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EDITORIAL

Let's clear the air of second hand smoke!

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At least as early as 1973, the tobacco industry identified "zealots" working to undermine the social acceptability of second hand tobacco smoke (SHS) in shared indoor public places as a significant threat to their business. A confidential report to the US Tobacco Institute concluded that public concern about SHS was "the most dangerous threat to the viability of the tobacco industry that has yet occurred".[1] The industry response has been to deny that SHS poses any serious health risks, to intimidate critics and subvert research, to promote non-interventionism and to prevent effective SHS control by working through front organisations and alliances with allied industries.[1-3]

Typically, the tobacco industry uses a three-pronged strategy of subversion.[3] One component of this strategy is to undermine and counter independent research through industry-directed 'sound science'. A study of 106 scientific reviews of the health effects of SHS found that, after controlling for article quality, topic, peer review status and year of publication, the only factor significantly associated with a conclusion that SHS was not harmful was whether an author was affiliated with the tobacco industry.[4] Industry writers were 88 times more likely to find no link.

A second component of the tobacco industry strategy is the use of public relations to shape opinion, manipulate the media and mislead the public. The success of this approach is illustrated by the bias observed in US print media reports towards viewing SHS research as "controversial" or "inconclusive".[5] Yet several major reviews present a consistent pattern of negative developmental, respiratory, cardiovascular and carcinogenic effects of SHS, and evidence continues to accumulate. In contrast, convincing evidence that ventilation can effectively eliminate these risks is lacking[6] and, given that SHS contains "5 regulated hazardous air pollutants, 47 regulated hazardous wastes, 60 known or suspected carcinogens, and more than 100 chemical poisons" under US standards, elimination is the rational response. SHS is classified as a known human carcinogen for which, along with asbestos, arsenic and mustard gas "There is sufficient evidence of carcinogenicity from studies in humans which indicates a causal relationship between exposure to the agent, substance, or mixture and human cancer."[7] Yet the tobacco industry continues to deny the risk, opposes clean air legislation and "promotes ventilation as a panacea" for SHS control.[6] The industry seeks to mislead by suggesting that SHS is merely an "annoyance" that can be addressed through the "accommodation" of smoking and "peaceful coexistence" of smokers and non-smokers in shared environments.

The third component of the tobacco industry strategy involves political tactics to prevent new restrictions on smoking. Lobbyists appeal to values, such as "freedom of choice" and "free enterprise",[8] while attacking taxation, regulation by the "nanny state" and the "tyranny of public health." The industry public relations apparatus works through "smoker's rights" and hospitality trade "front" organisations.[1] Underwriting the lobbying expenses of legitimate hospitality organisations is another tactic – hence the need for public disclosure of such involvement by organisations opposed to clean indoor air legislation. The tobacco industry works to arouse hospitality trade concerns about enforcement issues and the loss of business as a result of prohibiting smoking in indoor public places. A recent survey indicates that such concerns are held in New Zealand[9] despite overseas evidence that bans are largely self-enforcing and there is no loss of business in restaurants or bars, job losses or lost tourist revenue in jurisdictions where bans exist. On the contrary, smoking adds costs to business for cleaning, maintenance, ventilation and staff absenteeism as well as the risk of potential liability for the effects of an unsafe work place. Furthermore, many people avoid bars because of SHS and surveys undertaken for the Ministry of Health indicate that 75% of the population are non-smokers and most New Zealanders want stricter control of SHS.

In New Zealand, every year, around 400 premature deaths among non-smokers are attributed to SHS and approximately 140 of these are caused by workplace exposure.[10] The proportion of New Zealanders exposed to workplace SHS was almost halved by the Smoke-free Environments Act 1990, but little change has occurred since.

SHS controls challenge the tobacco industry and provide significant additional opportunities for public health gains.[9] A reduced number of places where smoking is permitted can lower smoking prevalence and intensity. Smoke-free environments provide an incentive to quit and a supportive context within which to do this. Restrictions on smoking in public places and enforced bans on smoking at school can help reduce youth smoking. One study has found that belief that SHS harms non-smokers more than doubles the chances of planning to stop or having stopped smoking among US youth.[11] Such gains would be valuable in New Zealand where tobacco smoking is the leading cause of death and youth uptake of smoking remains a serious problem.

The hospitality industry is central to efforts to eliminate SHS. Hospitality industry employees in New Zealand are among those workers most exposed to SHS and least protected from it. Electoral rolls indicate that at least 10 500 workers are likely to be exposed to SHS in bars and restaurants, alone. Their risks of avoidable premature death, acute and chronic health problems that result in greater use of health services, and time off work are increased. Many

New Zealand hospitality industry employees want better protection. It is unacceptable that workers, including pregnant women, continue to be exposed to the toxic cocktail of SHS. "Smoking bans remain the only viable control measure to ensure that workers and patrons of the hospitality industry are protected from exposure to the toxic wastes from tobacco consumption."[6] Yet statements from the leadership of the hospitality industry in New Zealand continue to promote ventilation as a solution and to ignore the effect of SHS on the health of their employees and patrons. A recent glossy Hospitality Association of New Zealand (HANZ) publication states that "Good ventilation and air filtering is good for business and much better than a ban on smoking in restaurants and bars, as promised by some politicians."[12] No scientific evidence is presented. It can only be assumed that the aim of that publication, widely distributed among politicians, is to undermine public health efforts to obtain legislation that will eliminate SHS from restaurants and bars. At a Wellington SHS workshop (July 10, 2000), Bruce H Robertson (HANZ Chief Executive) admitted that the tobacco industry had contributed to the production of at least one HANZ publication on ventilation.

Existing legislation that permits smoking in bars, restaurants, casinos, clubs and other venues inadequately protects staff and patrons against known serious hazards. Parliamentary consideration of the Smoke-free Environments (Enhanced Protection) Amendment Bill, currently before select committee, presents a valuable opportunity to include comprehensive controls. SHS control should create a 'level playing field' so that *all* indoor workplaces and *all* places to which the public have access, including restaurants, bars, cafes, clubs, housie halls, casinos etc, are free of SHS. A public education campaign about the risks of SHS should complement such legislation. Given the apparent opposition of HANZ to effective control, there is a need for informed and determined advocacy by health professionals and others concerned about the negative health effects of SHS. New Zealanders expect an unpolluted public water supply: why shouldn't we have clean air? We should settle for nothing less. The only acceptable compromise is to allow a transition period, after which SHS must be eliminated from all enclosed workplaces and shared indoor public environments.

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ORIGINAL ARTICLES

A serological survey of antibodies to Rabbit Haemorrhagic Disease Virus (Rabbit Calicivirus Disease) in two rural Central Otago communities

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Abstract

Aims. To determine whether individuals from two rural communities with heavy exposure to the Rabbit Haemorrhagic Disease Virus (RHDV) developed antibodies to this virus.

Methods. Sera were assayed using competition ELISA (cELISA) and solid phase ELISA (spELISA). Exposure estimates were based on answers to an interviewer administered questionnaire.

Results. Of the 104 participants, 79 were considered to have experienced high or medium exposure, many of whom described specific exposures. There were 58 people who reported contact with RHDV infected bait, organ homogenate mixtures or rabbit body fluids. A one-way analysis of variance (Kruskal Wallis) found that human cELISA results were differently distributed from both strongly RHDV positive rabbits (χ^2_1 = 27.37, p<0.001) and weakly RHDV positive rabbits (χ^2_1 = 27.35, p<0.001). The distribution of assay results in each exposure group did not differ in either cELISA (χ^2_2 = 2.49, p = 0.29) or spELISA (χ^2_2 = 1.70, p = 0.43). Relatively fewer results were categorised as reactive (two 'barely' positive and two doubtful) than in a previous survey of 493 unexposed people. None of the five positive results categorised by the less specific spELISA occurred in people described as 'barely' positive or doubtful by cELISA.

Conclusions. No serological evidence of infection with RHDV was found in a cohort including many heavily exposed individuals.

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The Rabbit Haemorrhagic Disease Virus (RHDV) is a typically fatal disease of European rabbits *(Oryctolagus cuniculus)* that is now established in New Zealand.[1] The disease is also known as Rabbit Calicivirus Disease (RCD) in Australasia, although this term is now more commonly used to refer to the non-pathogenic virus related to RHDV.

RHD was first recognised in China in 1984, and is now distributed across most of the world. A high mortality rate is observed in adult rabbits, while young rabbits usually survive and maintain immunity. Investigations have failed to identify clinical illness in any species other than rabbit.

No human antibody response has been found in the regular serological surveys of laboratory staff working with RHDV, some of whom have experienced sharps injuries and splashes with infected material.[2] The single, anecdotal report of a low, transient antibody response may be the result of a test artefact.[3]

An Australian study[3] of 269 workers attempting to control RHDV spread after its escape from quarantine found no serological evidence of infection or increased risk of illness amongst those most highly exposed. A reanalysis of data has challenged these results,[4,5] but has in turn been rebutted.[3,6]

A New Zealand serological study of two communities with an endemic, RHDV-free, rabbit population was undertaken in early 1997.[7] The results established a baseline for unexposed human sera, and showed that the cELISA was a suitable tool for examining antibody reactions to RHDV in human sera.

The suitability of this organism as a cost-effective rabbit control method in New Zealand had been the subject of joint investigations with Australia for some years, until the escape of virus from quarantine in Australia in September 1996. An application to import the virus legally into New Zealand was declined in early July 1997. The presence of RHD was first confirmed in late August, although there were reports that RHDV had been in use for the two months prior.[8] Roadblocks, no-fly zones and restricted places notices were used in an attempt to control spread of the virus. However, once the extent of spread was recognised, these measures were discontinued. A feature in New Zealand was the apparent extent of human involvement in spreading RHD. Farmers who admitted assisting the spread of RHD discussed injecting live rabbits, homogenising infected rabbit organs and applying these to a bait, such as carrot or oats, which was then distributed across the land. Others simply opened up infected rabbits where they lay.

National media attention was focused on Central Otago, and the Ministry of Agriculture and Fisheries and Police were interested in identifying anyone involved in illegally importing the organism. An ongoing debate about the legal status of people assisting its spread ensued, and legislation was enacted to clarify the situation.

Methods

Two rural communities (Cromwell and Wanaka) some 50 km apart were chosen as research sites because of their apparent central location in RHDV discoveries.

A prominent local lawyer sought people likely to have had extensive contacts with rabbits. The families of potential participants were invited to take part on a confidential basis, and the names of those who agreed were provided to one of the authors (RB). Information was provided about the purpose and methods of the study, including how their anonymity could be guaranteed, and where they could seek further advice or assistance. These people were reminded about the study and how they could take part by a local researcher who was also able to assist in answering queries.

The unusual sampling strategy was necessary to gain the confidence of the highly exposed potential participants who may have been liable for prosecution. This meant that participants were not randomly selected, though we assume that the observations are subject to random variation. Testing was undertaken over two days in early December 1997, some fifteen weeks after the formal identification of the virus. People arriving at the research centres were again informed about the study and given an opportunity to ask questions. A unique code was allocated to each participant once informed consent was given. An interviewer administered questionnaire asked about contact with rabbits, possible instances of consumption or direct contact with RHD infective material, any RHD associated illness and demographic data. Individual exposure levels were estimated based on participant's descriptions of several key activities (Table 1).

Table 1. Numbers of participants eligible for each exposure category.

Exposure grouping criteria	eligible number	total
High exposure		**52**
worked with bait, distributing mixture, or rabbit body fluids excluding those known to wear gloves; or	45	
handled, skinned or processed >7 rabbits per week which were shot, or trapped and considered 'a lot' likely to have RHD; or	7	
handled, skinned or processed >7 rabbits per week which were found dead and considered 'a lot' likely to have RHD; or	12	
a specific exposure such as cut hands, inhalation, consumption, needlestick, or 'carelessness'	38	
Medium exposure		**27**
any work with bait or distributing mixture; or	58	
handled, skinned or processed >1 rabbit per month and ≤7 rabbits per week which were shot, or trapped and considered 'a lot' likely to have RHD; or	17	
handled, skinned or processed >1 rabbit per month and ≤7 rabbits per week which were found dead and considered 'a lot' likely to have RHD; or	39	
someone in the family processed or stored in kitchen or shared eating area; or	28	
handled >3 sick rabbits over 3 months.	30	
Low exposure		**25**
Total		**104**

Two phlebotomists collected 17 mL samples in a sterile tube marked with the individuals code, the serum was separated and stored in chilled containers then couriered to Canterbury Healthlabs in Christchurch. Each sample was separated, aliquoted, and stored at -70°C, for PCR testing if ELISA testing of RHDV specific antibodies indicated a suspected positive result.

The primary assay was the Office International des Epizooties (OIE) standard cELISA for determining RHDV antibody levels in rabbits, which was also used in the NZ baseline survey.[9] A second assay, spELISA (an ELISA with the antigen directly absorbed to the solid phase), was performed both as a confirmatory test and to detect antibodies produced against the inner part of RHDV (common antigens of *lagomorph* caliciviruses). Serological tests were undertaken by the Office International des Epizooties (OIE) reference laboratory for RHD in Italy and included positive and negative rabbit sera as controls in each test bank. The results of both assays were described using cut-off values established using rabbit sera and previously in connection with the sera of both exposed and unexposed human populations. Actual cELISA assay values from human sera, as well as strongly and weakly RHDV positive rabbits, were used in a non-parametric analysis of variance.

