

Lymphoedema: prevalence,  
risk factors and management:  
A review of research

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## Contents

List of tables and figures	ii
<b>1 Introduction</b>	<b>1</b>
<b>2 What are the consequences of lymphoedema for women?</b>	<b>3</b>
<b>3 Prevalence of lymphoedema</b>	<b>5</b>
<b>4 Risk factors and the prevention of lymphoedema</b>	<b>14</b>
<b>5 The management of lymphoedema</b>	<b>19</b>
<b>6 Conclusions and recommendations</b>	<b>26</b>
References	28
Appendices	
1 Review of evidence	32

### **Tables**

1	Studies examining lymphoedema in women receiving axillary surgery (either sampling or dissection) and axillary irradiation	10
2	Studies examining lymphoedema in women receiving axillary surgery only	12
3	Studies examining lymphoedema in women receiving axillary irradiation only	13
4	Studies examining demographic and disease risk factors	15
5	Other proposed risk factors for lymphoedema	18
6	Summary of the outcomes for the intervention studies for the treatment of lymphoedema	21

### **Figures**

1	Prevalence of lymphoedema over time	7
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## 1 Introduction

### What is lymphoedema?

Lymphoedema is a swelling of the arm caused by damage to or removal of the lymph vessels or lymph nodes in the armpit. It can occur following surgery to the breast or axilla, from radiotherapy to these regions or from a combination of both. It can also be caused by a recurrence of the breast cancer. Occasionally, lymphoedema can be congenital and it can occur following other conditions such as massive cellulitis.

When blood passes into a limb, such as the arm, there is an exchange of fluids through the capillaries or tiny vessels in the arm. Most of the fluid is then returned to the heart, through the veins. However, some fluid accumulates in the tissues in the arm and this drains back slowly to the veins through the lymphatic system. The lymphatic system is a passive drainage system; the fluid in this system is called lymph and contains a significant amount of protein.

Normally, the lymph nodes filter out foreign material and bacteria from the lymph fluid as they allow it to drain back to the bloodstream near the heart. If the lymph nodes are damaged during treatment, the filter system cannot work as effectively, which leads to reduced ability to deal with infection. The build up of fluid and protein in the arm causes the swelling.

Women may experience lymphoedema as limb swelling, heaviness, pain, pitting of the skin, tightness or hardness in the limb; the skin may feel hotter or drier or inflamed and there may also be reduced mobility in the arm or shoulder.

### Purpose of the report

There is considerable concern among women treated for breast cancer about lymphoedema.<sup>1</sup> There is a view that lymphoedema occurs more commonly than is recognised by health professionals and that appropriate steps to prevent the occurrence of lymphoedema are not always taken.<sup>1</sup> The aims of this report are to:

- review the evidence about the consequences to women of developing lymphoedema;
- review the evidence about the prevalence of lymphoedema among women treated for breast cancer;

- review the evidence about possible risk factors for the development of lymphoedema and to identify any potential strategies for prevention;
- describe the existing management strategies for lymphoedema and evaluate the evidence about their effectiveness ; and
- make recommendations to develop clinical management, research and patient information about lymphoedema.

### **Review of evidence**

This report is based primarily upon a detailed review of the evidence about lymphoedema which was undertaken on behalf of the NHMRC National Breast Cancer Centre by Dr Colette Browning of Thomas and Associates. Copies of this review are available from the NHMRC National Breast Cancer Centre; the method used by Thomas and Associates in undertaking the review is described in detail in the Appendix. It included extensive computer and manual searching and all articles were evaluated against methodological criteria by two independent coders before inclusion in the review. However, the majority of research about lymphoedema identified had considerable methodological problems. Dr Jane Turner provided the review about the consequences to women of a diagnosis of lymphoedema.

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## 2 What are the consequences of lymphoedema for women?

For many women, lymphoedema may be one of a number of arm symptoms which adversely affect quality of life. A recent study assessed 69 women presenting for rehabilitation treatment for lymphoedema, all of whom had undergone surgery and/or radiotherapy and/or chemotherapy, but with no current evidence of active breast cancer.<sup>2</sup> Study instruments included the Brief Symptom Inventory (BSI), the Derogatis Sexual Functioning Inventory (DSFI), the Functional Interference Questionnaire (FIQ), the Social Support Questionnaire (SSQ6), the Interpersonal Support Evaluation List (ISEL - General Population Form), and the Dealing with Illness - Coping Inventory (DWICI).

