This publication was rescinded by National Health and Medical Research Council on 08/3/2006 and is available on the Internet ONLY for historical purposes.

**Important Notice**
This notice is not to be erased and must be included on any printed version of this publication.

- This publication was rescinded by the National Health and Medical Research Council on 08/3/2006. The National Health and Medical Research Council has made this publication available on its Internet Archives site as a service to the public for historical and research purposes ONLY.

- Rescinded publications are publications that no longer represent the Council’s position on the matters contained therein. This means that the Council no longer endorses, supports or approves these rescinded publications.

- The National Health and Medical Research Council gives no assurance as to the accuracy or relevance of any of the information contained in this rescinded publication. The National Health and Medical Research Council assumes no legal liability or responsibility for errors or omissions contained within this rescinded publication for any loss or damage incurred as a result of reliance on this publication.

- Every user of this rescinded publication acknowledges that the information contained in it may not be accurate, complete or of relevance to the user’s purposes. The user undertakes the responsibility for assessing the accuracy, completeness and relevance of the contents of this rescinded publication, including seeking independent verification of information sought to be relied upon for the user’s purposes.

- Every user of this rescinded publication is responsible for ensuring that each printed version contains this disclaimer notice, including the date of rescission and the date of downloading the archived Internet version.
THE MANAGEMENT OF Uncomplicated Lower Urinary Tract Symptoms in Men

February 2000

NHMRC
National Health and Medical Research Council
Clinical Practice Guidelines

The management of uncomplicated lower urinary tract symptoms in men

February 2000

National Health and Medical Research Council

NHMRC
The strategic intent of the NHMRC is to work with others for the health of all Australians, by promoting informed debate on ethics and policy, providing knowledge-based advice, fostering a high quality and internationally recognised research base, and applying research rigour to health issues.

First published 1996
reprinted with additions May 2000

NHMRC documents are prepared by panels of experts drawn from appropriate Australian academic, professional, community and government organisations. NHMRC is grateful to these people for the excellent work they do on its behalf. This work is usually performed on an honorary basis and in addition to their usual work commitments.

This document is sold through AusInfo Government Info Bookshops at a price which covers the cost of printing and distribution only. For publication purchases please contact AusInfo on their toll-free number 132 447, or through their internet address:

Contents

Summary............................................................................................................................... ix

Objective............................................................................................................................. ix
Options ................................................................................................................................. ix
Outcome............................................................................................................................... ix
Evidence............................................................................................................................... ix
Values ................................................................................................................................. x
Anticipated benefits........................................................................................................... x
Sponsors............................................................................................................................... x
Guidelines........................................................................................................................... xii

1 General aspects of these guidelines................................................................. 1

1.1 Their purpose........................................................................................................ 1
1.2 Definition of LUTS .............................................................................................. 2
1.3 Scope of the guidelines.......................................................................................... 4
1.4 Data evaluation........................................................................................................ 6
   1.4.1 Outcome measures ......................................................................................... 7
   1.4.2 Rationale ......................................................................................................... 8
   1.4.3 Levels of evidence.......................................................................................... 10
1.5 Information for consumers and general practitioners ....................................... 12

2 The spectrum of LUTS.............................................................................................. 15

2.1 What is uncomplicated LUTS?............................................................................ 15
2.2 Reason for consulting a doctor............................................................................ 15
2.3 Symptoms of uncomplicated LUTS..................................................................... 15
2.4 Conditions not covered by these guidelines....................................................... 18
2.5 Natural history of untreated LUTS...................................................................... 19
2.6 Morbidity and mortality of LUTS........................................................................ 20
2.7 Medical conditions that may increase the severity of LUTS................................ 21

3 Causes of LUTS........................................................................................................... 25

3.1 What causes LUTS?.............................................................................................. 25
3.2 Benign prostatic hyperplasia................................................................................ 26
3.3 Detrusor hyperactivity......................................................................................... 27
9 Conservative management ................................................... 71
  9.1 Reassurance and advice .............................................. 71
    9.1.1 Natural history of LUTS ................................ 71
    9.1.2 Quality and quantity-of-life issues ................. 72
    9.1.3 The need for review ....................................... 72
    9.1.4 Reassurance as definitive management ............... 73
  9.2 Lifestyle modification ................................................ 73
  9.3 Bladder training .......................................................... 74

10 Pharmacological management ............................................. 77
  10.1 Introduction ................................................................ 77
  10.2 Alpha-adrenergic blocking agents .............................. 78
    10.2.1 Introduction .................................................... 78
    10.2.2 Terazosin ........................................................ 79
    10.2.3 Prazosin .......................................................... 83
  10.3 Alpha-reductase inhibitor — finasteride .................... 85
  10.4 Anticholinergic medication ........................................ 89
    10.4.1 Propantheline bromide ................................... 91
    10.4.2 Oxybutynin chloride ....................................... 92
    10.4.3 Tricyclic antidepressant agents ...................... 93
  10.5 Phytotherapy ............................................................... 94
    10.5.1 *Serenoa repens* ............................................... 95
    10.5.2 Certinin ........................................................... 95
    10.5.3 *Pygeum africanum* ......................................... 96
    10.5.4 Beta-sitosterol ................................................ 96
    10.5.5 Toxicity of phytotherapeutic agents............... 96

11 Standard surgical intervention ............................................. 99
  11.1 Introduction ................................................................ 99
  11.2 Assessing surgical data ............................................. 100
  11.3 Indications for surgery ............................................. 101
  11.4 Transurethral resection of the prostate ..................... 102
  11.5 Transurethral incision of the prostate ....................... 104
  11.6 Open prostatectomy .................................................. 106
  11.7 Complications of surgery ........................................ 107
  11.8 Mortality rates following surgery ............................ 111
  11.9 Selection of surgical procedure ............................... 112
### 12 Alternative forms of treatment

**12.1 Introduction** .............................................................. 117

**12.2 Laser prostatectomy** .................................................. 118  
12.2.1 Morbidity ..................................................... 119  
12.2.2 Transurethral ultrasound guided laser prostatectomy ....................... 120  
12.2.3 Visual or endoscopic laser assisted prostatectomy ....................... 121  
12.2.4 Transurethral evaporation of the prostate .............................................. 123  
12.2.5 Transurethral balloon laser thermotherapy .............................................. 124  

**12.3 Microwaves** .............................................................. 124  
12.3.1 Transrectal or transurethral hyperthermia ................................................ 124  
12.3.2 Transurethral microwave thermotherapy .............................................. 125  