Results

There were 104 participants (70 men and 34 women) from 70 families. The median age was 48 years, with only four people older than 70 and two younger than 20 years. There was no obvious difference in the distribution of participants by sex, exposure, or their final serological results according to which location they were tested (Cromwell n=72; Wanaka n=32). Of the participants, 94 had some contact with rabbits, and over half (n=66) had handled, skinned or processed rabbits which they thought were 'a lot' likely to have RHD. A large number (n=29) believed they may have had direct contact with the virus and quite a few felt (n=14) it was possible they had consumed an infective mixture. The use of a kitchen or shared eating area to process or store rabbit was recalled by nineteen people, in whose families there were 28 people. 58 participants appeared to have worked with organ homogenates, RHDV infected bait or rabbits bodily fluids. Excluding the thirteen people who wore gloves, there were 30 participants who mentioned either broken skin on their hands or not wearing gloves and fifteen were not clear whether gloves were worn. Anecdotal reports indicated there were many opportunities for exposure to RHDV infected material in it's manufacture and distribution. For some, this involved getting RHDV infected blood in and around cuts; carrying buckets of RHDV infected mixture; shovelling infected bait mixtures; and mixing bait in concrete mixers. Others worked with tons of contaminated carrots; 'feeding out' bait mixtures off the back of motorcycles; tasting and smelling contaminated sprays blown in their face for hours. Two people reported needlestick injuries from syringes containing infected material, and one recalled consuming infected bait.

Eight people considered that their or their infant's health problems may have been due to rabbit or RHD contact, with seven descriptions of a health problem. These were: urinary infection; persistent bronchitis; Helicobacter associated gastritis; enteric adenovirus (six month old baby); coincidental 24 hour flu about the same time as RHD exposure; viral illness; and an unusual flu. Others commented on the ill health in the community due to the effects of rabbits on farming.

Exactly half of the participants were estimated to have had high exposure, a result of more than one type of activity in most cases (Table 1). Men accounted for 83% in the high exposure group. The range of human responses from the cELISA was distinct from that of both strongly and weakly positive rabbit control sera, which in turn were distinct from each other (Figure 1). Non-parametric analysis (Kruskal Wallis one-way analysis of variance) demonstrated a significant difference between the five groups of sera (χ^2_4 = 52.40, p<0.001). The distribution of cELISA results from the human group were significantly different from those of high titre rabbits (χ^2_1 = 27.37 , p<0.001) and low titre rabbits (χ^2_1 = 27.35 , p<0.001). However, the distribution of human cELISA results did not vary significantly according to estimated exposure (χ^2_2 = 2.49, p = 0.29).

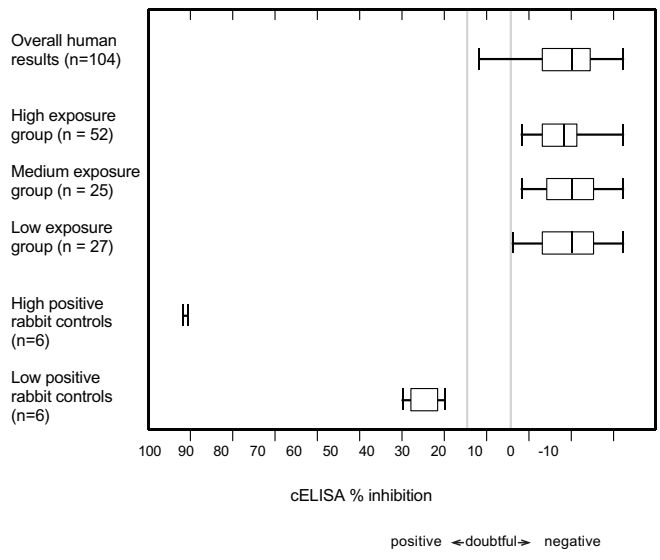

Figure 1. Box plot of cELISA results from study participants and rabbit control sera.

Even adjusting the significance level to 0.05/5 to allow for the *multiple a posteriori* comparisons, there was a clear distinction between rabbit and human sera but there was no apparent difference in the distribution of antibodies between humans with high, medium or low exposure.

cELISA results were categorised as positive (two), doubtful (two) and negative (100) according to the cut-off points established for rabbit RHD serology and verified in pre-RHD

human serology of the New Zealand baseline study. Both positive results were classified as doubtful on repeat assay, while one of the initially doubtful results was classified as positive. All positive results were so close to being classified as doubtful that a rounding approximation (to the 0.05 level) used in the original assay results could have masked a different classification.

This study found relatively more negative samples than were observed in either the estimated multiple retesting result or the initial test result of the New Zealand baseline survey (Table 2). The proportion of negative samples was most similar to that found in Italian human sera originating from an RHDV endemic area.[7] The distribution of categorical cELISA results across exposure groups (Table 3) showed that the high and low exposure groups contained one 'barely' positive and one doubtful cELISA response.

The results from the more broadly reactive spELISA found 27 borderline and five positive responses (Table 4), again using cut-off points developed using rabbits. However, all of the negative rabbit control sera in the test were also classified as borderline. Most of the human sera were negative (n=72), and none of the human assay values overlapped positive control rabbit sera.

Of the five positive responses, three occurred in people with low exposure and two in those with medium exposure. In addition, 27 borderline spELISA results were identified, with sixteen in those with high exposure, six medium and five low exposure. Overall, each exposure category had a similar proportion of negative results; low (68.0%), medium (70.3%), and high (69.2%). No difference was detected in the distribution of the actual spELISA assay results between the exposure groups (Kruskal Wallis χ^2_2 =1.70, p = 0.43).

When the assay results were considered together, none of the five positive spELISA results were doubtful or positive by cELISA. Most of the sera (70) were negative by both tests. All of the seven people who thought that they may have had illness due to RHD or contact with rabbits failed to show any antibody response in either cELISA, or spELISA.

Discussion

This study found no evidence of RHDV infection from serum samples of a population including people who had contact with RHDV infected material. The distribution of human sera cELISA results was significantly different from both strongly and weakly positive rabbit sera. No difference was found in the distribution of results in the three exposure categories for either cELISA or spELISA. Two cELISA results were classified as 'barely' positive and both were considered doubtful upon re-testing. Of the two initially doubtful results, one was considered positive after re-testing. All three sera which tested 'barely' positive were so close to the cut-off as to be within the margin of rounding error in the assay. This 'technical' classification of 'barely' positive does not indicate the presence of RHDV specific antibodies. The cELISA is an OIE reference assay that was standardised using rabbit sera. In the absence of the positive human sera which are necessary to establish a definite cut-off point for human sera, the classification of sera as positive only means that they are able to interfere in the reaction between the RHDV antibodies in the test and the virus.

Table 3. Distribution of categorical cELISA results across exposure.

Assay result	estimated exposure low	medium	high	total
cELISA - positive	1	0	1	2
cELISA - doubtful	1	0	1	2
cELISA - negative	23	27	50	100
Totals	25	27	52	104

Table 4. Distribution of categorical spELISA results across exposure.

Assay result	estimated exposure low	medium	high	total
spELISA - positive	3	2	0	5
spELISA - doubtful	5	6	16	27
spELISA - negative	17	19	36	72
Totals	25	27	52	104

In order to demonstrate that the interference is actually due to RHDV antibodies rather than a non-specific reaction, it is necessary to use a confirmatory serological test or look directly for the virus using high sensitivity techniques like PCR.

The low, but distinct reactivity observed in this study occurred at a titre of 1/10. In contrast, RHDV infected rabbits that survive demonstrate positive reactions at much higher titres of (1/2,560 - 1/5,120) in the 10-40 days post infection.

The baseline survey of an unexposed population demonstrated that the cELISA is a suitable assay for use with human sera, and had a relatively greater proportion of doubtful and positive outcomes than was found in the present study. The classification of apparently false positives in the baseline survey,[7] and again in this study, highlights the difficulty of interpreting borderline cELISA results from human sera, such as the low transient antibody response referred to by Mead et al.[2]

The spELISA is a less standardised test than the cELISA, and is subject to the same absence of positive human control.

Table 2. Comparison of cELISA results, NZ pre-RHD baseline‡ and Italian blood donor results.[7]

	Present study	Estimated results after multiple retesting (4x) of New Zealand pre-RHD Baseline survey, (n=493)	Initial test result of New Zealand pre-RHD Baseline survey,‡ (n=493)	Italian blood donor group[7] (n=100)
cELISA – positive	1.9%*	4.7%†	8.9%	2.0%
cELISA – doubtful	1.9%	12.6%	6.5%	1.0%
cELISA – negative	96.2%	82.8%	84.6%	97.0%
Total participants	100.0%	100.0%	100.0%	100.0%

* These results both bordered on doubtful. † Only six of these 23 were positive in each of the five tests. ‡ Capucci L, personal communication July 1999.

The results of this assay are more difficult to interpret in the absence of a baseline survey, and as a result no statistical comparisons of human and rabbit spELISA results have been made. The five positive spELISA results gave consistently higher readings than the rest of the sera, but remained clearly distinct from the RHD positive rabbit sera controls. None of these five sera were classified as positive by cELISA. Importantly, the spELISA classification of all negative rabbit control sera as borderline means that little weight can be attached to the finding of 27 human borderline results, and raises questions about the cut-off values.

The sampling procedure yielded volunteers from a high risk local area and enabled us to enrol a relatively large number of exposed people, and their families, in the necessary short period of time. There is no reason to believe that the resultant sample is not reasonably representative of adults with exposure to RHDV infected material and their adult families. More families eventually took part in the study (70) than were originally invited (60). Whether these are the same families is not clear, and it is possible that some people, in particular those with high exposure or no exposure, may have refused to take part. As only one child (15 years) participated, it is not possible to generalise the results to younger age groups.

Consistent with the results of the largest previous study of human health and RHD,[3] we found no serological evidence of infection, despite an apparently high level of exposure. This study provides evidence to support the hypothesis that even humans who may have been heavily exposed to likely RHD transmission routes do not develop antibodies to this organism.

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Patterns of alcohol use and misuse among elderly rest home residents in Christchurch

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Abstract

Aims. To determine the prevalence of alcohol use and misuse among elderly rest home residents in Christchurch.

Methods. A cross-sectional prevalence survey was conducted among 175 residents aged 65 years and over, randomly selected from 30 rest homes in Christchurch, in 1998. Hazardous patterns of alcohol consumption in the past twelve months were determined by the Alcohol Use Disorders Identification Test (AUDIT) questionnaire, and alcohol dependence in the past 12-months and lifetime was determined by a structured clinical interview using DSM-IV criteria.

Results. Of 246 eligible participants, 175 (71.1%) residents were interviewed, 115 women and 60 men, mean age, 82.6 years (SD=7.8) compared with 83.2 years (SD=6.3) for non-participants. The prevalence of hazardous patterns of alcohol consumption in the past twelve months by the AUDIT (cut-off score 8) was 5.1% (95% CI=1.8-8.4). According to DSM-IV criteria, the prevalence of lifetime alcohol dependence was 20.5% (95% CI = 13.5-27.6) and for the past twelve months was 0.5% (95% CI = 0-1.7). The prevalence of lifetime alcohol dependence was significantly higher in men 36.7% (95% CI = 23.2-50.1) than women 12.2% (95% CI = 5.6-18.8) (p=0.0001).

Conclusions. In spite of advanced age, a small proportion of elderly rest home residents consumed quantities of alcohol that put them at risk of future damage to physical or mental health. Lifetime prevalence of alcohol dependence was comparable to the general population estimates and was higher in men than women.

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Alcohol problems are often not identified and diagnosed in elderly people[1,2] despite their being more vulnerable to its effects than younger people.[3] Medication use is also very common among elderly people,[4] putting them at risk of possible adverse drug-alcohol interactions.[5]

The consequences of heavy and long term alcohol consumption include increased risk of strokes,[6] dementia,[7] depression,[7] some types of cancer,[8] falls,[9,10] hip fractures,[11] hypertension,[12,13] cardiomyopathy,[13] cardiac arrhythmias[13] and suicide.[14]

Little research has been undertaken worldwide on alcohol-associated problems in long-term care settings. The reported prevalence of alcohol abuse and dependence in United States Veterans Affairs nursing homes ranged from 2.8% to 49% depending on the settings and methods of study.[15,16] A recent study in old age homes in Germany indicated a 3.4% prevalence of current alcohol abuse or dependence according to home staff assessment.[9]

Alcohol is the most commonly used drug in New Zealand.[17] A recent New Zealand Health Survey in a non-

institutionalized elderly population reported that elderly people drink regularly but less on single occasions than younger people and indicated a 4.1% prevalence of current hazardous patterns of alcohol intake according to the Alcohol Use Disorders Identification Test (AUDIT).[18] There are no published surveys investigating the patterns of alcohol use and misuse in rest homes in Australasia. The aim of this study was to determine this prevalence using a validated instrument and by conducting a survey among randomly selected rest home residents within one city.

Methods

This cross-sectional study used a two-stage cluster sampling design.[19] At the first stage, 44 rest homes were randomly selected from a list of all rest homes in Christchurch and at the second stage residents were randomly sampled within each rest home. The clusters were selected proportionally to the number of individuals in the rest home (Figure 1). All residents aged 65 years or older who could give informed consent were included in the sampling frame for study. Residents were excluded if they were demented, terminally ill, dysphasic, severely deaf or currently psychotic. Residents were also excluded if they were discharged or re-hospitalized before the interview could be conducted.