The onset of lymphoedema was a mean of 3.36 years following surgery. Women with lymphoedema in their dominant hand reported more illness-related or lymphoedema-related distress than women with lymphoedema in their non-dominant hand. However, the severity of lymphoedema proved not to be an important factor in determining psychological distress, social or sexual dysfunction. The significant predictors of difficulties in these areas were the presence of pain, lack of social support, and use of avoidant coping mechanisms. The authors strongly suggest that rather than focusing on the severity of the condition per se, an assessment of pain, as well as social support for coping, may help to identify those in need of consultation by psychiatry and pain specialists.<sup>2</sup>

An earlier study examined 50 women with breast cancer-related arm swelling, matching these with 50 control subjects.<sup>3</sup> Measures used included the Karnofsky Performance Scale, Hospital Anxiety and Depression Scale (HADS), the Psychosocial Adjustment to Illness Scale (PAIS), the Clinical Interview Schedule (CIS), and the Social Stress and Support Inventory. Overall, patients with arm swelling suffered significant impairment in psychosocial adjustment.<sup>3</sup> A smaller study examined the adjustment of 37 women who had breast cancer-related arm swelling.<sup>4</sup> These subjects completed a self-rating questionnaire, beginning the study six months after treatment for swelling. They also completed the Psychosocial Adjustment to Illness Scale (PAIS). Eighty-six percent of patients had psychosocial maladjustment in one or more domains at referral, this persisting in 81%, six months after treatment.

The smallest study was of 25 patients.<sup>5</sup> This study focused more on physical response to treatment, although quality of life was assessed with a Functional Living Index - Cancer (FLIC). Quality of life was generally stable throughout the 12 months, but that specific to lymphoedema declined during the intensive phase of treatment, recovering and surpassing pre-treatment levels during the self-management phase of treatment. The study highlighted the fact that for many women, lymphoedema of the arm made ordinary tasks difficult, putting a patient at a disadvantage, rather than handicapping her.

In summary, lymphoedema can result in major psychosocial problems and difficulties in daily activities for women who suffer from it.

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## 3 Prevalence of lymphoedema

### Methodological issues

Analysis of research about the prevalence of lymphoedema is complicated by the lack of comparability between studies and methodological problems in individual studies. The methodological problems include:

#### Definition and measurement

Three different strategies for defining and measuring lymphoedema have been used:

- **Women's self report**

Self report has been assessed in a variety of ways and no detailed self questionnaire was located. However, responses to the simple item "Have you ever had any swelling of your arm on the side of your breast surgery and radiotherapy?" have been shown to have high agreement with case notes and with physical examination.<sup>6</sup> This simple question would therefore appear to be of considerable use.

The results of this study are also of interest because it is sometimes argued that women over report the occurrence of lymphoedema. In this study, there were no examples of over-reporting and indeed self report appeared to be more accurate than case notes using clinical examination as the gold standard. Similarly, Kissin et al found that 14% of their sample self reported lymphoedema compared with 25% of women who were judged to have lymphoedema based on arm volume differences.<sup>7</sup>

- **Clinical judgement**

Likewise no validated clinical scales for assessing lymphoedema were identified. Some of the studies included in the review used case notes accessed retrospectively. These studies may underestimate the prevalence of lymphoedema since it may not be routinely recorded in a standard manner. Mortimer et al, for example, found that 12% of patients without a clinical record of lymphoedema reported having experienced the problem and were judged by an independent clinician to have lymphoedema.<sup>6</sup> No

direct comparisons of clinical judgement against objective assessment were located.

- **Objective assessment**

The most frequently used objective assessments are comparisons of the volume of the affected limb with the non-affected limb or with its pre-treatment volume. Most studies either measure the arm circumference or the amount of fluid displaced using a water displacement technique. Different cut-off points have been used to categorise lymphoedema and, of course, this will affect the reported prevalence; most usually, a range of 1.5-2.5cm difference in arm circumference at any measurement position and/or an increased fluid displacement of 150-200 ml has been used as the cut-off point. Under normal conditions, there is a difference in fluid displacement depending on handedness that is accounted for in some studies but not others. One study compared the agreement between arm circumference and volume differences and found poor agreement with a correlation coefficient of 0.35.<sup>6</sup> Likewise Kissin and colleagues found poor agreement between the two techniques with volume assessments showing greater agreement with clinical judgement and better sensitivity.<sup>6</sup> Prevalence estimates based on volume assessments are therefore probably more reliable and are probably not comparable with those using circumference measures.