**12.4 Transurethral vaporisation of prostate** .............................................. 127  

**12.5 Transurethral needle ablation** .............................................. 128  

**12.6 High intensity focused ultrasound** .............................................. 129  

**12.7 Prostatic stents** .......................................................... 129  

**12.8 Balloon dilatation** ..................................................... 130  

**12.9 Summary of alternative treatments** .............................................. 132

### 13 Economic aspects

**13.1 Introduction** .............................................................. 133

**13.2 Unit costs of therapy** .................................................. 133  
13.2.1 Transurethral resection of the prostate .............................................. 133  
13.2.2 Open prostatectomy .................................................. 134  
13.2.3 Transurethral incision of the prostate .............................................. 135  
13.2.4 Pharmacotherapy .................................................. 136  

**13.3 Economic burden of illness** .............................................. 136  

**13.4 Economic evaluations of treatment options** .............................................. 137  

**13.5 Potential economic impact of guidelines** .............................................. 140
14 Where to from here? ................................................................. 151
  14.1 Guideline dissemination and implementation ........ 151
  14.2 Research ................................................................. 155

Appendixes ......................................................................................... 157
  A Working party terms of reference and membership....... 159
  B The guideline development process ............................. 161
  C American Urological Association seven-point
    symptom score ............................................................. 173
  D Voiding diary .................................................................... 175

Abbreviations ..................................................................................... 177

Glossary ............................................................................................. 179

References .......................................................................................... 189

Tables

Table 1 Probability of good symptomatic outcomes of
  surgery for men diagnosed by preoperative pressure
  flow testing as obstructed or unobstructed ....................... 55

Table 2 Acceptable studies of the association between
  prostate cancer and lower urinary tract symptoms in
  men (and proportion of cancers among men with and
  without lower urinary tract symptoms) ....................... 59

Table 3 Complication rates following surgical management ...... 108

Table 4 Complication rates following surgery ....................... 145

Table 5 Unit cost estimates for treatment options ................. 147

Table 6 Estimated health care costs of uncomplicated LUTS
  in Australia, 1994–95 ....................................................... 148
While it is considered that the guidelines represent the best advice regarding the evaluation and management of men with uncomplicated LUTS based on current evidence, they cannot be considered as definitive. Thus they should be used as they were intended — to provide a guide to management based on the best available evidence. It remains the prerogative of the man or his practitioner to modify the recommendations according to the specific circumstances of the case.
Summary

Consistent with international trends, this Summary is presented as a structured abstract (Hayward et al 1993).

Objective

The guidelines were developed to assist men, general practitioners and urologists to make decisions about the clinical management of uncomplicated lower urinary tract symptoms.

Options

Two broad groups of investigations were considered including those which have traditionally been performed to exclude the presence of serious disease and those used to predict the outcome of intervention. Three major types of treatment were also reviewed (reassurance, pharmacological intervention and surgery).

Outcome

As uncomplicated lower urinary tract symptoms rarely result in a serious health threat, the main outcome measure considered by the working party was a man's perception of the degree of ‘bother’ caused by his urinary symptoms.

Evidence

All evidence published subsequent to the publication of the Agency for Health Care Policy and Research (AHCPR) guidelines (McConnell et al 1994) was retrieved and studies were summarised in a review and in tabular form by a technical consultant (Jackson 1996). Generally, all studies were considered except for small case-series and those with high attrition rates. Technical reports about investigations and economic aspects of management, as required by NHMRC’s Guidelines
for the Development and Implementation of Clinical Practice Guidelines were commissioned.

Values

Where evidence for a clinically important effect on patient outcome was insufficient, the working party opted for a conservative approach, reducing conventional test-ordering and early intervention. There were no dissenting views by working party members of the recommendations made.

Anticipated benefits

These guidelines recommend fewer investigations and greater caution before intervention than previous guidelines. The implementation of the guidelines in clinical practice should reduce community concern about a common condition which is rarely life-threatening; reduce anxiety about a perceived association between uncomplicated urinary symptoms and early prostate cancer; reduce test-ordering without benefit for the patient in general practice; increase consideration of conservative approaches to clinical management; and reduce unnecessary surgery.

Sponsors

The NHMRC funded the preparation of these guidelines and the Commonwealth Department of Health and Family Services funded baseline studies. Members of the working party have no financial conflict of interest in the recommendations of the guideline.
Guidelines