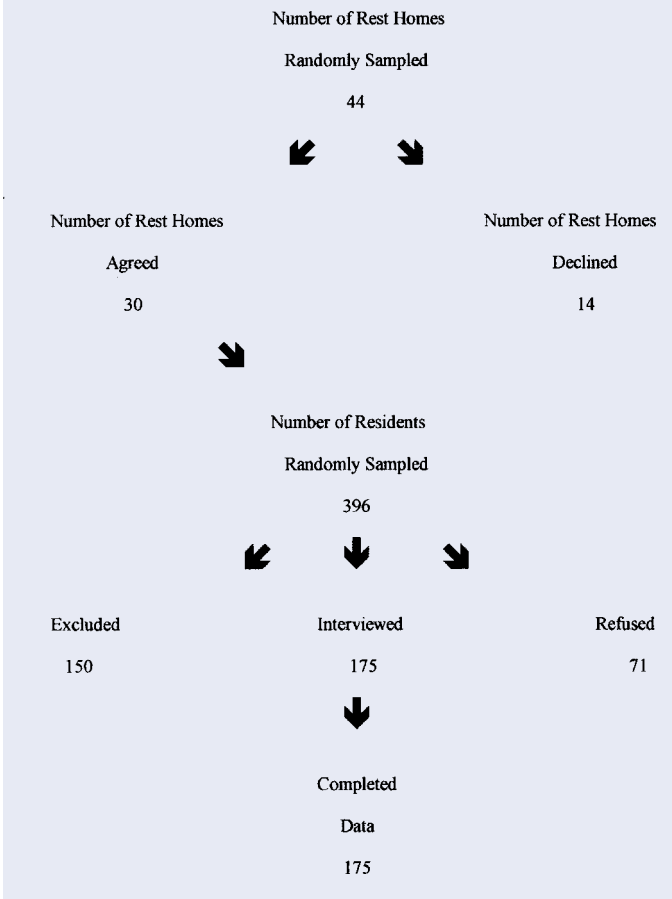

Figure 1. Sample method used to identify 175 study subjects.

We posted invitation letters, self addressed postage paid envelopes and information sheets specifically designed for the rest home managers to explain the nature, purpose and procedures of the study. This mail out was followed by telephone calls to give further information and to attend to any queries. Where necessary, the interviewer visited rest homes personally to talk about the study.

Of 44 randomly selected rest homes, 30 agreed to participate. The managers of rest homes who agreed to participate provided a list of all residents. The study residents were randomly selected from this list using a random number table. Following resident selection, the managers were then requested to identify any residents who met the study exclusion criteria. Each study resident was approached individually and the nature and purpose of the study was explained. Participating residents provided written consent, which was witnessed by the rest home staff on duty.

The principal investigator was blinded to the drinking habits of participating residents; rest home staff were asked not to disclose the drinking habits of participating residents prior to the interview. Once data collection was completed, rest home managers were asked to comment on present and past alcohol drinking habits of those people who were excluded or declined. A pilot study was conducted prior to the main survey.

The interview lasted approximately fifteen minutes with a focus on hazardous alcohol use and alcohol dependence. Hazardous alcohol use was defined as an established pattern of alcohol use carrying with it a high risk of future damage to physical or mental health, but which had not yet resulted in significant medical or psychological ill effects.[20] Alcohol dependence was defined as a condition in which an individual may continue to consume alcohol, despite adverse consequences, often to avoid or relieve symptoms of withdrawal.[21] The rest home residents were interviewed using the 10-item AUDIT (Alcohol Use Disorders Identification Test)[20] developed by the World Health Organization. A validation study showed a score of eight or more on the AUDIT indicates hazardous alcohol use.[22] The AUDIT was followed by a structured clinical interview using DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth edition) criteria for alcohol dependence[21] including some quantity/frequency questions and a question about treatment. The heaviest twelve months period of alcohol use in the lifetime was identified and then DSM-IV diagnostic criteria were applied for alcohol dependence. The cut off score of three or more DSM-IV criteria was used to make a diagnosis of alcohol dependence in the past twelve months, as well as in the lifetimes of rest home residents.[21] To standardize for the different alcohol contents of different beverages and for differences in glass size, we used photographs of standard spirit, wine, beer and spirit glasses with markings for equivalent amounts of alcohol.[23]

We calculated that a sample size of 175 would allow the prevalence to be estimated to within five percentage points with 95% confidence, assuming a true prevalence of 10% and allowing for a modest clustering effect.[19] We assumed that the effect of the cluster sampling would be modest, since the probability of sampling more than ten residents from each rest home was low. We used a Jackknife method, appropriate for cluster sampling, to calculate 95% confidence intervals.[24] We analyzed categorical outcome data between groups with the Chi-squared test. We used Student's t test and analysis of variance (ANOVA) to compare continuous outcome data.

This study was approved by the Southern Regional Health Ethics Committee, Canterbury.

Results

44 rest homes were selected. The managers of 30 (68.2%) agreed to participate. Reasons for refusal were 'Not interested' (7), 'Residents are not interested' (3), 'Renovation work is going on' (2), 'Tired of surveys' (1), and 'Recently converted into dementia-specific unit' (1). The initial random sample for the 30 rest homes included 396 residents, of whom 246 (65.2%) met the inclusion criteria. Of these eligible residents, 175 (71.1%) gave consent to participate and were interviewed.

The mean age of participants was 82.6 (95% CI 81.4-83.7) years. The mean age for those who declined was 83.2 (95% CI 81.7-84.6) years and for those who were excluded was 84.7 (95% CI 81.2-84.3) years. 168 (96.0%) were European, two (1.1%) were Maori and five (2.8%) were from other ethnic groups. There were more women (65.7%) than men (34.2%). This gender distribution was not significantly different for the non-participants with more women (71.8%) than men (28.2%) declining to take part. Similarly, there were more women (78.0%) than men (22.0%) among those who met the exclusion criteria.

Reasons for excluding 150 residents were: dementia (97), terminal illness (22), dysphasia (11), current psychotic disorder (7), hospitalized (5), severe deafness (4) and life-long intellectual handicap (4). Only one of the 97 residents who had dementia had a history of alcohol problems in the past as determined by the rest home staff. None of those who were excluded (150) were identified as having alcohol problems by rest home staff. Among the 71 people who declined, 64 residents had no reason or were not interested and one was terminally ill. Six residents declined specifically because they had a present or past alcohol problem. These same six residents were also reported by rest home staff to have past alcohol problems; one of the six also had a current alcohol problem.

Current alcohol use was infrequent among the participating residents. Of the 175 residents, 24 had had no alcohol in their lifetime. Only 47 residents had had alcohol more than ten times a month during the year of heaviest alcohol use in their lifetime. The mean age of first use for those who drank alcohol in their lifetime was 19.0 years.

88 residents had not drunk any alcohol in the past twelve months. Of the remaining 87 residents, only five had had six or more drinks on one occasion during the past twelve months.

Four previously alcohol dependent residents had received treatment for alcohol problems in the past. Each had had one inpatient treatment.

According to the AUDIT, nine residents (5.1%, 95% CI = 1.8-8.4) were identified as having hazardous patterns of alcohol consumption in the past 12 months.

According to the DSM-IV criteria, only one resident (0.5%, 95% CI = 0-1.7) was identified as having alcohol dependence in the past twelve months. According to DSM-IV criteria, 36 out of 175 residents, (20.5%, 95% CI = 13.5 – 27.6) were identified as having had alcohol dependence earlier in their lives. The prevalence of lifetime alcohol dependence according to DSM-IV was 36.7% (22/60) (95% CI = 23.2-50.1) among men, compared with 12.2% (14/115) (95% CI = 5.6-18.8) among women (p=0.0001).

Discussion

This is the first study to examine patterns of alcohol use in New Zealand rest homes. It showed that 20.5% of elderly residents in Christchurch rest homes had lifetime alcohol dependence and 5.1% continued to drink alcohol in a pattern which put them at risk of future damage to physical or mental health. Only one resident (0.5%) had alcohol dependence in the past twelve months. Of 175 residents, 24 had never used alcohol in their lifetime.

The prevalence of hazardous patterns of drinking alcohol reported here for rest home residents is comparable with the prevalence of 4.1% reported for community-dwelling respondents aged 65 years and over in a New Zealand health survey.[18] This is in spite of the age distribution of the rest home sample being older than the household health survey sample.

Alcohol problems among the people who declined, (8.4%) as reported by the rest home staff, were significantly lower than the prevalence of alcohol dependence determined using DSM-IV (20.5%). This is likely to be due to rest home staff using different criteria to define alcohol abuse and dependence; however, we cautiously conclude that the sampling method was not biased towards missing people with alcohol problems.

There has been very little research into alcohol abuse and dependence in long-term care settings. It is difficult to compare our analysis with others due to different age distribution, difficulty in establishing a representative sample, relative lack of standardized instruments, variable definitions of 'alcoholism', 'alcohol abuse', 'alcohol dependence', 'heavy drinking', 'drinking problems' and inherent bias in data collection methods. As a result, there is wide variation in prevalence estimates. Nevertheless, the results of this study are broadly consistent with those of others, which show that the prevalence of alcohol use and misuse declines in old age.[25,26] A decline observed in cross sectional studies, however, could represent a decline in alcohol use with time or a cohort effect; that is people born at one time may have had different lifelong drinking practices from those born at other times. However, longitudinal studies have also confirmed that heavy alcohol use declines with increasing age.[27,28] The finding that men had a higher lifetime prevalence of alcohol dependence than women is consistent with gender differences found generally.[29]

Some potential limitations in this study must be noted. The ability to remember present and past drinking events may decline with advancing age and long standing alcohol use and misuse. Although dementia was an exclusion criterion to maximize accuracy of data, recalling past events might have influenced the reporting of lifetime alcohol dependence to some extent. Recall bias might have affected the finding in either direction. Only one out of 97 residents who was excluded because of dementia was reported by rest home staff to have a history of alcohol problems in the past.

Self-report data are subject to bias. The validity of self reported information on alcohol consumption is a major concern.[30] This inaccuracy might be because of memory problems, difficulties in mental averaging or denial. Deliberate underreporting could have reduced the detected prevalence of alcohol dependence in the study. Interviewer bias is of less concern in this study as the interviewer was trained and blinded to individual residents' alcohol status prior to the interview.

An attempt was made to minimize potential sources of bias by using a random selection process for rest home selection and resident selection. The response rate of rest homes agreeing to participate was reasonable (68.1%). It is possible that participating rest homes might be interested in the study because of alcohol problems within their institution. If this bias were present, it would result in an overestimation of the prevalence rate. This seems unlikely, as the reasons for refusal were not related to characteristics of the residents. There was an acceptable resident response rate (71.1%). The majority of non-participants mentioned 'not interested' as a reason for refusal. There was a low prevalence of alcohol problems in the non-participants; only six of these were reported by rest home staff to have had alcohol problems. Only one resident out of these six had a current alcohol problem. Any bias resulting from the resident response rate would therefore result in an overestimate of prevalence.

Reasons for the observed low prevalence of a current hazardous pattern of alcohol consumption in rest homes could be due to lack of direct access to alcohol. This might be due to limited mobility and reliance on friends and family for access. Although the social life of rest homes continues to promote "Happy Hour" as part of the process of social integration into the leisure subculture, access to alcohol is controlled and maintained by the rest home staff.

It is possible that early mortality among lifetime abusers might have left a surviving elderly population that consumes less alcohol, and has fewer alcohol related problems. However, the 20.5% lifetime prevalence of alcohol dependence in this surviving population suggests this is not a significant factor.

Since this study was conducted at a single point in time any age related differences might not have reflected the effects of ageing. There is a possibility of a generational effect in the findings. Those who were brought up in times when abstinence was common are more likely to show fewer problems with alcohol today. Many from the present elderly population grew up when drinking was less socially acceptable and they may be reluctant to admit even limited consumption. The results of this study support the findings that men are generally more at risk than women.

Despite significant lifetime alcohol dependence among the rest home residents surveyed, there is a low prevalence of current hazardous patterns of alcohol consumption in Christchurch rest homes and the rates are comparable to those seen among older people living at home.

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The rapid whole blood agglutination d-dimer assay has poor sensitivity for use as an exclusion test in suspected deep vein thrombosis

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Abstract

Aims. Several clinical studies have proposed using d-dimer as an initial screening test to exclude thrombosis in cases of suspected (DVT). In published series, these assays have variable sensitivity, raising concerns that they may not be sufficiently robust for clinical practice. The aim of the study was to examine the sensitivity of two commercially available d-dimer assays and to assess their value and safety as initial screening tests in suspected DVT.

Methods. In this prospective study, blood samples were collected for d-dimer measurement (SimpliRED assay and IL test d-dimer) in all patients presenting to the emergency department over a twelve month period. All patients underwent compression ultrasound scanning as the primary diagnostic procedure.

Results. 235 patients were included in the study. 51(22.8%) had a DVT confirmed on ultrasound. The SimpliRED assay was positive in only 33 cases, with seventeen cases of confirmed DVT giving a negative result (six cases with proximal vein thrombosis). Assay sensitivity was 66%, with a negative predictive value of 88.9%. The IL test gave three false negatives (all below knee thromboses) giving assay sensitivity and negative predictive value of 94.1% and 96.8% respectively.