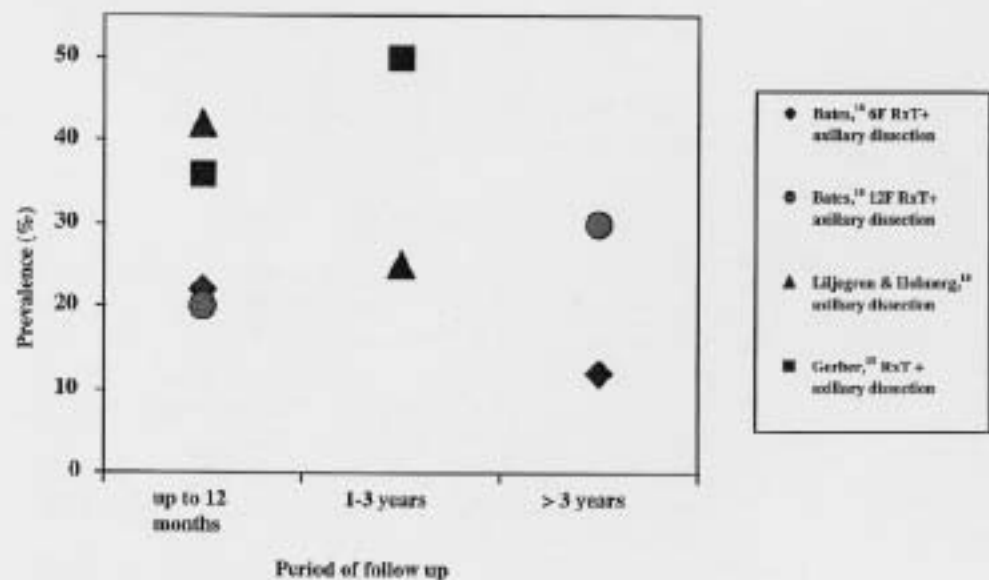
Other research has used a more functional approach to defining lymphoedema by assessing shoulder joint mobility.<sup>9</sup> The relationship between joint mobility and other measures is unclear.

It is evident that the lack of a standardised approach to defining and measuring lymphoedema makes comparisons between estimates of prevalence from different studies very difficult. The International Society for Lymphology has drafted a typology for lymphoedema; this was ratified at a meeting in Sao Paolo in 1995, but is rarely referred to in research.<sup>10</sup>

### **Follow up period**

Although acute oedema and/or lymphoedema may occur immediately following surgery, chronic lymphoedema usually has a delayed onset. Therefore, the timing of follow up may have a critical influence on the observed prevalence of lymphoedema. For example, Figure 1 shows data from several studies demonstrating changes in the prevalence of lymphoedema over time.

**Figure 1**  
Prevalence of lymphoedema overtime



### Sampling

There are a number of problems with the sampling strategy used in most of the studies reviewed. For example,

- **Small subsample size**

Many of the studies reviewed included women who received diverse treatments; when the sample was analysed separately by different treatment combinations the sample size was frequently very small. For example, one study reported an initial sample size of 57 reducing down to 13 in the subgroup receiving axillary dissection and irradiation.<sup>11</sup>

- **Sample frame problems**

Few studies reported their sample frames or consent rates and so assessment of the generalisability of the results is difficult. In some studies, the follow up rate was low raising the possibility of bias. Most often, participants represented a series from a particular clinic and therefore the results may not be generalisable to the population of breast cancer patients.

- **Poor differentiation of subgroups**

Some studies focused only on women with early breast cancer, others studied advanced breast cancer and in some all types of breast cancer were included together. Details of age and other patient characteristics as well as tumour characteristics were often missing.

All of these factors might be expected to influence the reported prevalence rate.

### **Details of treatment of breast cancer**

It appears that axillary sampling, axillary dissection and irradiation may all influence the prevalence of lymphoedema. The dose of radiotherapy and the dose per radiotherapy treatment may be important as is the degree of axillary surgery performed. It is therefore necessary to analyse the research according to the treatment provided. A number of studies did not provide sufficient information about treatment to be included in the review; even among those which are included, there is considerable variation between studies in the details of the therapies delivered.

### **Results of prevalence studies**

The estimates of prevalence of lymphoedema based on the studies included in the review are shown in Tables 1, 2 and 3 separately according to the types of surgery and axillary irradiation given.

#### **Axillary surgery plus axillary irradiation**

Table 1 summarises the studies looking at the prevalence of lymphoedema among women who received axillary surgery and axillary irradiation. The methodologically stronger studies which provided adequate details of treatment and information about the sampling strategies, and which were more likely to be prospective, are shown at the top of Table 1.

It is evident that most studies reported that a substantial proportion of women experienced lymphoedema following a combined treatment of axillary dissection and axillary irradiation. Among the methodologically stronger studies, the estimated prevalence of lymphoedema following full axillary dissection ranged from 12% to 60% of the sample, with most suggesting that more than one third of the women experienced lymphoedema.

