has generated a wealth of data on many other interesting aspects relating to heart

disease in this country, and these aspects have been receiving priority over the 'water story'. Some analyses have been done, however, aggregating the data on a town-by-town basis rather than at an individual level. The outcome variables considered have been the mortality from ischaemic heart disease amongst the total population in the study towns in the period 1979-82, and the prevalence of ischaemic heart disease amongst the RHS subjects. The results so far show that, even in the presence of new factors such as smoking habits and blood pressure, water hardness still appears to play a significant role in 'explaining' heart disease. These results were presented at a conference on inorganics in drinking water and cardiovascular disease at Amherst, Massachusetts, in May 1984, and the Department has been informed.

2.4 LEAD

One study at an individual level has been undertaken using the RHS water data. This considered the effect of tap water lead and other variables on blood lead. Since there is as yet no known link between blood lead levels and CVD, this cannot strictly be considered as meeting the objective of this project. The results, however, provide a useful contribution to the available information on the relationship between blood-lead and water-lead in middle-aged men. The results have been fully described elsewhere (7).

3. PRACTICAL IMPLICATIONS

A paper on the practical implications of the research into CVD was presented to MAWQ in September 1981 (MAWQ/145). The paper was favourably received, and the committee asked that the information be presented to a wider readership. Two papers were therefore published, one in the medical press (8), the other for the benefit of those in the water industry (9). The main conclusions of these papers were:

1. Recent work had strengthened the evidence that CVD mortality is influenced by a water quality factor related to water hardness. There is, however, considerable uncertainty as to the precise nature of the water components involved, and there is therefore no rational basis for introducing specific water treatments aimed at reducing the risk of CVD.
2. If water hardness itself is protective against CVD, then limitation of central softening is desirable but the new EEC regulations would be sufficient to control this in the UK. An agreement by domestic water softener manufacturers to provide a hard water supply for drinking and cooking is also helpful. These two measures involve little expense.
3. There does not appear to be any justification at present for recommending water hardening. Moreover, because water hardening is costly and because its maximum potential effect on CVD appears to be relatively small, it is unlikely that water hardening on an experimental basis is a practical proposition.

These conclusions still hold.

4. ADDITIONAL STUDIES

4.1 NEW FIELD STUDIES

During this contract, ideas were suggested for two additional studies, both in collaboration with the Royal Free Hospital. The first study was of blood-pressure variations between selected RHS towns, with the measurements on children rather than adults. The purpose of this study would have been to examine whether there is an early onset of regional differences in blood pressure and other CVD risk factors. The RFH decided, however, not to pursue this idea, at least not for the moment.

The second proposed study would have tried to take advantage of a large change in hardness of the water supplies to an area near Oswestry to see if any corresponding change in, for example, blood-pressure, could be detected. At the time, however, there was little evidence to suggest that that water hardness is associated with variations in blood-pressure, as against the well-established relationship with CVD mortality.

As it would not have been an easy study to design and carry out in the short time available, it was decided not to proceed.

4.2 'CHANGES'

In connection with studies of situations where water hardness has changed over a period of time, one further publication (10) has appeared during the time of this contract which used data collected for the earlier phase of the project. This paper offered a slight variation on the material previously reported to the Department (11), but the conclusions were essentially the same.

5. OUTCOME OF THIS CONTRACT

The contract period has seen the publication of a number of research papers based mainly on information generated by the earlier stage of the contract. The lead paper (7) was new.

WRC has provided the water data for Phase II of the Regional Heart Study, and offered interpretive advice on it to the research team at the Royal Free Hospital. An initial examination of this data on a town-by-town basis suggests that, even in the presence of personal risk factors such as smoking and blood pressure, water quality still 'explains' some of the regional variation in cardiovascular disease. Further exploration of this data is possible, but will have to take place outside of the present contract.

The practical implications of research to date have been widely publicised, as have the results of the 'changes' work.

It was unfortunately not possible to mount any new epidemiological studies, even when opportunities seemed to present themselves. The decision on these matters, however, has not been within the WRC's control.

6. GENERAL CONCLUSIONS AND FUTURE PROSPECTS

This report brings to an end a programme of contractual research on cardiovascular disease which WRC has carried out since 1977. The foundations for the work had been laid earlier with the development, during 1974-77, of a collaborative relationship between the WRC and the team of researchers led by Dr A G Shaper. During that time his team became the Department of Clinical Epidemiology and Social Medicine (later General Practice) at the Royal Free Hospital School of Medicine and was grant-aided by the MRC to undertake the Regional Heart Study. WRC's contribution to this research started as part of the Centre's general research programme but became part of a DOE contract in 1977. The Centre's involvement in this field thus spans about a decade of research. It is appropriate to take stock of what has been achieved and what may be recommended for the future.

At the time that WRC entered this field there had already been a number of studies of the possible relationship between water quality and cardiovascular disease. Some of these studies had obvious defects. Others, particularly those based on the 1961 Census and undertaken by Drs. M D Crawford and M J Gardner, appeared to be soundly based, although they were restricted to the county boroughs of England and Wales and had not characterised water supplies and their quality in a very critical way. The size of the difference in cardiovascular death-rates between soft and hard water areas appeared from some of these studies to be large enough to be of importance, if it could be shown to be the result of a causal connection between hardness and CVD. Further studies were, however, considered necessary:

- (a) to determine whether the same relationships could be observed for a larger set of communities and at a different epoch,
- (b) to attempt to refine and separate the role of water hardness from those of socio-economic or geographical trends,
- (c) to try to identify the particular water constituent that might be involved,
- (d) to ascertain whether factors that appear to be operating at the community level are actually interpretable in terms of risk to the individual.

The outcome of the studies assisted by the DOE contract has been to confirm the existence of a water-related factor, seemingly independent of the socio-economic or geographical influences on CVD. Estimates of the strength of this factor have however been smaller than suggested in some of the earlier research, and it has not been possible to identify a specific water constituent as responsible. The studies have thus partly fulfilled requirements (a) and (b), but have failed at (c). Research into (d) must be based on studies of individuals as well as communities and in this respect the work of the Regional Heart Study is not yet complete.

Because of the strong inter-correlations between the concentrations of different determinands in the range of waters supplied to communities in the UK, there is little hope of gaining further clarification of (c) by epidemiological research. What is needed is a deeper understanding of the mechanism responsible for the 'water story', and this must come from biochemical, physiological or pathological research. The studies in these fields are unlikely to be within the scope of WRC.

For research on (d) there may yet be information that could be gained from epidemiology, particularly from studies of individuals

who are followed for long periods of time, but the initiation of such studies does not really come within the remit of WRC. We do not therefore have recommendations for further studies of this kind, although we would remain open for discussion with any medical or other research group that might wish to explore new approaches to the intractable questions in this field. Based on our experiences, we are also well equipped to advise other groups on the 'water quality dimension' of their respective research projects.

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