The following tables set out the guidelines as determined by the working party and indicate the level of evidence on which the guidelines are based (see page 10). Abbreviations used can be found at page 177 and a Glossary of terms can be found at page 179.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical assessment of symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>The man's perception of the degree of bother he suffers because of his LUTS is the most important variable which needs to be determined. It is recommended that practitioners should adopt a score for the degree of bother and use this for the initial and subsequent assessment of the severity of the man's symptoms.</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Investigations to assess LUTS</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Urine analysis</strong></td>
<td>IV-2</td>
</tr>
<tr>
<td>Every man with urinary symptoms should have his urine tested.</td>
<td></td>
</tr>
<tr>
<td><strong>Voiding diary</strong></td>
<td>IV-2</td>
</tr>
<tr>
<td>Keeping a voiding diary is a useful tool to assist in the management of a man who thinks that his symptoms cause sufficient bother for him to consider management options for his LUTS.</td>
<td></td>
</tr>
<tr>
<td><strong>Serum creatinine testing</strong></td>
<td>N/A</td>
</tr>
<tr>
<td>The routine estimation of serum creatinine at the time of the initial presentation of a man with uncomplicated LUTS is not recommended. A decision regarding this testing should be determined by the importance the man and his practitioner place on a 1.8% prevalence of detecting a relevant abnormal test finding.</td>
<td></td>
</tr>
<tr>
<td>Guideline</td>
<td>Level of evidence</td>
</tr>
<tr>
<td>---------------------------------------------------------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Clinical assessment of symptoms (contd)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Ultrasound imaging</strong></td>
<td>N/A</td>
</tr>
<tr>
<td>The routine ultrasound imaging of the urinary tract at the time of the</td>
<td></td>
</tr>
<tr>
<td>initial presentation of a man with uncomplicated LUTS is not recommended.</td>
<td></td>
</tr>
<tr>
<td>A decision regarding this testing should be determined by the</td>
<td></td>
</tr>
<tr>
<td>importance the man and his practitioner place on a 0.8–2.5% prevalence</td>
<td></td>
</tr>
<tr>
<td>of detecting a relevant abnormal test finding.</td>
<td></td>
</tr>
<tr>
<td><strong>Cystourethroscopy</strong></td>
<td>N/A</td>
</tr>
<tr>
<td>Cystourethroscopy should not form part of the initial evaluation of a</td>
<td></td>
</tr>
<tr>
<td>man presenting with uncomplicated LUTS. It is an essential part of</td>
<td></td>
</tr>
<tr>
<td>surgical procedures.</td>
<td></td>
</tr>
<tr>
<td><strong>Post-void residual urine volume</strong></td>
<td>II</td>
</tr>
<tr>
<td>The assessment of post-void residual urine volume should not form part</td>
<td></td>
</tr>
<tr>
<td>of the routine assessment of men presenting with, or considering</td>
<td></td>
</tr>
<tr>
<td>treatment for, uncomplicated LUTS.</td>
<td></td>
</tr>
<tr>
<td><strong>Uroflowmetry</strong></td>
<td>II</td>
</tr>
<tr>
<td>The routine measurement of peak flow rate in the evaluation of the</td>
<td></td>
</tr>
<tr>
<td>patient is not recommended.</td>
<td></td>
</tr>
<tr>
<td><strong>Filling cystometry (cystometrography)</strong></td>
<td>IV-I</td>
</tr>
<tr>
<td>The use of filling cystometrography is not recommended as an independent</td>
<td></td>
</tr>
<tr>
<td>measure for the evaluation of uncomplicated LUTS.</td>
<td></td>
</tr>
<tr>
<td>Guideline</td>
<td>Level of evidence</td>
</tr>
<tr>
<td>--------------------------------------------------------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Clinical assessment of symptoms (contd)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Pressure flow studies</strong></td>
<td>III-2</td>
</tr>
<tr>
<td>Based on the studies available and the absence of any other compelling evidence for the benefit of pressure flow studies in predicting clinically significant outcomes of treatment, it is recommended that pressure flow studies should not form part of the routine evaluation of a man before pharmacological or surgical intervention. Where it is thought that a man may still find the difference in predicted outcomes for surgery helpful in assisting him to make a management decision, such a study could be offered to him for this purpose.</td>
<td></td>
</tr>
<tr>
<td><strong>Concerns about prostate cancer</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Prostate cancer</strong></td>
<td>IV-I</td>
</tr>
<tr>
<td>Men with uncomplicated LUTS should be advised that current data suggest that they have little or no increased risk of prostate cancer.</td>
<td></td>
</tr>
<tr>
<td><strong>PSA testing</strong></td>
<td>IV-2</td>
</tr>
<tr>
<td>It is not recommended to estimate serum PSA as part of the normal evaluation of a man with LUTS. Serum PSA testing should only be done after a man with LUTS has been fully informed of the consequences of such testing. It is important that he understand that there is no scientific evidence of a relationship between LUTS and presence of early prostate cancer.</td>
<td></td>
</tr>
</tbody>
</table>
## Management options

### Selection of treatment

Men whose LUTS cause a moderate degree of bother requiring intervention may, in the first instance, consider a trial of pharmacological intervention.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men whose LUTS cause a moderate degree of bother requiring intervention may, in the first instance, consider a trial of pharmacological intervention.</td>
<td>IV-2</td>
</tr>
</tbody>
</table>

### Conservative management

Reassurance and advice regarding conservative measures to minimise the degree of bother is a viable option for all men with uncomplicated LUTS. It is most appropriate for those men with a mild degree of bother or only anxious about their symptoms.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reassurance and advice regarding conservative measures to minimise the degree of bother is a viable option for all men with uncomplicated LUTS. It is most appropriate for those men with a mild degree of bother or only anxious about their symptoms.</td>
<td>IV-2</td>
</tr>
</tbody>
</table>

### Pharmacological management

#### Terazosin

Terazosin has been shown to be a moderately effective agent in reducing the degree of bother caused by uncomplicated LUTS.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terazosin has been shown to be a moderately effective agent in reducing the degree of bother caused by uncomplicated LUTS.</td>
<td>II</td>
</tr>
</tbody>
</table>

#### Prazosin

Before starting a course of prazosin medication, men should be fully informed of the lack of evidence supporting the efficacy of this drug.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prazosin</td>
<td>IV-2</td>
</tr>
</tbody>
</table>

#### Finasteride

Finasteride only has a statistically significant beneficial impact on the severity of LUTS if the prostate volume is greater than 40 mL. It is likely that a clinically perceptible benefit will only occur if the prostate volume is greater than 60 mL.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finasteride</td>
<td>I</td>
</tr>
</tbody>
</table>

# Management of LUTS
<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmacological management (contd)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Anticholinergic agents</strong></td>
<td>IV-3</td>
</tr>
<tr>
<td>Men with predominantly irritative symptoms, and who request pharmacological intervention, can be offered a trial of an anticholinergic agent. Such men should be informed that there is no definitive evidence that the treatment will be of benefit.</td>
<td></td>
</tr>
<tr>
<td><strong>Phytotherapeutic agents</strong></td>
<td>IV-2</td>
</tr>
<tr>
<td>The use of phytotherapeutic agents is not recommended because of the absence of long-term randomly controlled trials and the absence of reliable toxicological and safety data.</td>
<td></td>
</tr>
<tr>
<td><strong>Standard surgical intervention</strong></td>
<td>II</td>
</tr>
<tr>
<td><strong>Indications for surgical intervention</strong></td>
<td></td>
</tr>
<tr>
<td>Surgery should only be considered for:</td>
<td></td>
</tr>
<tr>
<td>• men severely bothered by their symptoms;</td>
<td></td>
</tr>
<tr>
<td>• men who are moderately bothered but do not improve after pharmacological management; or</td>
<td></td>
</tr>
<tr>
<td>• men who do not wish drug therapy and yet request active intervention for their LUTS.</td>
<td></td>
</tr>
</tbody>
</table>
### Standard surgical intervention (contd)

#### Selection of surgical procedures

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on currently available evidence, TUIP is an appropriate operative procedure for men with small glands (&lt;30 grams estimated weight).</td>
<td>II</td>
</tr>
<tr>
<td>For men with glands estimated to be larger than 30 grams, or those with a middle lobe component, the current evidence favours the performance of a TURP. While it may be appropriate to offer such men a TUIP, they should be informed that there are no reports of data comparing outcomes of TUIP to TURP in such conditions.</td>
<td>II</td>
</tr>
<tr>
<td>Open prostatectomy should be considered the procedure of choice where operative time for TURP is expected to exceed 75 minutes and where the gland is estimated to be larger than 100–150 grams.</td>
<td>III-2</td>
</tr>
</tbody>
</table>

#### Alternative forms of treatment

**Transurethral ultrasound guided laser prostatectomy**

TULIP is not recommended at present because of the lack of long-term randomised controlled trials. IV-2
**Guideline**