Only five studies were located which looked at lymphoedema among women who received axillary sampling followed by axillary irradiation and these tended to be the methodologically weaker studies.<sup>7,9,12-14</sup> The reported rates appear to be lower than those following full dissection and are in the vicinity of 6-32%. The study by Aitken et al reported a rate of 32% in those women who received axillary irradiation, although the oedema was generally minor, and no woman rated herself as inconvenienced by it.<sup>9</sup> Arm oedema was greater in those who had positive nodes compared with those with negative nodes. There was, however, no statistically significant subjective difference by node status or treatment group.<sup>9</sup>

### **Axillary surgery only**

Five studies explored the prevalence of lymphoedema among women receiving surgery to the axilla but no irradiation as shown in Table 2.<sup>7,8,13,15,16</sup> These estimates are more variable; among women receiving axillary sampling only estimates ranged between 0% and 21%. Among women receiving axillary dissection only, estimates of between 0% and 42% were reported, with most studies reporting 20-30% after 12 months.

At first glance, estimates for axillary surgery alone appear to be slightly lower than those for axillary surgery plus irradiation. However, the small number of studies and the lack of direct within-study comparisons make it difficult to draw conclusions.

### **Axillary irradiation only**

The one study examining this question reported low rates (8%) of lymphoedema among women who received axillary irradiation alone as shown in Table 3.<sup>7</sup>

### **Irradiation of the breast**

A recent study<sup>16</sup> has explored the impact of post-operative radiotherapy to the breast following axillary dissection on lymphoedema, among women who had already received axillary dissection. This study was a prospective randomised trial and it found that the addition of radiotherapy to the breast had no impact on the occurrence of lymphoedema.

**Table 1**  
**Studies examining lymphoedema in women receiving axillary surgery (either sampling or dissection) and axillary irradiation**

Study	Measurement and definition of lymphoedema	Follow up	Axillary sampling and axillary radiotherapy	Axillary dissection and axillary radiotherapy
			N	Prevalence
			N	Prevalence
<b>Methodologically stronger studies:</b>				
Basos, 1988 <sup>18</sup>	Clinical rating scale; lymphoedema defined as slight (no alteration in sleeve size), moderate (needs a larger sleeve size) or severe (very large arm causing serious incapacity)	10 yr Prospective	n/a	n/a
			411	6F: 22% 1yr 12% 10 yrs 12F*: 20% 1 yr 30% 10 yrs
Segenstrom et al, 1992 <sup>19</sup>	Objective > 150 ml	17 mths-5yrs	n/a	n/a
Grerber et al, 1992 <sup>15</sup>	Circumference - 2 cm	1 year	n/a	n/a
		2 years Prospective	57	60%
		19 months	38	36%
Golhaer et al, 1988 <sup>20</sup>	Various objective measures	5-10 yrs	79	22%
Olsen et al, 1990 <sup>12</sup>	Objective measure: 2 cm difference in circumference between arms		200	42%
			n/a	n/a

\* F=fractions

Table 1 (continued)

Study	Measurement and definition of lymphoedema	Follow up	Axillary sampling and axillary radiotherapy N Prevalence	Axillary dissection and axillary radiotherapy N Prevalence
<b>Methodologically weaker studies:</b>				
Aitken et al, 1989 <sup>6</sup>	Subjective judgement: lymphoedema defined as degree of arm swelling and impairment Objective measure: arm circumference (difference not defined)	5-6 years	54 32% with radiotherapy	n/a n/a
Kissin et al, 1986 <sup>7</sup>	Clinical judgement: lymphoedema defined from difference in size between operated & non-operated arms as no lymphoedema, moderate or severe retrospective	1-10 years	22 9%	47 38%
Larson et al, 1986 <sup>13</sup>	Clinical judgement: lymphoedema ranked on scale	6 years	165 6%	33 36%
Chiverton & Perry, 1987 <sup>14</sup>	Self report: linear analogue scale	2½ yrs - 5½ yrs retrospective	97 19%	n/a n/a

**Table 2**  
**Studies examining lymphoedema in women receiving axillary surgery only**

Study	Measurement and definition of lymphoedema	Follow up	Axillary Sampling		Axillary Dissection	
			N	Prevalence	N	Prevalence
Larson et al, 1986 <sup>13</sup>	Clinical judgement: lymphoedema ranked on scale	6 years	26	11%	16	0%
Kissin et al, 1986 <sup>7</sup>	Clinical judgement: lymphoedema defined from difference in size between operated & non-operated arms as no lymphoedema, moderate or severe retrospective		17	0%	94	7% axillary clearance
Liljegren & Holmberg, 1997 <sup>16</sup>	Arm circumference	3-36 months Prospective	n/a	n/a	3-12mo 13-36mo >36	181 42% 168 23% 63 16%
Hoe et al, 1992 <sup>8</sup>	Objective measure: volume	1-126 mths	n/a	n/a	118	8%*
Siegel et al, 1990 <sup>21</sup>	Objective measure: 1.5 cm difference in circumference between arms	1 month to 7 years	n/a	n/a	259	2.7%
Gerber et al, 1992 <sup>15</sup>	Circumference - 2cm	1 year 2 years			67 31	43% 58%