Conclusions. The precise role of d-dimer testing in the diagnosis of venous thrombosis has yet to be established. From our results and a review of published series, we conclude that the SimpliRED assay is too insensitive to use as a reliable exclusion test in cases of suspected DVT, however, the more sensitive automated IL test d-dimer may have a role in the initial assessment. We propose that the IL d-dimer test is used in conjunction with a pre-test probability score to identify patients at low risk of DVT and recommend that this approach is tested in a clinical study before introduction into practice.

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In many centres, compression ultrasound scanning has largely replaced venography as the first line investigation in cases of suspected deep vein thrombosis (DVT).[1] As ultrasound is non-invasive, well tolerated and can provide results rapidly, junior medical staff tend to request this investigation to exclude DVT, even in patients with a low clinical probability of thrombosis. In our hospital, this change in clinical practice has led to a marked increase in ultrasound scanning requests and put considerable pressure on the ultrasonography department. In an attempt to alleviate this problem, we have looked at alternative methods that could be used in the initial assessment of patients with suspected DVT. By far the easiest approach would be a simple blood test taken at presentation to either confirm or exclude thrombosis. To date, the only test that has shown promise is the measurement of the plasma d-dimer concentration.[2] D-dimer is a break down product of crosslinked fibrin and its level in blood is raised in patients with thrombosis. Unfortunately, elevated d-dimer concentrations are not specific for DVT or pulmonary embolus, but are raised in many other conditions. However, the d-dimer assay may have a place in clinical practice

because of its high negative predictive value. As a result, it has been proposed that patients with a normal plasma d-dimer concentration are unlikely to have a thrombosis, making further investigation unnecessary.

In order to use this type of assay reliably the sensitivity must be high, so that all cases of DVT are identified. To date, the reported sensitivity of d-dimer assays has shown considerable variability; as a result we were concerned that it would be difficult to directly translate the results of these clinical trials into practice in a busy general hospital. Therefore, we performed a clinical evaluation of two d-dimer assays in all patients presenting with a suspected DVT over a twelve-month period. The aim of the study was to determine the sensitivity of these assays in this clinical setting and to assess their value and safety as the initial screening for patients with suspected DVT.

Methods

This was a prospective study of all patients presenting with suspected DVT to the emergency department of Palmerston North Hospital from 11th April 1999 to the 10th April 2000. All patients were entered into an established clinical pathway for suspected DVT, involving clinical assessment followed by compression ultrasound scanning. We elected to use a single scan for diagnosis, but advised patients with persistent symptoms to return for further assessment. We previously showed that this strategy was safe with a low thromboembolic risk at three months.[3] If the results of the ultrasound were deemed inadequate, the patient proceeded to venography. This decision was at the discretion of the radiologist.

All patients had blood samples collected into citrated anticoagulant for d-dimer estimation, prior to any radiological investigation. The radiologists were not aware of the d-dimer results at the time of scanning. The d-dimer assays were performed by trained laboratory staff, who were not aware of the ultrasound scan results. Patients were excluded from the study if they failed to have blood samples collected at presentation, if they were already taking oral anticoagulant therapy, or if ultrasound scanning was considered unnecessary by the admitting clinician.

The d-dimer concentration was measured using two assay methods. A rapid red cell agglutination test (SimpliRED, Agen Biomedical Ltd, Brisbane, Australia) was performed according to the manufacturer's recommendations. This is a qualitative assay. The presence of agglutination signifies a d-dimer concentration above 0.12mg/L (as stated by the manufacturer). The result is reported as either positive (d-dimers present) or negative (the concentration of d-dimer is below the level of detection).

The second assay was a quantitative assay (IL test D-dimer, Instrumentation Laboratories) performed on the ACL Futura. The assay is a turbidometric immunoassay using latex beads coated with a specific d-dimer antibody. It was performed according to the manufacturer's specifications. This is performed on plasma and the result expressed as the plasma concentration of d-dimer in µg/L.

Results

During the study, a total of 264 patients presented to the emergency department with a history suggestive of venous thrombosis. 235 patients fulfilled the criteria for admission to the study by having an adequate compression ultrasound and at least one of the two d-dimer assays performed. 29 patients were excluded: fourteen had no blood samples collected; twelve did not undergo an ultrasound scan; and three patients were already on oral anticoagulant therapy.

Compression ultrasound scanning confirmed venous thrombosis in 51 patients (22.8%). In 27 cases, the DVT was situated in the proximal vessels (popliteal vein and above) and in 23 patients the thrombosis was confined to vessels below the knee (calf veins below the popliteal fossa). One patient had an axillary vein thrombosis. Only one patient, with an initial negative scan, returned with persistent symptoms (after two days). A repeat ultrasound confirmed a small below knee DVT.

The SimpliRED assay was performed in 231 cases (50 with a DVT, 181 with a negative ultrasound scan). Of the 50 cases of confirmed DVT, the SimpliRED assay was positive in 33 and negative in seventeen (Table 1), giving an assay sensitivity of 66% and a negative predictive value of 88.9%. 181 patients had a negative ultrasound scan, of whom 137 had a negative SimpliRED assay result, giving a specificity of 75.6%. In the seventeen patients with a DVT but a negative SimpliRED result, six had proximal vein thrombosis, ten had below knee thrombosis and one had an axillary vein thrombosis.

Table 1. Results of the SimpliRED d-dimer assay.

	Patients with confirmed DVT	Patients without DVT
Positive	33	44
Negative	17	137

Sensitivity 66%
Specificity 75.6%

The IL-test d-dimer was performed in 232 patients (51 with a DVT, 181 with a negative ultrasound scan). The results ranged from 15.6 to >34 000 mg/L. A cut-off value of 250 mg/L was taken to distinguish between a positive and negative result. Of the 51 cases of confirmed DVT, the IL test d-dimer assay was >250mg/L (positive) in 48 and <250mg/L (negative) in three (Table 2), giving an assay sensitivity of 94.1% and a negative predictive value of 96.8%. Of the 181 patients with a negative ultrasound scan, 93 had a negative IL-test d-dimer assay result, giving a specificity of 51.5%. Three patients with a confirmed DVT gave a negative IL-test result. In all three, the thrombosis was confined to the vessels below the knee.

Table 2. Results of the IL-test d-dimer assay (cut-off value of 250µg/L)

	Patients with confirmed DVT	Patients without DVT
Positive >250µg/L	48	88
Negative <250µg/L	3	93

Sensitivity 94.1%
Specificity 51.5%

Discussion

In our series of 235 patients, a definite diagnosis of venous thrombosis was confirmed in 22.8% of cases. This is a similar incidence to other recently reported series (Table 3), but is in contrast to studies reported 10-15 years ago, where 40-50% of patients investigated had a confirmed thrombosis. This lower detection rate probably results from a more conservative approach to the investigation of suspected DVT. Ultrasound is often requested merely to exclude thrombosis, even in patients with a low clinical probability of thrombosis. This has led to an increased demand on ultrasonography services, prompting the search for an alternative first line test to exclude low risk patients from further investigation.

Several studies have proposed that the measurement of plasma d-dimer can be used as an initial screening test in patients with suspected DVT.[2,4] The diagnostic performance of these assays, however, shows considerable variation, making it difficult to select an appropriate one for clinical practice. The ideal is an assay with sensitivity approaching 100%, meaning all cases of DVT give a positive result, and a negative result could be used to confidently exclude thrombosis. To date, the assays with the highest sensitivity are ELISA methods designed for batch analysis. These have a sensitivity between 97-100%,[5-7] but have proved too

cumbersome and expensive for rapid emergency use. More recently, rapid assays have been developed. Probably the simplest is the SimpliRED red cell agglutination test. This could theoretically be used at the bedside and gives results within a few minutes. This test has been evaluated in screening for pulmonary embolus, with a reported sensitivity of 97%,[6] however, the sensitivity in suspected DVT is far more variable, ranging from 56-100% (Table 3).

Table 3. Sensitivity of the SimpliRED assay in cases of suspected DVT from previously published reports.

Published studies	No. of Patients in study	Percentage with DVT	Sensitivity
Harper et al (2001)	235	22.8%	66%
Carter et al (1999)[16]	200	28%	87%
Stey et al (1999)[17]	100		87.5%
Wildberger et al (1998)[18]	250	32.8%	96.3%
Freyburger et al (1998)[5]	100	50% (DVT+PE)	79%
Brimble et al (1997)[19]	262	22.5% (DVT+PE)	86%
Wildberger et al (1997)[20]	122	30%	94.6%
Jacq et al (1997)[14]	50	38%	58%
Mayer et al (1997)[21]	108	30%	100%
Turkstra et al (1996)[22]	234 (180 DVT)	28.6% (DVT&PE)	100%
Brenner et al (1995)[23]	86	58%	94%
Wells et al (1995)[24]	214	24.7%	93% Proximal 70% distal
Farrell et al (2000)[15]	173	33% (DVT+PE)	56% DVT 68% PE
Van der Graaf et al (2000)[7]	99	50%	80%
Fiessinger et al (1996)[25]	30	23%	71%
Reber et al (1997)[26]	100	23% (DVT+PE)	87%
Kraaijenhagen et al (1997)[27]	552	20%	93%
Chunilal et al (1999)[9]	151	22.5%	82% finger prick 94% citrate 97% EDTA
Lee et al (1999)[28]	121 947	48.8% (with cancer) 14.6% (without cancer)	86.4% (with cancer) 82.2% (without cancer)
Janssen et al (1997)[6]	132	67%	61% (63% proximal)

PE = pulmonary embolism.

In our series, we found this test had poor performance, with a sensitivity of only 66% and a negative predictive value of 89% (Table 1). Had we used this assay as the initial screening test to exclude low risk patients from further investigation, seventeen cases of DVT would not have been detected. Our major concern was that six of these cases had extensive above knee thromboses. The reason for this poor performance is unclear, but in part could be explained by the subjective interpretation of this type of assay. Recent studies have shown that there can be marked inter-observer variation.[8,9]

The IL-test d-dimer is a fully automated quantitative assay that takes approximately 20 minutes longer to perform than the SimpliRED test but is not dependent on subjective interpretation. In our hands this assay proved more sensitive (94.1%; Table 2) than the SimpliRED test and was 100% sensitive for proximal vein thrombosis. This is in line with earlier evaluations of the assay.[7] Had this been used as the initial screening test, only three cases of below knee DVT would have been missed. Although these were clinically important, they were unlikely to embolise. In practice, the quantitative assay is also more informative and allows for some clinical discretion, especially for interpreting borderline results.

In order for this type of exclusion test to be useful and cost effective, its introduction must result in a significant reduction in the number of ultrasound requests. An indication of this benefit can be gauged from the assay specificity. A high specificity implies a low false positive rate and results in more patients being identified as low risk for thrombosis, in whom further investigation is unnecessary.

From our evaluation and a review of the published data (Table 3), we concluded that the SimpliRED test cannot be relied upon to exclude thrombosis in the initial assessment of suspected DVT. Although this assay is highly specific (75.6%) and in practice would lead to a 50% reduction in ultrasound requests, it failed to detect 34% of venous thromboses referred to our unit. Such a high failure rate is unacceptable. The IL test had better sensitivity, missing only 6% of cases and could have a role in the initial assessment of suspected venous thrombosis. Although specificity is only 51.5%, in practice this would still lead to a 30% reduction in ultrasound requests.

The precise role of d-dimer tests in assessing cases of suspected DVT has yet to be established. A recently published algorithm proposed that all patients with a negative d-dimer could be assumed to have a low risk of thrombosis and do not require further investigation.[10] The problem with this approach is that the initial assay must have sensitivity approaching 100% and that a major clinical decision is based entirely on the results of a single investigation. This may be appropriate in a trial setting but is less acceptable in routine clinical practice.

We propose that a safer approach is to use this type of assay as an adjunct to a detailed clinical assessment. Several reports have shown that a clinical scoring system can be used to categorise DVT patients into high, medium and low risk groups[11] and that this can be used in conjunction with ultrasound scanning and d-dimer measurement in the work-up of suspected DVT.[12,13] From the results of our study, we propose a clinical algorithm (Figure 1) for patients with suspected DVT which needs to be further evaluated by an appropriately designed clinical trial.

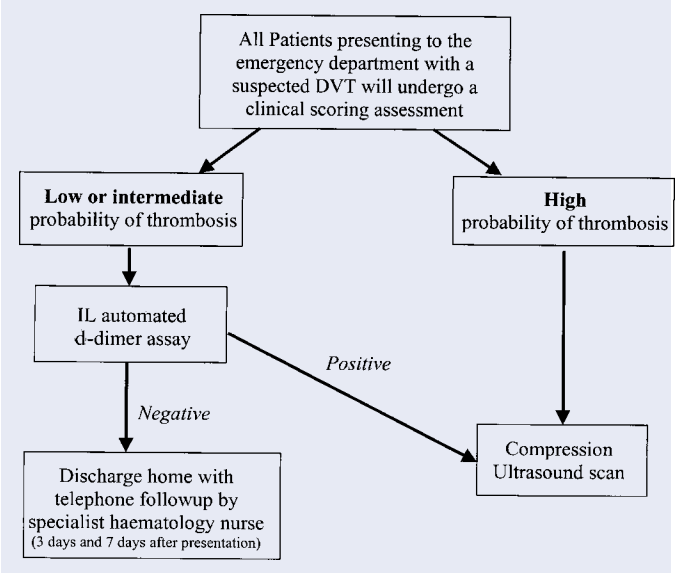

Figure 1. Proposed algorithm for patients with suspected DVT. All patients with a high probability of DVT proceed directly to an ultrasound scan. Low and intermediate probability patients only undergo an ultrasound if the d-dimer assay is positive.