<table>
<thead>
<tr>
<th>Alternative forms of treatment (contd)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Laser assisted prostatectomy</strong></td>
</tr>
<tr>
<td>There is now sufficient data to permit the use of VLAP in a clinical rather than experimental setting. It is important that men considering this form of therapy clearly understand:</td>
</tr>
<tr>
<td>• the absence of data regarding long-term efficacy (beyond 12 months);</td>
</tr>
<tr>
<td>• an undefined but significant incidence of early morbidity; and</td>
</tr>
<tr>
<td>• the probability that this therapy offers similar results to TURP and, where the gland is small, TUIP, the latter also having a low morbidity profile.</td>
</tr>
<tr>
<td><strong>Level of evidence</strong></td>
</tr>
<tr>
<td>II</td>
</tr>
</tbody>
</table>

| **Transurethral evaporation of the prostate** |
| At present the use of TUEP is not recommended because of the absence of data from long-term randomised controlled trials. |
| **Level of evidence**                      |
| IV-3                                    |

| **Transurethral balloon laser thermotherapy** |
| TUBAL-T is not recommended at present because of the absence of data from long-term randomised controlled trials. |
| **Level of evidence**                      |
| IV-3                                    |

| **Transrectal or transurethral hyperthermia** |
| The use of transrectal or transurethral hyperthermia is not recommended at present because of the lack of data from long-term randomised controlled trials. |
| **Level of evidence**                      |
| IV-3                                    |
## Alternative forms of treatment (contd)

### Transurethral microwave thermotherapy
There is now sufficient data to permit the use of TUMT in a clinical rather than experimental setting. It is important, however, that men considering this form of therapy clearly understand:

- the absence of large studies showing a long-term efficacy; and
- an undefined but ‘significant’ incidence of early morbidity.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transurethral microwave thermotherapy</strong></td>
<td>II</td>
</tr>
<tr>
<td>There is now sufficient data to permit the use of TUMT in a clinical rather than experimental setting. It is important, however, that men considering this form of therapy clearly understand:</td>
<td></td>
</tr>
<tr>
<td>- the absence of large studies showing a long-term efficacy; and</td>
<td></td>
</tr>
<tr>
<td>- an undefined but ‘significant’ incidence of early morbidity.</td>
<td></td>
</tr>
</tbody>
</table>

### Transurethral vaporisation of prostate
The use of TUVP is not recommended at present because of the lack of long-term RCTs. More data will be important as there are potential hazards from using high frequency power, such as burns, nerve and muscle stimulation and urethral strictures.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transurethral vaporisation of prostate</strong></td>
<td>IV-3</td>
</tr>
<tr>
<td>The use of TUVP is not recommended at present because of the lack of long-term RCTs. More data will be important as there are potential hazards from using high frequency power, such as burns, nerve and muscle stimulation and urethral strictures.</td>
<td></td>
</tr>
</tbody>
</table>

### Transurethral needle ablation
TUNA is not recommended at present because of the absence of data from long-term randomised controlled trials.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transurethral needle ablation</strong></td>
<td>IV-3</td>
</tr>
<tr>
<td>TUNA is not recommended at present because of the absence of data from long-term randomised controlled trials.</td>
<td></td>
</tr>
</tbody>
</table>

### High intensity focused ultrasound
HIFU is still experimental and not recommended at present because of lack of data from long-term randomised controlled trials.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High intensity focused ultrasound</strong></td>
<td>IV-3</td>
</tr>
<tr>
<td>HIFU is still experimental and not recommended at present because of lack of data from long-term randomised controlled trials.</td>
<td></td>
</tr>
</tbody>
</table>

### Prostatic stents
Stents may have a role in the management of patients with urinary retention or with severe LUTS who are in poor general health and may not tolerate any form of surgical intervention.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prostatic stents</strong></td>
<td>IV-2</td>
</tr>
<tr>
<td>Stents may have a role in the management of patients with urinary retention or with severe LUTS who are in poor general health and may not tolerate any form of surgical intervention.</td>
<td></td>
</tr>
</tbody>
</table>
Alternative forms of treatment (contd)

Balloon dilatation
The use of balloon dilatation is not recommended. Trials have been of short duration with few patients but suggest that there is little response and this is not maintained.

Level of evidence

II

Research recommendations

Measure of bother
Future research should be aimed at the development and psychometric testing of a measure of ‘bother’ and quality of life which is valid, reliable, responsive to changes in health status and practical for serial measurement in clinical trials conducted in Australia, while also addressing the need for culturally appropriate outcome measures.

Natural history of LUTS
Epidemiological studies should be carried out of urinary symptoms, bother and quality of life to determine the natural history of LUTS in ageing Australian men.

Diagnostic tests
There should be rigorous appraisal of diagnostic tests using established methodological criteria (Jaeschke et al 1994).

Prostate cancer
Epidemiological studies are required in Australia to determine the association between urinary symptoms and early prostate cancer.
Research recommendations (contd)

**Patient information**
Research is required to develop and evaluate patient information that reduces anxiety about prostate cancer; supports clinical decision-making for LUTS and enhances clinician and patient satisfaction with care.

**Pharmacological intervention**
Randomised controlled trials to assess durability of treatment are required using 'bother' as an outcome measure of pharmacological interventions for men severely bothered by urinary symptoms.

**Comparison of TURP and TUIP**
Long-term randomised clinical trials are recommended which should be appropriately funded and designed to compare TURP and TUIP using clear and standardised eligibility criteria based on bother, standardised surgical procedures and serial outcome measures.

**Alternative treatments**
Further randomly controlled trials are needed to evaluate the more promising of these procedures. They should be compared to conventional surgery and sham interventions.

Design of these trials should involve larger sample sizes and consider comparison with conventional surgery, standardised interventions, validated outcome measures and duration of treatment effectiveness.
1 General aspects of these guidelines

1.1 Their purpose

Thirty-seven per cent of Australian men over 45 years of age report troublesome lower urinary tract symptoms and the frequency increases with age (Pinnock and Marshall 1997, Garraway et al 1993). At least one-third of male patients over 50 years seen in general practice have some of these symptoms (Ward and Sladden 1994). Possibly because the pathophysiology of lower urinary tract symptoms is not well understood, there has developed over the years a wide range of investigations and treatment strategies which at times may be inappropriate or unnecessary.

In the report of the Australian Health Technology Advisory Committee, *Treatment Options for Benign Prostatic Hyperplasia* (NHMRC 1994), the National Health and Medical Research Council drew further attention to significant variations in the management of this condition.

This report also recommended the urgent development of clinical practice guidelines for the management of Australian men with urinary symptoms and noted that similar guidelines had been developed by the Agency for Health Care Policy and Research (AHCPR) in the United States (McConnell et al 1994) and by the World Health Organization (Cockett et al 1994).