\*A small number received irradiation

**Table 3**  
**Studies examining lymphoedema in women receiving axillary irradiation only**

Study	Measurement and definition of lymphoedema	Follow up	N	Prevalence
Kissin et al, 1986 <sup>7</sup>	Clinical judgement: lymphoedema defined from difference in size between operated & non-operated arms as no lymphoedema, moderate or severe	1-10 years	12	8%

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## 4 Risk factors and the prevention of lymphoedema

Several types of risk factors have been suggested as contributing to the development of lymphoedema including demographic and health risks, clinical treatment and other lifestyle factors as follows:

### Demographic and health risks

A number of studies have investigated the role of patient characteristics in predisposing women to the development of lymphoedema. Factors assessed include the age of the patient, whether the patient was overweight and whether the patient had a history of infection or wound complications. Some of these studies also have methodological problems such as including only univariate analyses and small sample sizes.

The studies have not reported consistent relationships between the potential risk factors studied and the occurrence of lymphoedema. Of the four studies which investigated age as a predictor of lymphoedema,<sup>12,19,22-24</sup> three found that older patients were more likely to develop lymphoedema<sup>12,22,23</sup> and the other reported no association between age and lymphoedema.<sup>19</sup>

Both wound complications and increased wound drainage appear to be associated with an increased risk of lymphoedema.

Two studies explored the relationship between obesity and lymphoedema: one found no association<sup>22</sup> and the other that being overweight increased the risk of lymphoedema.<sup>19</sup>

One study found a prior history of infections in the arm to be a significant predictor of lymphoedema.<sup>19</sup> These studies are summarised in Table 4.

**Table 4**  
**Studies examining demographic and disease risk factors**

Risk factor	Study	N	Results
Age	Pezner et al, 1986 <sup>22</sup>	74	Increased risk in women over 60 yrs
	Olsen et al, 1990 <sup>12</sup>	79	Increased risk in older women
	Clarysse, 1993 <sup>23</sup>	390	Increased risk in older women
Wound	Segerstrom et al, 1992 <sup>19</sup>	136	No association
	Pezner et al, 1986 <sup>22</sup>	74	Postoperative wound complications led to increased risk
Obesity	Tadych & Donegan, 1987 <sup>24</sup>	49	Greater wound drainage led to increased risk
	Pezner et al, 1986 <sup>22</sup>	74	Weight not associated
Other factors	Segerstrom et al, 1992 <sup>19</sup>	136	Increased risk in overweight women
	Segerstrom et al, 1992 <sup>19</sup>	136	Previous history of arm infection increases risk Operation on dominant side not associated

### Clinical issues

As previously described, the relationship between axillary surgery and irradiation and the subsequent development of lymphoedema has been examined. Lymphoedema appears to be more common among women who have received axillary dissection and axillary irradiation.

There are currently few guidelines about when axillary dissection and irradiation are necessary.

Lymphoedema can also occur as a result of a recurrence of breast cancer in the lymph nodes in the supraclavicular fossa and axilla. Whilst such relapses are uncommon, lymphoedema, persisting until death, is a symptom in 50% of such relapses.<sup>17</sup>

## Lifestyle factors

Many other 'lifestyle' factors have been proposed as increasing the risk of lymphoedema including those listed in the *NHMRC Clinical Practice Guidelines for the Management of Early Breast Cancer* as shown in Table 5.

Some of these factors are biologically plausible; for example, an affected limb may be subject to an increased risk of infection as the fluid in the limb provides an environment for the growth of bacteria introduced by cuts and burns. Therefore protection from infection appears to be a reasonable precaution. Similarly vaccination might be avoided as poor absorption may render it ineffective.

However, there is no methodologically adequate epidemiological evidence linking any of these factors to increased risk of lymphoedema. It may be that these recommendations cause some women to experience unnecessary restrictions due to a fear of precipitating or exacerbating lymphoedema. Two interesting small studies were found; the first is a case study reporting on the treatment of a woman who received a redback spider bite in her lymphoedematous arm.<sup>25</sup> She required anti-venom to be given into the bite site, which would normally be proscribed. The second study explored the impact of hand surgery on the affected side on lymphoedema among 15 women.<sup>26</sup> None developed any post operative infection or had any worsening of pre-existing lymphoedema or the onset of new arm swelling. In contrast, in a similar group of women who had not undergone previous surgery for breast cancer, some problems with infection were reported. While these studies are small, they illustrate the likely complex relationships among lifestyle factors and the development of lymphoedema and caution against unsubstantiated recommendations.