In conclusion, we are concerned that the d-dimer test is creeping into clinical practice without clinicians being aware of the poor sensitivity of some assay methods. In fact, this type of assay could be seen as dangerous by lulling the unsuspecting clinician into a false sense of security believing that a negative result equates to no DVT, which is clearly not always the case.

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The clinical significance of Atypical Squamous cells of Undetermined Significance: a laboratory audit of cervical reporting

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Abstract

Aim. To determine the outcomes in women diagnosed with 'Atypical Squamous Cells of Undetermined Significance' (ASCUS) on cervical smears.

Methods. All diagnoses of ASCUS on cervical smears made at Southern Community Laboratories (SCL) in Christchurch in 1996 were retrieved from the SCL database and correlated with all available previous and subsequent smear and biopsy results from these patients. The outcome was reported as the most significant (highest grade) cervical smear or biopsy over the following two year period.

Results. 278 women had smear results of ASCUS in 1996, reflecting 2.3% of total cervical smear diagnoses at SCL (Christchurch) for that period. Follow-up was available for 260 (94%). 61% had benign (normal or inflammatory) changes, 6% had persistent ASCUS (smear only), 18% had a Low Grade Squamous Intraepithelial Lesion (LSIL), and 15% had a High Grade Squamous Intraepithelial Lesion (HSIL). All women with ASCUS who subsequently developed HSIL had persistent abnormal smears.

Conclusions. An ASCUS smear result indicates a group of women who have an increased risk for detection of HSIL. The effectiveness of routine Pap smears for detection of cervical cytologic abnormality is confirmed.

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Most (93%) women in New Zealand who have cervical smears have a benign result and a small minority (4%) have an abnormal result. Another small group (3.4%) have a result which does not give a definitive diagnosis but indicates 'Atypical Squamous Cells of Undetermined Significance' (ASCUS).[1,2]

The term ASCUS was coined as a result of the Bethesda conferences in 1988 and 1991. The Bethesda system for reporting cervical cytologic diagnoses was developed at these conferences to provide a uniform diagnostic terminology that would facilitate communication between the laboratory and clinician. These criteria are illustrated in the Bethesda System monograph.[3] ASCUS is defined as: "Cervical abnormalities that are more marked than those attributable to reactive changes but that quantitatively or qualitatively fall short of a definite diagnosis of squamous intraepithelial lesion (SIL)." Because the cellular changes in the ASCUS category may reflect an exuberant benign change or a potentially significant lesion which cannot be unequivocally diagnosed, they are interpreted as being of undetermined significance.

Perhaps the greatest clinical dilemma associated with cervical screening relates to the management of borderline cervical abnormalities, namely ASCUS. An uncertain proportion of women with ASCUS will be found to have a High-Grade Squamous Intraepithelial Lesion (HSIL) at colposcopy. Published studies report a wide range of outcomes, with 25-60% of women with ASCUS reported to have SIL on biopsy with 15-30% of these SIL's representing HSIL.[4-6] Although immediate referral for colposcopy following an initial report of ASCUS is advocated by some, it remains to be proven that this is necessary or cost effective. There are also valid concerns that many women with minor cervical abnormalities are being tested repeatedly

or unnecessarily, resulting in increased cost to the health system. Nevertheless, persistent mildly abnormal cervical cytology is an important indication for referral to colposcopy because although not diagnostic of early cervical neoplasia, this seems to identify patients at risk for its subsequent detection.

In an effort to determine the local clinical significance of the ASCUS diagnosis, and to provide information for referring practitioners and their patients, an audit was conducted at Southern Community Laboratories, Christchurch, to correlate cervical smears with a diagnosis of ASCUS and available follow-up in a subsequent two-year period. The aims of the audit were first, to monitor the rate of cervical smears with the diagnosis of ASCUS; second to identify follow-up outcomes where available; and third to provide the results of this audit to guide ongoing patient management.

Methods

Cervical smears at Southern Community Laboratories are screened by qualified cytotechnologists. For quality assurance, each smear is re-examined by a second cytotechnologist. All smears found to contain abnormal cells are then examined by a cytopathologist. This system of 100% rescreening is regarded as the most cost-effective strategy in reducing the rate of 'false-negative' smears.[7]

All cases coded as ASCUS in 1996 were retrieved from the laboratory database which was also searched for available follow-up cervical smears or biopsies over the subsequent two-year period. The National Cervical Screening Programme (NCSP) also provides follow-up data for quality-assurance purposes which is incorporated into the laboratory database.

We use cytologic criteria for ASCUS as specified by the Bethesda system terminology committee: "...squamous cells most often of intermediate or superficial type with nuclear enlargement 2.5-3 times the size of a normal intermediate cell nucleus, with a slight increase in the nuclear/cytoplasmic ratio. Variation in nuclear size and shape, and binucleation. Mild hyperchromasia may be present, but the chromatin remains evenly distributed without granularity. Nuclear outlines are usually smooth and regular; very limited irregularity may be observed:"...[3]

In most cases, the cytologic differential diagnosis of ASCUS is between a reactive lesion and LSIL. There is a small subgroup of ASCUS cases in which an HSIL cannot be excluded and in whom colposcopy is recommended.[8,9] These cases were included in our study as at the time they were coded as ASCUS.

The outcome was recorded as the most significant (highest-grade) cervical smear or biopsy over the following two years.

Results

General. 278 women had cervical smears reported as ASCUS in the calendar year 1996, which represents 2.3% of all cervical smears examined in this laboratory during that year. The screened population was from a low risk community, with 85% of smears coming from general practitioners and nurse smear takers, and 15% from gynaecologists.

Two-year follow-up was available in 260 (94%) women. 18 (6%) were lost to follow-up. 106 (41%) had cervical biopsies and the remainder had smear-only follow-up. With two year follow-up, the outcomes in women with smears showing ASCUS were:- 39 (15%) women had HSIL, 46 (18%) had LSIL, 16 (6%) had persistent ASCUS (no biopsy), and 159 (61%) had benign changes (Figure 1). 37 of the 39 diagnoses of HSIL were confirmed by histology.

Age-group. Stratified by age-group there were 86, 101 and 73 women respectively with available follow-up in the under 26 years, 26-39 years and over 39-year old age-group categories. Rates of HSIL for these groups were 17%, 17% and 10% respectively (Table 1). The differences in outcomes between the different age-groups are not statistically significant (Chi squared = 8.7).

Subcategorisation of ASCUS. The ASCUS result was subcategorised by the most likely diagnosis on the basis of morphology into 'favour SIL', 'favour HPV', 'favour reactive' groups. The category of 'ASCUS favour reactive' had the highest number of benign smears (59%) but 10% of this category still turned out to have an HSIL. Figures for the 'ASCUS favour SIL' category were 37% benign and 24% HSIL respectively. Figures for the 'ASCUS unspecified' and 'ASCUS favour HPV' were intermediate between these (Table 2). The differences in outcome between different ASCUS subcategories do not achieve statistical significance (Chi squared = 11.1).

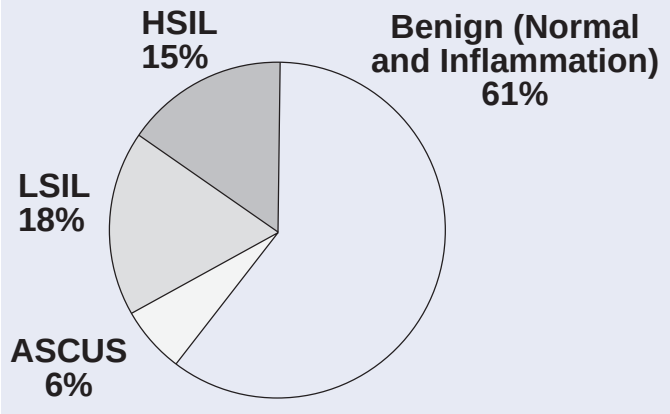

Figure 1. The most significant smear and/or biopsy result within two years following on ASCUS smear result.

Table 1. Follow-up outcomes of different age groups.

	Follow-up Outcome						
	Normal		ASCUS + LSIL		HSIL		Total
Age-group (years)	No.	%	No.	%	No.	%	No.
<26	42	49	29	34	15	17	86
26-39	51	50	33	33	17	17	101
>39	51	70	15	21	7	10	73

Table 2. Follow-up outcomes for patients with different ASCUS subgroups.

	Follow-up Outcome						
	Benign		ASCUS + LSIL		HSIL		Total
	No.	%	No.	%	No.	%	No.
Favour Reactive	58	63	25	27	9	10	92
Unspecified	28	48	18	31	12	21	58
Favour HPV	41	59	18	26	10	14	69
Favour SIL	5	37	16	39	10	24	41

Persistent Abnormal Smears with HSIL. Follow-up smears after the initial diagnosis of ASCUS were analysed in women in whom the final outcome was HSIL. All 34 women with a final outcome of HSIL had at least one further abnormal smear following their initial ASCUS smear. The mean elapsed time from the initial ASCUS smear until final diagnosis of HSIL was 11.5 months (range 4 to 26 months). However, four women also had at least one negative follow-up smear, and three had negative colposcopy and negative biopsy before the final diagnosis of HSIL was made.

Discussion

This audit was performed to better understand the characteristics and outcomes in women diagnosed as ASCUS in our laboratory. The results are congruent with those of previous studies. Published data indicates ASCUS rates ranging from 0.6% to 5.8%, with an average of 3.4% reported by community laboratories in New Zealand in 1995

and a median ASCUS rate in 1993 of 2.8% in American laboratories.[1,10]

We followed the approach of similar studies, examining cytology and histology outcomes, rather than only the histologic correlation of ASCUS.[11] Although histology may be regarded as the 'gold standard', in fact, there may be discrepancies between cytology and histology results due to sampling.[12,13]

Our two-year follow-up rate of 94% compares very favourably with other published studies which report rates of 41-84%.[11,14] It is worrisome that some patients lost to follow-up will have high-grade lesions. Alanen et al conducted a retrospective review of cytology, colposcopy and follow-up. Of 6319 smears, 320 (5%) had ASCUS. 28% of patients with ASCUS were lost to follow-up. After a two-year follow-up period, 78.6% of patients with ASCUS reverted to normal or benign cellular changes. 3.9% of women with an index Pap smear diagnosis of ASCUS had HSIL on colposcopic biopsy.[11]

Williams et al reported 668 patients with a diagnosis of ASCUS for the calendar year and followed them up over a two-year period. 41% of patients underwent colposcopic biopsy of whom 4% showed HSIL.[6] Our rate of association of ASCUS with HSIL of 15% falls within the range reported by other authors of 5.2% to 18%.[6,11,15] However, it is emphasised that the majority of women with ASCUS had benign outcomes.

The diagnosis of ASCUS thus defines a group of patients with an increased rate of diagnosis of HSIL, a lesion which is important to identify, investigate and treat. This is in contrast to LSIL, which is increasingly believed not to be a biologically significant lesion.[16]

We studied the outcomes in different age groups using the same ranges as other published data. Our findings show similar rates of abnormality in the under 26, and 26 to 39 year old groups, with HSIL rates of 17%. The over 39 year old age-group had a rate of HSIL of only 10%, although the differences in outcomes between these age groups were not statistically significant. Results from the NCSP and other overseas studies also showed the under 26 year-old age group to have similar rates of abnormality to the 26 to 39 year old group, declining thereafter. Although the incidence of ASCUS and the frequency of underlying dysplasia is lower in older women, there is still a real risk that women in this age-group have an underlying lesion.[1,6,17,18]

Women in the older age-group have a lower rate of enrolment in the NCSP, although they have a significant incidence and mortality rate of cervical carcinoma, emphasising the importance of appropriate screening and follow-up in this group.[1]

Subcategorising ASCUS as to the likely diagnosis appears to have limited ability to guide management in our practice, with 10% of cases diagnosed as 'ASCUS favour reactive' and 24% of cases diagnosed as 'ASCUS favour SIL' subsequently demonstrating HSIL. Gonzales et al divided patients with ASCUS into those favouring a reactive process or LSIL. No HSIL were identified in patients in whom a reactive process was favoured. 15% of patients with ASCUS favouring LSIL had CIN (cervical intraepithelial neoplasia) 1 or 2 on biopsy.[19] In other studies addressing the issue of subcategorising ASCUS, HSIL was found in 2-4% of patients with 'ASCUS favour reactive', and in 12-23% of 'ASCUS favour SIL' smears.[20,21]

In a patient with a cytologic diagnosis of ASCUS favouring a reactive process, a repeat smear that is normal is reassuring, as women with normal repeat smears were less likely to have HSIL. However, subcategorising ASCUS does not appear to have major predictive value for individual cases.

The finding of persistent abnormality in repeat smears of all women with HSIL confirms the effectiveness of routine Pap smears for follow-up. However, some of these women had false-negative smears, biopsies, and colposcopies before HSIL was diagnosed. Several studies have examined non-correlation of paired cervical smears and biopsies and have found discordant results in 11-14% of cases.[12,13,19] The cause of the discrepancy is mostly attributed to differences in cytology and biopsy sampling which are reported as occurring at similar frequencies. Ibrahim et al studied 3404 consecutive paired cervical smears and biopsies of which 481 had a discordant diagnosis. 446 discordances were attributed to sampling differences. The cytologic smear contained the diagnostic lesion in 40%, and the biopsy in the remainder.[13] Thus it would appear that the practice of obtaining paired smears and biopsies at colposcopy should increase the sensitivity in detecting an abnormality.