With these recommendations in mind, and given the prevalence of urinary symptoms in ageing men, it was felt important to establish a more uniform approach to their management. It is hoped that these guidelines will assist men, general practitioners and urologists in
making decisions about clinical assessment, investigation and treatment of uncomplicated LUTS.

Given the prevalence of urinary symptoms in ageing men, it was felt important to establish guidelines for a more uniform approach to their management. Support for the development of guidelines was provided by the two medical organisations whose members are most closely associated with the treatment of these men, the Urological Society of Australasia and the Royal Australian College of General Practitioners.

In November 1995 a Working Party on Voiding Dysfunction in Men was convened under the auspices of the NHMRC’s standing committee, the Quality of Care and Health Outcomes Committee, to develop evidence-based recommendations. So that all the potential stakeholders were represented the working party comprised representatives from urology, general practice, consumers, health economics and health services. The working party was supported by an NHMRC secretariat and consultants commissioned to undertake specific technical and economic reviews of the scientific literature. The terms of reference and membership of the working party are given in Appendix A.

1.2 Definition of LUTS

The natural history of urinary tract symptoms in men as they grow older is not well understood although it is accepted that these symptoms are seldom life-threatening. There is no consensus about the underlying pathological processes causing these changes in urinary function. Terms such as benign prostatic hyperplasia (BPH) and ‘prostatism’ inadvertently suggest that enlargement of the prostate is the only cause of the symptoms.

Studies have demonstrated that the severity of urinary symptoms does not correlate with the presence of BPH or the degree of prostatic enlargement (Barry et al 1993, Girman et al 1995, Simpson et al 1996). Also, symptoms and signs of lower urinary tract dysfunction are evident in both men and women of similar ages. Studies have shown that proxy measures such as prostate size, urine flow rate, residual
urine, the visual appearance of the prostate at cystoscopy and the findings of pressure flow urodynamics do not necessarily correlate with urinary symptoms. Historically, however, these measures were used to define a clinical condition.

Thus, a complex of clinical symptoms was prematurely linked to a histological condition and inadvertently reduced to a set of invalid proxy measures. More perturbing, these flawed proxy measures were used as substitute outcome indicators for change in patient symptoms in case-series and clinical trials. For example, men were entered into clinical trials because they had large prostates, even though the link between an enlarged prostate and symptoms compromising their quality of life had not been convincingly established. Interventions changing prostate size were considered ‘successful’ by their proponents although patient symptoms, or quality of life, were neither measured nor reported.

More recently, Abrams coined the more helpful term ‘LUTS’ (lower urinary tract symptoms) in recognition of the need to reduce controversy (Abrams 1994). This permitted a return to a useful clinical definition of a symptom complex without necessarily implying a full understanding of its underlying pathology in all cases (Barry et al 1996). This perspective allowed the working party to emphasise that the health outcomes of importance were the severity of the urinary symptoms and the experiences of the man himself, despite imperfect objective measures of this experience, poor understanding of its aetiology and flawed proxy measures.

Uncomplicated LUTS

These guidelines only refer to a specific set of lower urinary tract symptoms — those which do not usually give rise to any serious health threat (see Section 2.4). The working party has therefore used the term ‘uncomplicated LUTS’ to define the set of symptoms to which these guidelines refer.
1.3 Scope of the guidelines

The guidelines contain detailed recommendations, as developed by the working party, for the physical evaluation, investigation and treatment of men presenting with uncomplicated LUTS. Conditions excluded from these guidelines are discussed in Section 2.4. Where it can be categorised, the strength of the evidence on which the recommendations were made is presented so that doctors can provide guidance to their patients, and together they can make informed decisions regarding the management of the condition.

The patient’s subjective sense of bother from his symptoms is important in defining that a problem exists. Physical signs *per se* or results of investigations should not be used independently of symptoms and the bother they cause to initiate treatment. This patient-centred approach is defensible on two grounds. First, when medical science has an imperfect understanding of the underlying pathology, it is appropriate to focus on the patient’s subjective experience. Second, it acknowledges the need to involve the patient himself in the process of making decisions about treatment options, as only he will know what he is prepared to risk for the current levels of symptoms and the bother they cause. This is especially so as we have, as yet, no better or more objective means of measuring either the symptoms, their impact, or the pathological process underpinning them.

The central tenet of these guidelines is:

...the consideration of how the patient weighs the likely consequences of his choice. There are substantial differences in the risks and benefits associated with different management choices; in order to make the right decision, men must be fully informed and empowered to base their decisions on their own values and expectations. (Patient Outcomes Research Team [Wennberg 1995])

A draft of these guidelines was subjected to specific consultation with all members of the Urological Society of Australasia, the Royal Australian College of General Practitioners and individual general
practitioners. The draft has also undergone review by international referees and a public consultative process. As a result of these consultations, a number of changes were made to achieve this final document.

While it is considered that the guidelines represent the best advice regarding the evaluation and management of men with uncomplicated LUTS, based on current evidence, they cannot be considered as definitive. Thus they should be used as they were intended — providing a guide to management based on the best available evidence. It remains the prerogative of the man or his practitioner to modify the recommendations according to the specific circumstances of the individual.

The guidelines are the basis from which the general practitioner and consumer guides have formally been developed and they are, in turn, underpinned by three technical reports. Two of these reports fully detail the outcome of the literature searches undertaken to arrive at the findings and recommendations made in the guidelines (Cummins 1996, Jackson 1996). The third defines the in-depth health economic review that was undertaken (Butler 1996).

Finally it is important to note the relationship of these guidelines to the issue of prostate cancer. The anxiety a man may suffer because he is concerned about the possibility that he may have prostate cancer is discussed in these guidelines because of its relevance for a man who consults his practitioner about LUTS. However, these guidelines are not intended to address the question of screening for prostate cancer or the management of a man with clinical or investigative findings suggestive that he may have that disease. The issues related to prostate cancer screening have been addressed by a recent report, *Prostate Cancer Screening*, produced by a standing committee of the National Health and Medical Research Council, the Australian Health Technology Advisory Committee (CDHFS 1996).
1.4 Data evaluation

Studies evaluating the effectiveness of management options were retrieved using recognised literature search strategies (McConnell et al 1994, Cummins 1996, Jackson 1996).

Greater emphasis was placed on studies reporting outcomes related to patients’ experience of LUTS (degree of bother). Therefore, studies reporting a degree of bother (or another self-reported or clinical assessment) and those reporting ‘symptom scores’ using internationally-recognised instruments (whether physician or patient completed), provided the most useful clinical information about the effectiveness of treatment. Less emphasis was placed on those studies reporting outcomes such as peak urine flow rate, residual urine volume or prostate size in the absence of any impact on the degree of bother. In this context, the patient's subjective sense of how bothered he is by his symptoms is most important in defining if a problem exists.