There is also some information available from self report studies of patients' views about the triggers for their lymphoedema. Unfortunately, women surveyed in these studies had previously been provided with information about 'likely triggers' for lymphoedema. It is therefore very possible that the results are biased with women looking for those factors to which they had previously been alerted. For example, a survey conducted by the Lymphoedema Association of Western Australia (n=214, using data collected over 1992-94) found that 30% of respondents reported aircraft flight as the trigger for lymphoedema, 25% reported infection as the trigger, 24% reported injury as the trigger and 8% reported an insect bite as the trigger.<sup>27</sup> Casley-Smith and Casley-Smith surveyed people with lymphoedema who were asked to identify the trigger for the condition.<sup>28</sup> Of the 490 people with primary and secondary lymphoedema, 5% nominated aircraft flight as the trigger and 2% nominated a long car trip. Of the

remaining 454 respondents, 30% nominated trauma, 20% said that the lymphoedema was present from the date of surgery or radiotherapy, and 40% could not identify the trigger for lymphoedema.<sup>28</sup>

In summary, there are a number of biologically plausible predisposing factors for the development of lymphoedema, such as the extent of axillary surgery, or a history of previous infections. However, the other restrictions frequently nominated as risk factors are not well founded in the literature, and require further research and clinical consideration on an individual basis.

**Table 5**  
**Other proposed risk factors for lymphoedema**

<p>Source: <i>NHMRC Clinical Practice Guidelines for the Management of Early Breast Cancer</i>. Canberra: National Health and Medical Research Council, 1995.</p>	<p>Other preventative and management techniques suggested in the educational material surveyed were:</p>
<ul style="list-style-type: none"> <li>• don't allow anybody to take blood, check your blood pressure, put a drip or give an injection or vaccination in the affected arm;</li> <li>• don't carry anything heavy with the affected arm;</li> <li>• don't garden without gloves or long sleeves;</li> <li>• don't wash the dishes without gloves;</li> <li>• don't let your arm become sunburnt;</li> <li>• avoid cuts, burns and insect bites;</li> <li>• wear loose clothing and loose jewellery;</li> <li>• use skin cream to keep the skin of your arm moist;</li> <li>• keep cool during hot weather;</li> <li>• if you cut your arm or develop an infection in the arm on the same side as your cancer, see your doctor immediately to get antibiotics.</li> </ul>	<ul style="list-style-type: none"> <li>• avoid long aircraft flights;</li> <li>• avoid sports that cause pain;</li> <li>• avoid holding a cigarette in the affected arm;</li> <li>• avoid heavy massage to affected limb;</li> <li>• keep weight under control; and</li> <li>• don't pick cuticles.</li> </ul>

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## 5 The management of lymphoedema

Several approaches to the management of lymphoedema have been evaluated, and the methodology and outcomes of these studies are shown in Table 6.

### Compression techniques

Five studies exploring the impact of compression on lymphoedema were located as summarised in Table 6.<sup>29-33</sup> These studies explored various strategies including: elastic sleeves alone; pneumatic compression; elastic sleeves and electrically stimulated drainage; ultrasound and pneumatic compression; and elastic sleeves, electrically stimulated drainage and pneumatic compression combined. While all of the studies demonstrated a reduction in lymphoedema from the baseline to post treatment measures, none of the studies included a non-intervention group. One study found that a compression sleeve reduced lymphoedema compared with an information and advice only group.<sup>30</sup> However, the sample size was very small (11 and 14 per group) and nearly half of the information/advice group only also showed reduced arm volume, illustrating the importance of appropriate control groups. Given the variation in lymphoedema over time, these studies can only be seen as providing limited support for the value of compression techniques. Simpler elastic compression would appear to be as effective as more invasive measures.

### Complex Physical Therapy (and variants)

Complex Physical Therapy (CPT) and its derivatives is a combination of physical therapies derived from the work of Michael Foldi and his colleagues. The aim of the therapy is to remove excess plasma proteins from the tissue. A typical treatment involves one hour, five to six days per week over 4 weeks; however, this can be very variable depending on the severity of the lymphoedema and the therapist's approach.

CPT involves four components:

- 1 skin care to cure and prevent infection;
- 2 massage (manual lymph drainage) to remove protein and excess fluid by opening collateral lymphatics to increase drainage.

Massage is light and in the direction of normal flow. The aim is to enlarge the size and capacity of collateral lymphatics;

- 3 compression bandages to increase tissue pressure and lymph flow. A compression elastic garment is prescribed at the end of treatment; and,
- 4 exercises, which are performed while wearing the bandages, to promote muscle and joint pumping.

Five studies investigating the effectiveness of CPT or variants in reducing lymphoedema were located as shown in Table 7.<sup>5,34-37</sup> All studies showed a pre-post treatment effect, and many reported changes were quite substantial. However, none of the studies included a control group and therefore the true magnitude of the treatment effect is unclear.