In conclusion, an ASCUS smear result identifies a group of women who are at increased risk of a current or subsequent diagnosis of HSIL relative to the general population. This applies to all age groups. The practice of regular cervical smear screening is a proven means of detecting pre-malignant changes. Our findings demonstrate that patients with ASCUS results who are ultimately found to have high-grade lesions will more likely have persistently abnormal Pap smears. These results support current recommendations for increased follow-up by Pap smear of patients with ASCUS smears. They also underscore the importance of systematic follow-up and repetitive screening by laboratories with good quality control and quality assurance programmes. The cornerstone of cervical carcinoma prevention most likely will remain the Pap smear.

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Getting the message across: sun protection information in media weather reports in New Zealand

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Abstract

Aims. To assess the public reach, awareness, understanding and response to the burn time and the Ultra Violet Index (UVI) in media weather reports in New Zealand.

Methods. Data from a representative sample (n=396), ages 16-44 years, were gathered over four consecutive summer weeks of 1999 via a random digit dialling telephone survey. Items collected included sources of weather reports and their frequency of use; knowledge, understanding, perception and use of the burn time and the UVI; sun-related beliefs, attitudes and behaviours.

Results. Exposure to weekend weather bulletins was sustained, and occurred mainly via television (83%) and radio (50%). There was greater awareness of the burn time than the more recent UVI (89% vs 43%). The UVI was less often used to guide sun protection actions (49% vs 63%) but better understood (94% vs 66%) and more often recalled along with sun protective messages (56% vs 32%) than the burn time. Few could describe the burn time or the UVI for the past Sunday. Self-perceived understanding of the burn time was higher than its measured, sub-optimal, comprehension (96% vs 65%).

Conclusions. Further efforts are needed to promote the UVI, particularly on TV1 and on radio, and to reach younger adults and less educated groups. For a transition period, presentation of the burn time should be restricted to complementing the UVI. Thereafter, the UVI should become the standard indicator of UV level in New Zealand.

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Skin cancer, in particular, its most lethal form, malignant melanoma (melanoma) is an important health issue in New Zealand,[1] where some of the highest incidence and death rates from melanoma are recorded[2] and about 1600 melanomas are registered each year.[3] Yet melanoma is one of the most preventable cancers, with over 90% attributable to sunlight exposure in Australasia.[4] The most efficient long-term strategy to reduce the melanoma burden lies in primary prevention that targets excessive sun exposure. In New Zealand, programmes combining primary prevention and early detection of melanoma have been in operation for over a decade.[5]

Three conditions are required to reduce harmful sun exposure: (1) wide dissemination of appropriate and accessible sun protection messages, (2) adequate public acceptance and understanding of these messages, and (3) their favourable and prompt impact on behaviour. Regular provision of public advice about ultraviolet (UV) levels can play a crucial role by drawing attention to UV as a health hazard, educating the community about ways in which UV intensity varies with daily weather, and assisting and prompting people to protect themselves adequately. New Zealand was the first country to use this communication strategy[6] and the time to burn (burn time) for fair-skinned individuals has appeared in media weather reports since 1989.

International authorities[7] have since devised and recommended the universal use of a standardised and objective measure of UV radiation at ground level, the Ultra Violet Index (UVI). UVI presentations generally link UV intensity ratings with risk of sunburn (ranging from no or minimal risk for values below three, to very high and extreme risk for values of 10+ and 12+, respectively).[8] The UVI, supported by several world organisations and many scientists, has been used in New Zealand from the summer of 1994-5 concurrently with the burn time.

Information on the extent, understanding and impact of sun safety messages presented in media weather bulletins, arguably the most readily accessible source, remains limited,[9,10] and this area has been identified as a research priority in New Zealand.[11,12] This paper describes the first exploration of the public reach and response to sun protection messages in media weather reports in New Zealand. In particular, the dual use of the burn time and the UVI provided a unique opportunity to compare respective awareness, comprehension and acceptance.

Methods

A nationwide telephone survey was conducted over four consecutive summer weeks of January 1999 and carried out by an experienced contractor (Phoenix Research) using random digit dialling and computer-assisted telephone interviewing (CATI). The CATI system allowed for the monitoring of interviews to help achieve good quality control. Interviews took place on Monday evenings, January 11 to February 1, with call-backs (up to five) made mainly on the next evening for those who were not contactable the previous day.

A sample size of about 400 was calculated to be statistically sufficient to obtain point estimates, with a 5% overall margin of error. Quotas ensured equal gender proportions and a representative participation of Maori (at least 12%) and by age group (16-19 years: 15%, 20-24 and 25-29: 20% each, 30-34, 35-39 and 40-44: 15% each). The study focused on young adults, who remain a key target group for primary prevention. The lower age limit was set to avoid any difficulties with parental consent.

The ten-minute questionnaire drew, in part, on US[10] and Australian[13] precedents. Questionnaire items sought socio-demographics, phenotypic characteristics, attitudes towards tanning, perceived risk of skin cancer, sunburn occurrence, sources of weather information, awareness, understanding and perception of both the UVI and the burn time. To avoid order effects, the sets of questions about burn time and UVI were asked in randomised order at widely separated points in the questionnaire.

Independence between discrete variables and compliance with the age, sex and ethnicity quotas were assessed by the Pearson chi-square statistic. A significance level of $p<0.05$ was accepted throughout. Two statistically dependent variables were termed associated when the values of one variable varied monotonically across the categories of the other.

Of 2679 households contacted, 755 people met the sex, age and ethnicity criteria and 396 interviews were completed (participation rate: 52.5%).

The study was approved by the Otago Ethics Committee.

Results

Participants. The age and sex distributions met set quotas (Table 1). The proportion identifying themselves as Maori

(14%) was commensurate with Maori representation in New Zealand. In terms of residence, 52% lived in the three most populated cities (28% in Auckland, 12% each in Wellington and Christchurch). Most respondents (73%) were in paid employment and, of these, 80% worked full time. A majority (58%) considered they would burn then tan if exposed, unprotected, to the sun for 30 minutes (Table 1).

Table 1. Distribution of participants and awareness of the burn time and of the UV Index (UVI) by socio-demographic and phenotypic characteristics.

Variable	Distribution %	(n)	Aware of the burn time		Aware of the UVI	
Gender						
Male	48%	(192)	87%		45%	
Female	52%	(204)	92%		40%	
Age				bs		
16-19 years	16%	(65)	78%		35%	
20-24 years	19%	(74)	92%		42%	
25-29 years	19%	(75)	89%		34%	
30-34 years	15%	(59)	90%		52%	
35-39 years	15%	(60)	93%		50%	
40-44 years	16%	(63)	93%		46%	
Ethnicity*						
New Zealand European	77%	(304)	93%		44%	
Other European	6%	(22)	91%		50%	
New Zealand Maori	14%	(57)	84%		35%	
Pacific Island	3%	(13)	46%		23%	
Asian	2%	(10)	70%		22%	
Type of place of residence						
Metropolitan area†	52%	(206)	86%	*	39%	
Other	48%	(190)	93%		46%	
Education‡						
School certificate or below	31%	(108)	87%		35%	**
High school graduate or below	27%	(96)	85%		37%	
Tertiary level	42%	(149)	92%		52%	
Employment status						
Employed	73%	(283)	89%		45%	
Home duties	8%	(30)	97%		29%	
Students	14%	(55)	85%		35%	
Unemployed	6%	(22)	91%		48%	
Daily occupational sun exposure§						
None at all	34%	(97)	92%		47%	
Up to 1 hour	32%	(91)	89%		46%	
1-4 hours	17%	(47)	89%		40%	
5+ hours	17%	(48)	85%		40%	
Skin type						
High sensitivity	26%	(100)	92%	**	42%	
Moderate sensitivity	58%	(227)	92%		44%	
Low sensitivity	17%	(65)	76%		40%	
Natural skin colour						
Very fair	12%	(49)	94%	*	46%	
Fair	37%	(148)	91%		43%	
Medium	21%	(82)	93%		42%	
Olive	22%	(87)	86%		45%	
Dark/black	7%	(29)	71%		29%	

bs: borderline of significance ($0.05<p\leq0.1$), *: $p<0.05$, **: $p<0.01$
* Allowance of multiple ethnic affiliations, reported by 6% of the sample, hampered the calculation of a χ^2 test of heterogeneity for that variable. Also, 18 cases with other ethnic reporting were discarded.
† Metropolitan areas included the three largest cities (Auckland, Wellington and Christchurch).
‡ Those with unspecified or overseas qualifications (n=43) were excluded.
§ Only for those employed.

Sun-related beliefs and behaviour. Some 60% reported liking to get a suntan and 37% had attempted to get a tan that summer. A suntan was mainly perceived as providing moderate (41%) or non-existent (34%) protection against UV, although nearly 20% believed it afforded efficient protection. About 21% got sunburnt the previous weekend, generally in episodes of mild (redness without soreness) or moderate (redness with soreness) severity, and 60% considered themselves to be at average risk of skin cancer.

Weather reports. At least 60% of respondents paid attention to summer weather reports, at weekends. Awareness of last weekend weather forecasts was associated with age (p=0.007), increasing from about 50% among those below 30 years of age to 70% among older respondents. Television was the preferred source of weather information (83%), followed by radio (50%) and newspaper (36%). Of those primarily watching television weather forecasts, TV1 viewers were twice as numerous as TV3 viewers (73% vs 36%). No particular radio channel was favoured for weather bulletins. Participants generally read weather forecasts solely in the purchased local newspaper. Most (85%) found it useful to have a regular reminder of UV intensity and of recommended sun protection in weather bulletins, and 73% remembered whether the news report for the past weekend included any sun protection message.

Burn time and UVI: awareness and sources of information. Twice as many people were aware of the burn time as were aware of the UVI (89% vs 43%). Few (2%) did not know about these measures. Awareness of the UVI was positively associated with education (p=0.008). The relationship between burn time awareness and educational level was less clear (Table 1). Awareness of the burn time, but not of the UVI, varied significantly with residence, and skin type and colour. Awareness of both indicators was consistently lowest among teenagers, Pacific Island and Asian people, good tanners and those with a dark complexion and low perceived risk of skin cancer.

Television was the major source of information for UVI (45%) and burn time (47%). Compared to the burn time, the UVI was less frequently experienced through audio-visual media, particularly radio (19% vs 35%), but more often seen in printed media and remembered when presented along with sun protective messages (56% vs 32%). Those able to describe the burn time and the UVI for their local area for the last Sunday (the day before most interviews) were too few to validate their recall against the media.

Burn time and UVI: comprehension and attitudes. Of those aware of the burn time, most (96%) believed it to be an easy concept to understand. The corresponding proportion for the UVI was 64%, and 15% reported difficulty in comprehending this measure. Comprehension of the UVI, assessed via agreement/disagreement with standardised statements, was very high and associated with favourable sun-related attitudes (Table 2). Understanding of, and attitudes to, the burn time were less satisfactory than for the UVI. As UVI awareness, alone, was positively associated with a higher educational level than the sample average, results were corrected for education to improve comparability. This was achieved by restricting answers about the burn time to those aware of the UVI. Misunderstanding of the meaning of the burn time persisted and sun-related intentions were barely changed. Sun-related attitudes to UVI did not, overall, depend on demographic and phenotypic factors (data not shown). Attitudes to the burn time improved steadily with education ($p<0.01$ for statements on use of sun protection and duration of sun exposure) and the most sun-sensitive and the least occupationally exposed individuals (those most likely to be at risk of melanoma) reported the most protective attitudes.

Burn time and UVI: perceived usefulness. The burn time was perceived as slightly more useful than the UVI for helping to determine appropriate sun protection for oneself and one's family (63% vs 49%). Perceived usefulness of these indicators was unrelated to education, gender and age. Interest in further information was greater for the UVI than the burn time (68% vs 40%), but indecisiveness about this requirement was higher for the burn time (37% vs 7%). No

Table 2. Understanding of, and attitudes to, UV index and burn time in New Zealand.

Statements to assess understanding of, and attitudes to, the UV index and the burn time*	% who agreed†	corrected % who agreed‡
As the UV index increases, it means that:		
The intensity of the sun's UV rays increases	94	
I can spend more time in the sun	3	
I need to use more sun protection	95	
As the burn time increases, it means that:		
The time it takes for the sun to burn the skin is longer	65	66
I can spend more time in the sun	51	55
I need to use more sun protection	50	42

* The statements reflect the actual wording of the questions.
† People unaware of an indicator or aware of it but who neither agree nor disagree with a statement were excluded.
‡The correction was performed by restricting answers about the burn time to people aware of the UVI.

relationship was detected between awareness or availability of further information and understanding of these indicators. A significant association existed between finding both measures useful ($p<0.001$) or wanting more information about both indicators ($p<0.001$). More females than males (80% vs 66%, $p=0.002$) wanted further information about the UVI, but this was not so for the burn time.

Discussion

This study represents the first evaluation of the public reach and response to the burn time and the UVI in New Zealand. The generalisability of our results largely depends on sample representativeness. Data on non-respondents were unavailable, but crude comparisons with recent community surveys[14,15] and official statistics[16] indicate similar socio-demographic and phenotypic distributions, and fairly comparable sun-related attitudes and beliefs. Our findings should, therefore, be applicable to the New Zealand population aged 16-44 years.