Studies were ranked in order of methodological soundness. Greater weight was given to randomised controlled trials (RCTs) although the majority of retrieved studies were case-series or nonrandomised controlled trials. The limitations of these weaker study designs are well known (Elwood 1988, Andersen 1990). Case-series tend to overestimate the effect of treatment, which is frequently shown to be less substantial when subjected to controlled evaluation (Andersen 1990). Case-series also have potentially limited general application and are prone to selection and measurement biases (Andersen 1990). It was disappointing to note that promising interventions evaluated in case-series were rarely tested under more rigorous conditions of randomisation and blinded assessment with sufficient sample sizes. Surgical interventions were least likely to have been evaluated against nonsurgical interventions using randomised controlled designs, with or without sham operations.

Many of the articles reviewed use scores (such as those of Boyarski or Madsen Iversen) where the index values are different from the American Urological Association (AUA) Symptom Index or International Prostate Symptom Score (IPSS). It is therefore not
possible to compare absolute values across these different scores. The percentage changes were helpful, however, and taken as equivalent.

The working party considered that studies with fewer than 40 patients were unhelpful because their results are compromised by such wide confidence intervals that any demonstrated treatment effect could be uncertain (Sackett and Cook 1993). The choice of proxy outcome measures involving continuous data, such as urinary flow rates, can generate statistically significant differences before and after treatment even in small studies. However, the relationship of urinary flow to clinical outcomes and improvement in patient quality of life is not established and such studies are unhelpful. Small studies also are unlikely to detect relatively uncommon (<10%) complications or side effects (Levine et al 1994) and the working party was concerned about the validity of any study in which fewer than 50% of subjects were available for follow-up (Kraemer and Thiemann 1987).

1.4.1 Outcome measures

The pivotal outcome in the management of men with uncomplicated LUTS is the degree of improvement of the ‘bother’ he experiences. Unfortunately, objective measures of bother are not well defined or validated and one of the major difficulties encountered was the lack of RCTs in which degree of bother was reported as an outcome of intervention.

Measurements of bother have only recently appeared in the literature as outcomes reported in clinical trials. Some surgical studies did report bother (or an acceptable proxy measure) but rarely used controlled designs. In the absence of sound measurements of bother, proxy measures accepted by the working party included crude measures of bother, such as the single four-point index included in the IPSS or the AUA seven-point urinary quality-of-life score and symptom scores (see Appendix C).
Even in those studies where more acceptable outcome measures (such as symptom scores) are reported, the clinical benefits of any changes need to be assessed with caution. Although there is undoubtedly a relationship between symptom score change and change in the degree of bother perceived by a man, even statistically significant changes in symptom scores may not translate into a measurable change in the degree of bother experienced by the man if the score changes are numerically relatively small.

**Research recommendation — measure of ‘bother’**

Future research should be aimed at the development and psychometric testing of a measure of ‘bother’ and quality of life which is valid, reliable, responsive to changes in health status and practical for serial measurement in clinical trials conducted in Australia, also addressing the need for culturally appropriate outcome measures.

### 1.4.2 Rationale

Given the methodological limitations of much of the published scientific literature, the working party needed early to reach a consensus about the approach to be applied when having to derive a clinical recommendation from demonstrably inadequate evidence. As noted elsewhere (Naylor 1995), these so-called ‘grey zones’ appeared to outnumber those instances where evidence was irrefutable and the derived clinical recommendation strongly evidence-based and uncontroversial. Two types of reactions to these ‘grey zones’ have been described, reflecting fundamental differences in medical ethics (Davidoff 1996).

- An *interventionist* approach assumes that patients are best served by providing any or all services with any promise of benefit.

- A more *conservative* approach requires a greater certainty of benefit, based on a steady accumulation of scientific knowledge.
For treatments, this requires the increasingly rigorous evaluation of interventions found promising in clinical trials or uncontrolled case-series by replicable RCTs with blinded outcome measurement.

Thus, the working party could have taken a more interventionist position, recommending tests and treatments in the anticipation that net benefit would accrue over and above personal and societal costs even though published empirical evidence to justify such a position was not available. Understandably, respondents to the draft of these guidelines circulated for public consultation who advocated this approach, could not furnish any further evidence to support their criticisms other than Level IV-3. However, critics usefully identified that the core issue was the absence of definitive evidence. Some argued that the working party’s derived recommendations went against current practice. In response, the working party has acknowledged that current clinical patterns of care usually reflect an earlier era when rigorous appraisal of the scientific evidence was not expected before a test or therapeutic intervention was adopted in practice.

In the absence of definitive evidence to support a specific test or treatment, the working party elected not to recommend the test or treatment, even when anecdotal evidence suggested that the test was common practice or professional opinion considered it useful.

In response to the feedback obtained during the public consultation process, the working party has made this position more explicit in the final guideline. First, the evidence has been evaluated and its strength quantified. Second, the derived clinical recommendation based on the consensus of the working party using a conservative approach is stated. Those who wish to apply a more interventionist approach can proceed to do so. However, these guidelines make explicit the limitations of current knowledge when an evidence-based approach is advocated. In these grey zones, clinical management is a choice between conservative and interventionist interpretations of circumstantial evidence.

In taking the conservative approach, the working party also readily accepted its responsibility to identify gaps in empirical evidence which
urgently require methodologically sound research to be undertaken. These areas are identified in the appropriate sections of the text and in Section 14.2 and the working party encourages individual clinicians, the relevant professional colleges and consumers to accept the challenges of an evidence-based approach to health care and the need to plan for a responsive research program to ensure that better evidence exists when the guidelines are revised. Collaboration in relevant research by all parties will ensure than an evidence-based approach to health care is strengthened and sustained beyond initial guideline development.

### 1.4.3 Levels of evidence

A four-point rating system was applied to the quality of evidence on which the recommendations in these guidelines are based. The rating system has been adapted from the system developed by the United States Preventative Services Task Force and is recommended by the NHMRC (1995).

This hierarchy of evidence relates only to accumulating evidence about the effectiveness of interventions. While useful to evaluate studies of the outcomes of interventions, some limitations of the hierarchy were noted. For example, on those occasions where RCTs reported statistically significant improvements in outcomes but the working party doubted the clinical significance of these findings, the working party cited the evidence as an RCT (Level I or II) but interpreted the guideline conservatively. The hierarchy did not readily address this situation. It was also clear that descriptive studies with small samples were insufficient for measuring risks and adverse outcomes. It was not possible to communicate this detail with the hierarchy as given.