### Surgical techniques

Two studies investigating the impact of surgical techniques were located.<sup>39,40</sup> Both studies showed an improvement following treatment among women with lymphoedema that had been unresponsive to other therapies. The surgical techniques evaluated were microsurgical lymphatic venous anastomoses and lymphatic grafting as shown in Table 6. The results achieved appeared to be substantial, although not all women benefited and the side-effects of surgery were not reported. However, the absence of a control group in either of these studies raises concerns about the extent to which these improvements may have been observed in the absence of any treatment.

### Drug therapy

The main drug therapy used to treat lymphoedema has been oral benzopyrones such as *coumarin*. Benzopyrones are thought to increase proteolysis by macrophages, thereby removing excess protein and excess fluid from the affected limb.

There is some evidence from small randomised, double-blind cross-over trials that benzopyrones can be effective in reducing lymphoedema to some extent. However, these drugs have been withdrawn from use in Australia due to their significant toxicity to the liver: between July 1993 and May 1995 there were 10 reports of suspected adverse reactions related to the oral use of coumarin.<sup>40</sup> However, powder and creams containing *coumarin* are still available.<sup>41</sup> There are other forms of benzopyrones such as *flavonoids* (specifically rutosides) available which do not contain the *coumarin* which is believed to cause the liver function problems. (N. Piller, personal communication, December 1997.)

**Table 6**  
**Summary of the outcomes for the intervention studies for the treatment of lymphoedema**

Study	N	Methodology	Outcome
<b>Compression techniques</b>			
Lerner & Requena, 1986 <sup>29</sup>	150	Pre-post design Objective measurement: multiple circumference Treatment: pneumatic compression	80% showed a reduction in arm circumference.
Hornsby, 1995 <sup>30</sup>	25	Randomised trial (no control) - comparing information alone with information plus compression sleeve Objective measurement: volume	11 of the 14 women using compression sleeve showed a reduction in arm volume. In the control group, 5 of the 11 women showed a reduction in volume.
Bertelli et al, 1992 <sup>31</sup>	107	Randomised trial (no control) Objective measurement: circumference Group A wore an elastic sleeve six hours per day for 6 months and Group B also received electrically stimulated lymphatic drainage (ESD) treatment	The summed arm circumference difference reduced significantly after 2 months in both groups and the reduction was maintained at six months. However, there was no difference in arm circumference reduction between the two groups. At 6 months, 48% of Group A and 41% of Group B had achieved a 25% reduction in arm circumference relative to the unaffected arm.

Table 6 (continued)

Study	N	Methodology	Outcome
Bertelli et al, 1991 <sup>32</sup>	74	Randomised trial (no control) Objective measurement: circumference Treatment: elastic sleeve, ESD and pneumatic compression	At 6 months the mean summed circumference difference score was 17.2 cm which was significantly different from the mean at commencement. Pneumatic compression and electrically stimulated drainage did not add to the effect of the treatment by the elastic sleeve alone. About one third of women showed at least a 25% reduction in circumference. About 4% of the sample showed an increase of more than 25% in circumference.
Balzarini et al, 1993 <sup>33</sup>	96	Randomised trial Objective measurement: circumference Treatment: ultrasound (31) & mechanical pressure therapy (65)	There was no significant reduction in arm size at 12 months in either group. The use of an elastic sleeve did not add to the small reductions obtained in either group.
<b>Complex physical therapy</b>			
Boris et al, 1994 <sup>34</sup>	16	pre-post design Objective measurement: arm circumference	Reduction of excess volume of 73%

Table 6 (continued)

Study	N	Methodology	Outcome
Mirolo et al, 1995 <sup>5</sup>	25	Pre-post design Objective measurement: volume difference calculated from circumference measurements Treatment: complex physical therapy and pneumatic compression	40% decrease in excess volume immediately post treatment
Bunce et al, 1994 <sup>15</sup>	25	Pre-post design Objective measurement: volume difference calculated from circumference measurements Treatment: complex physical therapy and pneumatic compression	40% decrease in excess volume following treatment; 50% decrease at 6 months and 12 months
Carroll & Rose, 1992 <sup>36</sup>	22	Pre-post design Objective measurement: volume difference calculated from circumference measurements	45% decrease in excess arm volume significant decrease in pain symptoms and intensity and a significant decrease in arm of 45%.

Table 6 (continued)

Study	N	Methodology	Outcome
Casley-Smith & Casley-Smith, 1992 <sup>27</sup>	78	Pre-post design Objective measurement: volume difference calculated from circumference measurements, water displacement, tissue softness, skin temperature	Grade 1 lymphoedema changed from 121% to 107% of the unaffected arm (ie a 67% reduction in excess volume). Grade 2 lymphoedema changed from 153% to 123% of the unaffected arm (ie a 57% reduction in excess volume).
<b>Surgical techniques</b>			
Baumcister & Stoda, 1990 <sup>28</sup>	36	Pre-post design Objective measurement: volume difference calculated from circumference measurements, lymphoscintigraphy Treatment: lymphatic grafting	The treated arm reduced by 23% at 2 weeks; 25.5% at 2 years and 32.8% at 3 years. Lymphatic scintiscans indicated that the transport index changed from 33 to 23 over 16 months indicating an improvement of about 30%.
Filippetti et al, 1994 <sup>29</sup>	36	Pre-post design Objective measurement: circumference measurements, ultrasound, lymphoscintigraphy, tomography Treatment: microsurgical lymphatic venous anastomoses (LVA) and exercise plus elastic sleeve & low pressure compression therapy	Results were classified according to poor, fair or good. Seventy-four percent of patients were classified as good or fair at 6 months and 59% patients were classified as good or fair at 12 months.