Results indicated that the UVI was less known, but better understood than the burn time. Several factors may contribute to explain this latter finding. First, two statements for the burn time, alone, cued correct answers (respectively, "I can spend more time in the sun" and "I do not need to use more sun protection") which might have been perceived as being socially undesirable. Second, the more common dissemination of sun protection messages with the UVI than the burn time in weather bulletins during January 1999,[17] confirmed by the participants' recall, may have facilitated its understanding. The UVI is generally presented in terms of risk category rather than a number, thus tends to vary less during summer than the burn time. Unvarying messages and constant numbers are, plausibly, the easiest to grasp and remember. Third, the inverse relationship between burn time and sunburn risk (the risk decreases with increasing burn time) is counter-intuitive and may have confused some people. The consistent pattern of misunderstanding for the burn time and correct interpretation for the UVI lend support to this assumption. Unfortunately, the contributions made by these factors to the rather poor interpretation of the burn time cannot be separated. Comprehension of UV indicators was based on questions developed by an international expert group.[10] This evaluation tool may, however, need further validation, particularly for the burn time. Alteration of the questions, perhaps by expressing them in a more numerical and illustrative way, is possible. This would enable further assessment of any tendency to over-estimate understanding of the burn time and under-estimate comprehension of the UVI.

Awareness of UVI appeared to be somewhat lower than in the US[10] and Australia,[18,19] but its interpretation in terms of sun protection attitudes and behaviour tended to be more favourable in New Zealand. The unique, concomitant use of the burn time and the UVI in New Zealand limits international comparisons.

Exposure to media weather reports, particularly at weekends, was sustained and the usefulness of regular reminders of current UV level was hardly contested. Awareness of both measures was, generally, highest among the most sun-sensitive individuals and a sizeable proportion of people was interested in receiving further information. These are encouraging signs, indicative of good public acceptance, but optimism should be tempered as recall of the burn time or the UVI for the prior Sunday or of whether these measures were complemented by sun safety messages was infrequent. Respondents who remembered the recommended protective actions were considerably fewer than those probably exposed to these accompanying messages.[17] Burn time and UVI awareness was lowest among teenagers and adults aged less than 30 years, possibly due to less frequent exposure to weekend weather reports. These population groups experienced the greatest sun exposure and highest sunburn prevalence on summer weekends in New Zealand.[11,14]

Our results suggest that the extent and content of sun protection messages in weather bulletins may need refinement, possibly by being more explicit or prominent. The main channel of information for weather forecasts was TVI, a national television station which solely promotes the burn time, whereas TV3, with smaller audiences for weather bulletins, promotes the UVI. Availability of the UVI and the burn time from newspapers and radio stations differs between regions, demonstrating the role of the media in influencing access to, and familiarity with, these messages. Further work is warranted to assess how best to sensitise the public and the media to sun protection information conveyed in weather bulletins. A larger study to evaluate whether people are more receptive to UVI information presented in terms of interpreted risk (level, colour associated with level) or absolute risk (value of the index) would be useful.

Both public and professional opinion in New Zealand favours the use of a sole indicator of ambient UV hazard.[17,20,21] While the burn time is probably more intuitively 'user-friendly', the UVI presents several advantages.[22] First, it is a physical, accurate and well-defined measure of environmental risk that people have to interpret for themselves, like temperature. Second, the UVI is universally applicable, and not based on the physiological response for a sun-sensitive skin type. That awareness of the burn time, but not of the UVI, was found to be dependent on skin type and natural skin colour substantiates the belief that the burn time is of limited population scope. Sun-induced skin damage, such as sunburn,[11] is relatively common among Maori, despite their generally darker complexion. Third, the UVI is the international standard measure recommended[7] and adhered to by many countries.[23] A higher awareness and better dissemination nationwide would assist both New Zealanders travelling abroad and

overseas visitors in adopting adequate sun protection in unfamiliar environments.

The satisfying degree of understanding and acceptance of the UVI makes it a suitable proxy measure of ambient UV level, but limited awareness about it would benefit from an extended presentation in the media in conjunction with the more familiar burn time. This would warrant the widest dissemination (98% of respondents knew of at least one of these measures), provide an easy way of conceptualising the meaning of UVI values, and may help to improve comprehension of the burn time. Implementation of this communication strategy would, however, have to overcome apparent opposition among the more commercially- driven media, notably TV 1.[21] The comparatively low exposure to UVI via radio points to the need for further development of this portable medium, of great potential for conveying locally relevant weather information to people in various settings.[20]

New Zealanders rely more on burn time than UVI, so misinterpretation of the burn time can have larger scale behavioural consequences. Enabling people to suitably protect themselves from sunlight has become increasingly important now that a 12% increase in summer peak UV levels in New Zealand occurred during the 1990's[24] and that, concurrently, sunburn occurrence appears to be on the rise.[14]

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FROM MOLECULE TO MALADY

The future of high speed molecular biology in medicine

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The largest project ever undertaken in biology is nearing completion. The Human Genome Project will determine the DNA sequence of every human chromosome, thereby providing a major reference point for finding the genetic component of human disorders and disease. The Human Genome Project has also helped drive the development of high throughput technologies that explore the various levels of information in a cell. This development is important because although information about mutations and DNA sequence variations may explain the phenotype to some extent, the downstream processing of genetic information is also very important. To understand the downstream processing of genetic information, we need to look further than the DNA sequence to the cell's population of messenger RNA (mRNA) molecules, the transcriptome, and the population of proteins in individual cells, the proteome.

DNA microarrays and gene chips

We are experiencing a technology revolution which allows the simultaneous measurement of the expression levels of thousands of genes. Previously, scientists measured the expression levels of genes one at a time. Now with the DNA microarray and gene chip technologies, a global birds-eye view of the patterns of cellular gene expression is attainable. The background to this technology lies in the mechanism by which genes work. When a gene is functioning, it is transcribed into its corresponding mRNA with the amount of mRNA increasing as the expression levels increase. DNA microarrays simultaneously measure the individual mRNA expression levels of thousands of genes in a sample in a massively parallel manner.

There are, at present, two main microarray technologies. The basis of one of these technologies, DNA microarrays, is a simple glass microscope slide onto which thousands of different genes are robotically spotted at very high density (Figure 1). At the University of Otago, the Otago Genomics Facility has very recently been established to provide local researchers with access to DNA microarray technology. Gene chips, developed by Affymetrix, are similar except that short fragments of genes are synthesised at high density

directly on a prepared surface.[1,2] When mRNA is isolated from a tissue and layered over the glass slide under controlled conditions, individual mRNA molecules form hybrids with their corresponding gene by complementary base pairing (Figure 1). The ability of individual mRNA molecules to find and bind to their corresponding gene on the glass slide is the key to this technology. This selective binding allows many genes to be investigated in one experiment at the same time. The read out from the chip shows which genes are expressed and which are not and also provides information on the level of expression. In a typical DNA microarray procedure, RNA is isolated from two samples eg. normal tissue and diseased tissue. Each RNA sample is then labelled separately with two different fluorescent dyes. The two labelled RNA samples are then combined and hybridised to the arrayed genes on the glass slide (Figure 1). The amount of RNA bound to a gene on the array is measured using fluorescent excitation by lasers with the level of fluorescence emission giving a measure of the level of gene expression. By measuring the fluorescence ratio for both dyes, this provides a comparison between the gene expression levels in the two samples.

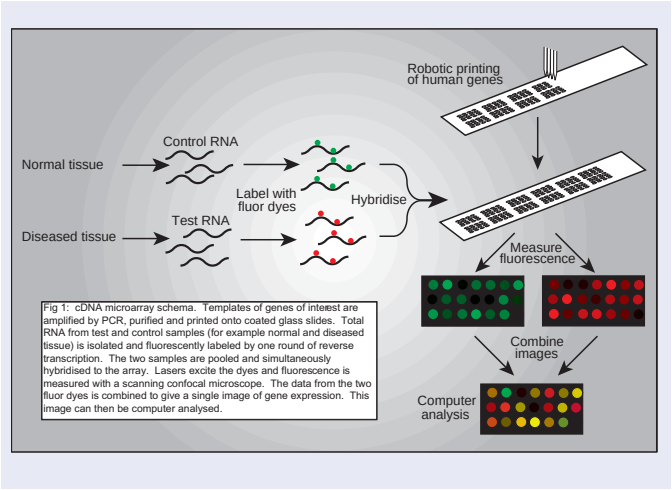

Fig 1: cDNA microarray schema. Templates of genes of interest are amplified by PCR, purified and printed onto coated glass slides. Total RNA from test and control samples (for example normal and diseased tissue) is isolated and fluorescently labeled by one round of reverse transcription. The two samples are pooled and simultaneously hybridised to the array. Lasers excite the dyes and fluorescence is measured with a scanning confocal microscope. The data from the two fluor dyes is combined to give a single image of gene expression. This image can then be computer analysed.

Microarrays produce enormous amounts of data which must be stored, analysed and displayed in a way such that the data can be mined to identify key genes and pathways involved in the disease process. It is this point in the process which is now proving to be the most challenging, and here is where the next technical advances must be made.

Application of DNA micoarrays

Microarrays have a number of applications. For example, gene expression assays with microarrays have already been used to determine gene function, analyse the distribution of gene expression in tissues, and determine gene interactions.[3] By examining how gene expression changes after administration of a drug or toxin, the mechanism of action of that compound can be investigated.[1] Microarray analyses may eventually be used as diagnostic tools, because it seems reasonable to assume that within a healthy population the mRNA from each gene will lie within a normal tissue specific range, much like different elements in a blood sample. Those mRNA species outside these concentrations may provide an indication of disease, predisposition to disease or a treatment outcome.[3]

DNA microarrays have already been used to accurately classify acute leukaemia into lymphoblastic and myeloblastic forms, and to identify two disease subtypes within diffuse large B-cell lymphoma, a form of Non-Hodgkins lymphoma.[4] Lymphoma and leukaemia have been some of the first cancers to be studied by microarray analyses because specimens are easily obtained and purified. In solid tumours, there are a myriad of different cells which have to be separated, making the analysis more complex.[5] This problem of tumour heterogeneity can be circumvented to some degree by use of laser capture microdissection. This technique enables the very fine dissection of different cell types within a tissue sample by circumscribing cells of interest with a laser.

Diseases other than cancer will also benefit from this ability to delineate subtypes. Many patients with common diseases including diabetes, atherosclerosis and neurodegenerative disorders receive the same diagnosis but often have vastly different clinical courses. The clinical heterogeneity of these diseases suggests that different molecular pathways may be an underlying factor. If these molecular pathways could be defined and subtypes identified the behaviour and clinical outcome for a particular patient may be able to be predicted more accurately. Microarrays show great promise in disease diagnosis, but the major test for microarrays will be to determine whether the information they provide can be clinically applied to improve patient management and outcome.

SNPs

Another exciting aspect of genetic research is finding associations between DNA sequence variations and a number of traits and common diseases. The most common DNA sequence variations in the human genome are single nucleotide polymorphisms (SNPs, pronounced Snip), which vary from one person to another by just one single nucleotide. SNPs are estimated to occur approximately once in every one thousand bases.[6] Some SNPs occur within the regulatory elements of genes and affect their levels of expression. Other SNPs are present within the gene itself and can modify the function of the gene in any of several different ways. In many cases, SNPs have no function at all but could be used as markers for different disease susceptibility alleles because of their close physical proximity to a susceptibility gene.[7] The clinical applications of a large scale genome map of SNPs associated with different phenotypic variants would not be limited to determining disease risks alone, but could be used to analyse a variety of patient traits.

Recently, the application of SNP technology to human disease was elegantly demonstrated in a study of duodenal ulcer disease, gastric cancer and *Helicobacter pylori* infection.[8] Two DNA polymorphisms were identified which are associated with an increased risk of progressing to gastric cancer with *H. pylori* infection. One of these polymorphisms is an SNP in the regulatory region of a gene encoding a pro-inflammatory cytokine that influences the environment of the stomach, making it more favourable for *H.pylori* colonisation and eventual progression to gastric cancer. If a screening test could be designed for this SNP, the risk of *H. pylori* infection progressing to cancer could be more easily assessed, and those with an increased risk could receive appropriate monitoring.

The future of high-throughput gene expression and proteomic technologies

Studies of gene expression and gene sequence are valuable, but usually it is protein, and not mRNA that ultimately determines phenotype. Moreover, the level of expression of a gene does not always correspond to the activity of the protein product from that gene in a cell. Proteomics studies

the total protein population of a cell and how this varies under different circumstances. For a number of reasons, high throughput proteomic technology has not yet reached the massive throughput of DNA microarray technology. Nevertheless, proteomics is used routinely in a number of academic laboratories and pharmaceutical companies to identify protein markers associated with common diseases such as respiratory diseases, diabetes, Alzheimer's some cancers and atherosclerosis (for example, see http:www.ogs.com/corporate/press/home.html). It is hoped that markers identified in this way will be used in a clinical setting to act as surrogate markers for toxicity or drug effects, thereby increasing the predictive value of drug trials and shortening the trial periods.