The working party also did not have available to it any accepted hierarchy of strength of evidence for diagnostic tests. When use of the NHMRC hierarchy was considered inappropriate for some diagnostic tests, the level of evidence for the relevant guideline appears as ‘not applicable’.
Thus, a guideline recommending a specific test on the basis of how good that test is in confirming a diagnosis, is not a guideline to which a level of evidence can be applied (ie ‘not applicable’).

<table>
<thead>
<tr>
<th>Level of evidence ratings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Level I</strong></td>
</tr>
<tr>
<td><strong>Level II</strong></td>
</tr>
<tr>
<td><strong>Level III-1</strong></td>
</tr>
<tr>
<td><strong>III-2</strong></td>
</tr>
<tr>
<td><strong>III-3</strong></td>
</tr>
<tr>
<td><strong>Level IV-1</strong></td>
</tr>
<tr>
<td><strong>IV-2</strong></td>
</tr>
<tr>
<td><strong>IV-3</strong></td>
</tr>
<tr>
<td><strong>N/A</strong></td>
</tr>
</tbody>
</table>
1.5 Information for consumers and general practitioners

The NHMRC will also be publishing modified versions of these guidelines for consumers (men and their families) and for general practitioners (GPs).

**Consumer guide:** *To Pee or not to Pee? — A Guide for Men about their Urinary Symptoms*

The working party also recognises that men themselves, being individual people, will have different levels of need for information, different preferences for the formats of such information and different types of social support and professional assistance when seeking treatment or discussing options. The working party encourages ongoing revision of the consumer guideline so it matches better these specific circumstances and needs. Different versions in a range of reading scores need to be developed. Versions are needed which are adequately translated and backtranslated in common community languages, respecting cultural sensitivities and health beliefs. Alternative information technology permitting more graphics, interaction and tailoring of information to individuals also holds promise in consumer empowerment. Resources precluded the development of such a comprehensive range of materials but the publication of a ‘prototype’ consumer guideline is an important first step.

**Guide for GPs:** *‘Is it my Prostate, Doc?’ — Assessing the Evidence*

Clinical practice guidelines are designed to assist clinical decision-making by summarising the current scientific evidence and deriving practical recommendations. In recognition of the variety of clinical contexts in which this guideline will be used, the working party encourages its local adaptation by individual general practitioners, group practices, divisions or other professional bodies in order that evidence-based medicine can progress beyond rhetoric to become reality. While the GP guideline was developed with substantial input from general practitioners, it could be improved further by ongoing
discussion, refinement and a strong sense of ownership at the local level. The working party requests that any group adapting the guideline through local activity document this process and keep the NHMRC informed of progress.

Copies of the GP and consumer guides can be obtained from Commonwealth government information (AusInfo) shops in all capital cities.
2 The spectrum of LUTS

2.1 What is uncomplicated LUTS?

The use of the acronym ‘LUTS’ to describe benign urinary symptoms is a recent innovation and the bulk of the literature related to this condition uses terms such as BPH or ‘prostatism’ (Abrams 1994). While BPH is frequently used loosely to apply to the clinical symptoms and also to changes in the prostate, in the literature review on which these guidelines are based, every effort has been made to discriminate between these various meanings. Conditions which are excluded from these guidelines are discussed in Section 2.4.

2.2 Reason for consulting a doctor

A man may visit his doctor for one or both of two reasons: he is bothered by his symptoms and/or he is concerned that the symptoms may signify a serious underlying disease such as cancer. It is important for the man to have every opportunity to express his reason for consulting the doctor. However, he may be reluctant to state clearly the reason because he is embarrassed by the symptoms or is afraid of their possible implications, and the doctor may need to overcome his reticence by specific questioning.

2.3 Symptoms of uncomplicated LUTS

The symptoms of uncomplicated LUTS comprise any or all of the following:
• the need to awake frequently from sleep to void (nocturia);

• voiding frequently during the time the man is awake — best identified by asking how many hours he is able to retain urine between voids;

• a feeling of urgency;

• urge incontinence;

• hesitancy — having to wait before voiding commences, on a regular basis;

• alterations in the nature and strength of the stream
  – its ‘bore’,
  – its ability to project forwards,
  – the need to strain,
  – continuous or interrupted, especially towards the end of voiding;

• postmicturition dribble — the leaking of urine into clothing after the apparent completion of voiding;

• feeling of incomplete emptying; and

• second void or ‘void encore’.

These symptoms are frequently described in the literature as being grouped into two categories known as ‘obstructive’ and ‘irritative’ (Madsen and Bruskewitz 1995).

The ‘obstructive’ symptom complex includes:

• hesitancy,
• reduced stream,
• postmicturition dribble, and
• feeling of incomplete emptying.

The ‘irritative’ symptom complex includes:
• nocturia,
• frequency,
• urgency, and
• urge incontinence.

This terminology may be confusing because similar descriptors are used to define two groups of urodynamic abnormalities. Unfortunately there is poor correlation between these two symptom complexes and the similarly-described urodynamic abnormalities. Some authors suggest that, for this reason, these symptom descriptors should not be used (Abrams 1995).

Key point
Where the terms ‘obstructive’ or ‘irritative’ are used, it should be clearly stated whether they refer to symptoms or have been defined using urodynamic tests.

Research recommendation — natural history of LUTS
Epidemiological studies should be carried out of urinary symptoms, bother and quality of life to determine the natural history of LUTS in ageing Australian men.
2.4 Conditions not covered by these guidelines

Patients with the following conditions, in association with LUTS, would not, in the first instance, be managed as suggested by these guidelines. Their specific management details are not discussed here.

Any of the following factors exclude a diagnosis of uncomplicated LUTS:

- haematuria;
- pain on voiding;
- other types of urogenital pain;
- urinary tract infections;
- urinary retention;
- urinary incontinence which is – severe, or – continuous;
- other disease states that may cause urinary symptoms directly, or as a consequence of a neurological disorder;
- men with conditions such as – cognitive disorders, – dementia, – Alzheimer's disease, – cerebrovascular accidents, – Parkinson's disease, – autonomic neuropathy, – multiple sclerosis, or – alcoholism.

It is important to note that if, following evaluation and management of any of the above conditions, the patient is not found to have any significant underlying pathology or his symptoms revert to those defined as uncomplicated LUTS, then management of his symptoms would follow the strategies proposed by these guidelines. Thus, this situation may apply where, for example, a man voids satisfactorily after...
an episode of urinary retention or when a urinary tract infection has been successfully treated and no other predisposing factors are found.

**Key point**

If, following evaluation and management of any of the above conditions, the patient is not found to have any significant underlying pathology or his symptoms revert to those defined as being uncomplicated LUTS, then management of his symptoms would follow the strategies proposed by these guidelines.