Table 6 (continued)

Study	N	Methodology	Outcome
<b>Drug therapy</b>			
Piller, Morgan, Casley-Smith, 1985 <sup>42</sup>	26	Randomised double-blind cross over trial of a benzopyrone Objective measurement: arm volume	Drug reduced volume of limb, skin temperature, and increased wellbeing
Casley-Smith, Morgan & Piller, 1993 <sup>43</sup>	31	Randomised double-blind placebo-controlled trial of a benzopyrone	Lymphoedema worse in the control group; decreased from 46% to 26% above normal in control group

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## 6 Conclusions and recommendations

Based on the evidence reviewed for this report, the following recommendations can be made:

### 1 There is an urgent need for further research about lymphoedema

There has been little research into the prevalence, prevention or management of lymphoedema. The little research that does exist is often limited by major methodological problems. There are several steps that should be taken to improve understanding in this area:

- Agreement should be reached about a standardised approach and/or measurement tool for defining and measuring lymphoedema;
- Using this measurement tool, a large-scale study of the prevalence of lymphoedema should be undertaken based on a representative sample of women identified through a cancer registry or other non-clinic list. It should include sufficient numbers of women and sufficient information about treatment modalities to allow categorisation of women into subgroups of sufficient size to permit appropriate comparisons;
- Large-scale studies, possibly using a cohort or case control design, should be undertaken to identify life-style factors that may be associated with the aggravation of lymphoedema; and
- Randomised controlled trials of the effectiveness of the commonly recommended strategies for managing lymphoedema should be undertaken.

### 2 Guidelines about the clinical indicators for axillary surgery and irradiation should be developed

The prevalence of lymphoedema among women receiving axillary dissection and axillary irradiation ranged from 12% to 60% of the sample, with most studies suggesting that more than one third of women in this group would develop lymphoedema. Given the distress and impairment experienced by women who develop lymphoedema, the use of axillary dissection and irradiation should be carefully considered. There is a need for recommendations about the use of these techniques. Women should be provided with information about the possibility of developing lymphoedema prior to axillary surgery or irradiation.

**3 Patient information materials about lymphoedema should indicate the current lack of information about risk factors**

There is little evidence to support current recommendations about the prevention of lymphoedema. Patient information resources should clearly indicate that, whilst these factors are biologically plausible, their role is currently not confirmed by evidence.

**4 As lymphoedema is a significant contributor to psychosocial distress, strategies for early detection should be developed**

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## Appendix 1

### Review of evidence

A detailed review of the evidence about lymphoedema was undertaken on behalf of the NHMRC National Breast Cancer Centre by Dr Colette Browning, Thomas and Associates. Copies of this review are available from the NHMRC National Breast Cancer Centre; the method used by Thomas and Associates in undertaking the review is as follows:

### Method of review

An initial search of MEDLINE for articles published in the period 1985 to 1996 was conducted via CD-ROM. This search was broad using the keyword lymphoedema and, in the first instance, only animal studies and non-English language articles were excluded. A joint manual search of the abstracts of these articles by two of the investigators was then conducted. Additional references were retrieved as a result of a survey of the references of each article and through consultations. Unpublished and in press research was sought from key researchers in the area. The contents pages of key journals in the area were also manually searched for the period 1986-1996.

### Inclusion/exclusion criteria

All articles were independently reviewed by two members of the three-person research consultant team on a randomised basis. Where disagreement occurred, the third member of the team decided the status of the article. Listed below are the inclusion and exclusion criteria for the literature included in this review.

Articles were eligible for inclusion if:

- Language: article available in English language
- Sample size: greater or equal to 20 participants
- Content: Primarily lymphoedema as a complication of breast cancer treatment. If sample includes other patients then at least 20 need to be breast cancer patients and these patients' data need to be reported separately.
- Participant characteristics needed to be specified including type of treatment for breast cancer.

The following types of articles were excluded:

- Articles using data already published
- Articles about physiological mechanisms of lymphoedema
- Review articles
- Articles discussing measurement techniques only
- Articles where the data were not interpretable (insufficient details about measurement techniques or breast cancer patients could not be assessed separately).