Skilful health professionals have always recognised variation in disease presentation, outcome and response to treatment. Part of the art of medicine is identifying these variations and modifying management accordingly. High throughput science is now being added to this art at a rapid pace, with the goals of identifying the genes and mutations responsible for variations, and finding ways to treat the disease causing variants. Now we can look at the genome, transcriptome and proteome together, rather than separately, to generate a more global view of the state of cells and tissues under different conditions, be it normal, diseased or treated. This greater knowledge base is promising to be of benefit to all.

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MEDICOLEGAL DIARY

Obtaining consent for epidural analgesia for women in labour

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The following scenario is a situation which obstetric anaesthetists face every day: You are an anaesthetist on duty, providing epidural analgesia for women in labour in the delivery suite. A request for epidural pain relief involves a patient who is extremely distressed with pain and anxiety. She has never before had an epidural, and has no prior information about it. You explain the potential complications and write in the patient's notes that these issues have been discussed. Has the anaesthetist obtained a valid consent from the patient?

In order for the patient's consent to be valid, three matters must be satisfied. First, the patient must be competent, or have the legal capacity, to provide consent. Second, the patient must be provided with sufficient information about the procedure. Third, the patient's consent must be voluntary, ie, free from duress.

There is a rebuttable presumption that all patients are competent to consent to or refuse medical treatment.[1] The anaesthetist must, however, consider whether the patient is sufficiently able to understand the nature, purpose, effects and likely consequences of the epidural.[2] The patient may have a diminished competence to consent due to either temporary or permanent factors such as pain, severe fatigue, shock, confusion or drugs. Where the patient does have diminished competence, she retains the right to make an informed choice to the extent appropriate to her level of competence.[3] The anaesthetist must make a reasonable assessment of this. He should consider whether the patient has taken in and retained the treatment information, and weighed up the needs and risks of the procedure.[4]

In order for consent to be valid, the patient must receive information about the epidural that a reasonable person in that patient's position would expect to receive. This includes an explanation of the options available, the expected risks and the side effects.[5] The anaesthetist must consider the particular circumstances of the patient which might make a certain side effect especially significant. Material risks will be those that are inherent in the procedure, and that the patient, if warned, would be likely to consider significant.

The Courts have been reluctant to put a percentage figure on a risk that should be disclosed, although a 10% risk of a stroke from an operation has been held to be clearly significant.[6] There has been learned comment in New Zealand indicating that risks exceeding a 1% probability need to be disclosed.[7] Whilst this may well be the case, it should not be treated as the legal demarcation point. Whilst anaesthetists would be well advised to disclose risks exceeding a 1% probability, less frequent side effects will be material to some patients. Nevertheless, significant neurological deficits directly attributable to an epidural, which have been found to occur in 1 patient out of 13 007,[8] need not ordinarily be disclosed.

Postdural puncture headaches can occur as a complication in approximately 1% of obstetric epidurals,[9] last for a median of eight days,[10] and can be severe enough to restrict ability to care for the baby. In that very few women would not attach significance to a side-effect that would restrict their ability to provide post-natal care for their baby, anaesthetists should discuss the risks of postdural puncture headaches with their patients as part of the consent process. As a general rule, if there is any doubt about the disclosure of a risk, anaesthetists should discuss the risk, remembering that many patients will want to have a statistical probability put on the identified risk.

The third requirement is that consent is obtained voluntarily and freely. Improper pressure, applied either by a member of the clinical team or the patient's personal support team, vitiates consent.

Where the patient is not competent, then a proxy must have been appointed as a welfare guardian or have the power of attorney to act in relation to the patient's care and welfare, in order to consent on the patient's behalf. A member of the patient's family is not automatically a valid proxy. Where the incompetent patient is a minor, the patient's parent(s) will be a valid proxy. Where there is no valid proxy, the anaesthetist can

perform the procedure if it is in the 'best interests' of the patient, provided that reasonable steps have been taken to ascertain the patient's views, or the views of others interested in the welfare of the patient.[11] What is in the 'best interests' of the patient will ultimately be a decision for the anaesthetist.

By far the best way to ascertain the patient's views will be through extensive discussion of potential pain relief as part of the ante-natal care, including any relevant risks. The patient's views should be recorded in her notes in case she becomes temporarily incapable of making a decision. An advance indication in the notes will not, however, remove the need for the anaesthetist to attempt to obtain consent at the time of the epidural.

While there needs to be shared responsibility amongst health professionals involved in ante-natal care for informing patients about epidurals and other pain relief, the responsibility for obtaining consent for an epidural is on the anaesthetist. Anaesthetists must take the time to discuss the procedure with the patient, and to sufficiently acquaint themselves with the patient's particular characteristics so that he or she is able to assess what risks should be disclosed. Wherever possible, consent should be obtained in writing. It is not, however, legally essential to obtain a written consent unless the patient will be under a general anaesthetic, there is a significant risk of adverse consequence, the patient is participating in research, or where the procedure is experimental.[12] Anaesthetists should always make detailed notes of the discussion with the patient in her records.

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3. Code of Health and Disability Services Consumers' Rights, right 7(3).
4. Supra note 2.
5. Code of Health and Disability Services Consumers' Rights, right 6(1).
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HISTORICAL PERSPECTIVE

The attitude of The Medical Association to medical services and the Social Security Act, 1938

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The Medical Association, as the mouthpiece of its members, strongly opposed the introduction of any scheme of social security which included medical services and which had universal coverage of rich and poor alike. It was feared that doctors' incomes would suffer, but there were important ethical and philosophical issues as well.

The Medical Association

The Medical Association in the relevant period was the New Zealand Branch of the British Medical Association (BMA), which was known, to its members, to the public, to the newspapers, to its supporters and its detractors alike, as 'the BMA.' I shall so call it herein despite the professional historians who call it 'the NZBMA'. It could fairly claim to be the mouthpiece of the profession, since its members comprised the vast majority of doctors in practice.

The expressions, 'social security' and 'general medical services,' came later. Earlier terms were 'national medical service' or 'national health insurance, (NHI).

Up to the 1930s, medicine was simple and cheap. There were few synthetic drugs and no expensive investigations. Even so, some members of the community could not afford medical treatment, particularly in the years of the great depression of the early 1930s, but it had long been the custom of the medical profession to treat the indigent without charge and to load the charges of wealthy patients accordingly.

In 1911, the United Kingdom introduced NHI, applying only to lower income groups. A similar scheme was vaguely considered in New Zealand, but World War I delayed serious discussion. In 1920, the BMA set up a special committee to counter what was emotively called "proposed political aggression."[1] The committee reported that: "The question of national medical service is prominent at the present time for various reasons, chief of which is the increased responsibility of the State to undertake the prevention of disease and the promotion of the health of the people."[2]

Thus there was recognition that the nation had moved away from the 'laissez-faire' principle of the nineteenth century that governments should not interfere with the way individual citizens lived their lives. It was recommended that: "A modified form of national service should be at once established for the benefit of poor patients in the cities and larger towns of the Dominion."[2]

In an introduction to that report, the editor of the New Zealand Medical Journal (NZ Med J) , Dr JS (later Sir James) Elliott, wrote: "The profession in New Zealand is opposed to a complete or extensive form of national medical service, but is in favour of a modified service."[2] He meant that any scheme should apply only to the poor and exclude those who could afford to pay for their own medical care.

Nothing further happened through the 1920s, but in 1933 Dr ES Stubbs of Oamaru wrote a paper in the NZ Med J in which he claimed, ignoring the women in medicine: "As the body of men best acquainted with all the facts of the situation, it is our special responsibility as a profession to get for the community the best possible medical service; best not only clinically, but best in organisation, best in efficiency, in ethics and in psychology."[3]

The Hospital Boards Association was interested and sent a report to the BMA. At the meeting at which the report was considered: "the majority of those present… were agreed that some scheme of National Health Insurance was likely to eventuate in the near future."[4] An NHI committee was set up with Professor CE (later Sir Charles) Hercus of Dunedin as convenor. This committee consisted of one representative from each of the fourteen divisions of the BMA, together with nine members of the Wellington divisional executive, the president and the honorary general secretary.[5]

The committee met for the first time on 12 June 1935 in Wellington. Hercus took the chair and suggested that this committee needed to be chaired by a general practitioner (GP). He nominated Dr JPS Jamieson who was unanimously elected.[5] From then on, Jamieson led the profession through lengthy discussions about the future form of medical services.

Jamieson was a Shetland Islander and compromise was not in his nature. As a point of interest, a brother produced the anatomical atlases which have been used by generations of students around the world. Dr SD Rhind, then editor of the NZ Med J, wrote: "The ideals of the profession, which have been developed in response to the urge of humanity in our Western civilisation are now, as they always have been, to maintain health and prevent disease; to cure disease; to alleviate suffering due to disease; and to save life."[6]

In the general election of 1935, the Labour Party swept into office for the first time. Looking back in 1960, Sir Douglas Robb considered in retrospect that the Labour Party found social security "a wonderful horse on which to ride to victory."[7] In his autobiography, Sir Fred Bowerbank wrote of the struggles which followed: "The British Medical Association, headed by Dr James Jamieson, of Nelson, fought what could only be described as a strategic withdrawal."[8] I very much doubt that Jamieson ever thought in those terms.

On the government's side was Dr DG McMillan, member of parliament and GP of Dunedin. During 1937, he toured the country addressing some 60 meetings of doctors, trying in vain to convert them to the universal scheme of health benefits which his party espoused.[9]

The profession stayed, to a surprising degree, united behind Jamieson as its leader. The NHI committee held many well-attended meetings, its members travelling to Wellington by main-trunk express train from Auckland or by ferry from Lyttelton, both overnight journeys. Otago and Southland members had to precede that by an all-day train trip to Lyttelton.

Jamieson told the 1937 annual meeting of the BMA that there was "almost unanimity" in the following statement: "By all means let the State ensure that no necessary medical service shall be unattainable by anyone from reason of lack of ability to pay for it; and by all means let the heavier costs be so spread that no one will be crippled financially by major calamities of sickness, but leave to those who can meet their own costs the responsibility of meeting their needs in their own way to their own satisfaction; and let the State concern itself more particularly in building a healthy, virile race, which cannot be done by running to the doctor and leaning on the State, but by education, disease prevention and encouragement of self-reliance…

"The profession has been bred for centuries with a tradition of charity which to a certain present trend of social thought has become repugnant, but which we have not cast off…The community, we are told, no longer desires our charity, and no longer wishes us to be able to give it…"[10]

The government would not yield on the universal scheme of health benefits which had been a major plank in their election platform. The BMA would not yield on what they saw as essential points in a medical service, which excluded subsidised services for the wealthy. The two ideas were incompatible. As the socialist Dr McCall Smith of Rawene put it: "The health objectives of the sick man and the financial objectives of the doctor are diametrically opposed."[11]

Of course members of the BMA were conscious of their own interests and incomes. Who is not? There were also, however, deeper issues involved, issues of ethics and of the long-standing humanitarian traditions of medicine. As Robb said, speaking to the Auckland division in 1941: "I suppose there is no member of the BMA who has not experienced considerable anxiety in recent years as to his own future and to the future of his profession. In common with many other time-honoured institutions we feel that our work is in the melting pot. We feel we may lose control over the changes that have taken place and seem likely to take place."[12]

The Social Security Act had been passed in 1938 and people were paying social security tax, but there was as yet no medical service under the act. Discussions on that issue continued.

In 1939, Bowerbank, as chairman of council of the BMA, accompanied Jamieson to a meeting with the Prime Minister, Michael J Savage, and Peter Fraser, Minister of Health. Bowerbank recalled that Savage and Jamieson "engaged in a heated argument while the rest of us, including Mr Fraser, looked on…[Savage] then threatened us with a State medical service."[13] It was little use engaging in heated arguments with a government which was in an unassailable position since they had, at the time, a majority of 55 to 25 in the 80-member House.

In 1941, Jamieson proclaimed: "The profession is determined that its traditions of service to the people as individuals and human beings, not as pathological entities, will be preserved in this country. It will not submit to a condition of state helotry."[14]

The government introduced a panel scheme of general medical services, which was regarded by the profession as "a condition of state helotry." So few doctors signed up to join it that the scheme was a failure. A fee-for-service scheme was then proposed. There were further arguments on the size of the fee: the original proposal of five shillings (50c) was increased to seven shillings and sixpence (75c). The amount of that increase, two shillings and sixpence, equalled 30 pence. That led to charges that the doctors were selling their souls for 30 pieces of copper.[15]

The important point, however, was not the size of the government's fee, but the fact that permission was given for the doctor to charge an extra fee at his or her discretion. It was that matter of principle which persuaded the BMA to advise its members to sign up, and the scheme began on 1 November 1941. Traditionally, the fee for a consultation had been half a guinea, ten shillings and sixpence ($1.05), and many doctors imposed an extra charge of three shillings (30c) to bring their fee up to that level.

Doctors carried on their practices as before, apart from the change in paymaster. There was no change in the doctor-patient relationship and GPs found, perhaps to their surprise, that they could still practise ethically and with professional satisfaction, as well as with profit.

Dr JO Mercer, editor of the NZ Med J, summed it up thus: "We have shown a united opposition to menaces and blandishments….There is, however, in the attitude of doctors to legislation which offers no guarantee against the degradation of medical practice, a spiritual value quite apart from other considerations. The brotherhood exemplified by the spirit of the Hippocratic Oath has survived the lapse of time and lives today without diminution or decay in this remote corner of the world."[16]

The last word ought to go to Jamieson: "the Association has striven consistently for the achievement of positive health."[14]

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