### 2.5 Natural history of untreated LUTS

The natural history of untreated LUTS can be considered for two somewhat different groups of men. Firstly there is the natural history of urinary symptoms in men in a community setting where they have not presented to a medical practitioner because of their LUTS. This presumably represents that large group of men who, for whatever reason, have not considered their LUTS sufficiently bothersome for them to present to a medical practitioner.

Secondly there is the natural history of LUTS where men have presented to a practitioner because of the nature or severity of their symptoms. This would therefore better represent the possible course of LUTS in men who seek medical advice because of their symptoms and who do not undergo any form of intervention. There are relatively few studies which report the natural history of uncomplicated LUTS in either of these settings.

A one-year community study of 266 untreated patients showed considerable within-subject variation in urinary symptomatology with a quarter of men reporting an improvement in irritative symptoms and a third a deterioration in other symptoms. Levels of bother caused by the LUTS did not, however, show much change during the period of follow up (Garraway et al 1993).
A recent community study assessed the longitudinal changes in the severity and bother of LUTS in over 2000 men over a 42-month period. The authors also assessed the linear changes in symptom scores at the baseline evaluation, with age. There was an increase of 0.10 AUA symptom index units with year of age at the study baseline. Longitudinally there was a slight decrease in symptom severity at an 18 months assessment while at the 42-month evaluation there had been an increase in symptom severity across all age groups. The average annual increase in AUA symptom index was 0.2 points per year over the observation period. It is important to note however that there was considerable variability in progressing with some men’s symptoms getting worse and some improving (Jacobsen et al 1996).

In a study which best represents the natural history of LUTS in men who have presented with these symptoms to a medical practitioner, 107 untreated men were followed for 5 years. Within this period, 10 required prostatectomy and a further 16 considered that their symptoms were worse at the end of the five-year period for a 24% incidence of symptom deterioration. Twenty-nine per cent (31 men) considered that their symptoms had improved and 47% (50 men) felt that there had been no significant change in the severity of the symptoms. The incidence of acute retention during the five years of follow up was 1.9% (Ball et al 1981).

From these data it seems possible that men can be reassured that although there may be some slow deterioration in their symptom severity with time, this is by no means inevitable and that many men will perceive that their symptoms improve. None of the studies were able to predict which men would undergo significant deterioration.

### 2.6 Morbidity and mortality of LUTS

A common cause for anxiety in men with urinary symptoms is that their LUTS may progress to acute urinary retention, although the reported annual incidence of this occurrence only ranges from 0.4–6%. Its occurrence is unpredictable and may follow a particular event such as excessive alcohol intake, prolonged travel, constipation and anal

Chronic retention may occur because of irreversible changes to the bladder wall leading to inefficient bladder emptying and increased residual urine (Jones and Georges 1992).

Retention with high bladder storage pressures may cause a functional obstruction of the drainage of the upper tracts. This will result in the development of hydronephrosis, usually bilateral, and may result in the deterioration of renal function. Unrecognised and untreated, such renal failure can eventually result in death. The incidence of upper tract dilatation in men with LUTS has been reported to be between 0.8% and 2.5% (de Lacey et al 1988, Koch et al 1996).

The incidence of renal insufficiency in men with LUTS has been reported to range from 0.3% to 30% with a mean of 13.6% (Roehrborn et al 1996a, McConnell et al 1994). Such a variable and high incidence of renal insufficiency is not surprising when the characteristics of the study population are considered. Many of the men are elderly and have well-established risk factors for renal deterioration which have nothing to do with the pathophysiology of LUTS.

Other values for the incidence of morbidity and mortality secondary to LUTS are reported but they are difficult to evaluate because the actual cohort of men being studied is poorly described (Guess 1995, Boyle et al 1996). Thus it is difficult to establish whether some of the causes of morbidity are directly related to the LUTS and its underlying causes, or to other coexistent factors in an ageing population of men.
2.7 **Medical conditions that may increase the severity of LUTS**

The severity of uncomplicated LUTS may be magnified because of extrinsic factors, not directly related to the man's urinary system.

For example, urinary incontinence is more common in frail elderly men. However, while the nature of the LUTS suffered by the frail elderly man may be similar to that of his younger counterpart, incontinence is not a normal part of ageing and there is always an underlying disorder or precipitating cause. Although the incontinence may be due to urological causes, it is probable that other factors may cause or combine to cause the incontinence.

Identification of factors that may increase the severity of uncomplicated LUTS requires a focus not just on the lower urinary tract but on the general health and functional ability of the patient. Such an assessment thus becomes an integral part of patient evaluation and may require specific questioning of the man and, where relevant, discussion with relatives and carers and visits to the man's home. Factors that may be responsible include:

- medications,
- confusion,
- impaired mobility,
- reduced manual dexterity including difficulty with clothing,
- constipation and/or faecal impaction,
- polyuria,
- acute medical illness, and
- environmental factors.

Frequently, one or a number of the causes that are usually responsible for LUTS combine with some of the above factors to increase the severity of the symptoms.

Similarly it is sometimes necessary to consider whether a specific disease process may be contributing to a man's urinary symptoms.
Some conditions will, by definition, exclude the description of the man's symptoms as LUTS. These include:

- Alzheimer's disease and other forms of dementia,
- cerebrovascular accidents,
- alcoholism,
- Parkinson's disease,
- cerebral tumours,
- multiple sclerosis, and
- autonomic neuropathy.
3 Causes of LUTS

3.1 What causes LUTS?

The symptom complex of LUTS is caused by a heterogeneous combination of changes in bladder, urethra and prostatic function. Although it is likely that outflow obstruction is the fundamental cause of uncomplicated LUTS in many men, the specific factors responsible for the symptoms are difficult to confirm using current diagnostic methods. Some of the changes are likely to be age related and others have not yet been clearly defined (Simonsen et al 1987).

Just as the underlying causes of LUTS are unclear, the dynamic abnormalities associated with the symptom complex have not yet been adequately identified. For many years it has been widely considered that the primary abnormality is an infravesical obstruction with, on some occasions, secondary changes to bladder function (Barry et al 1996). Much of this supposition probably derives from the fact that previously men more frequently presented with urinary retention and the obstruction was in turn relieved by prostatectomy. This strengthened the view that all urinary symptoms were due only to bladder outflow obstruction.

It is now clear that the pathophysiological processes responsible for LUTS may include one, or a combination, of the following:

- detrusor hyperactivity (see Section 3.3);
- detrusor hypoactivity (see Section 3.4);
- infravesical pathology (see Section 3.5) resulting from
  - increased urethral sphincter activity,
  - increased prostatic volume (see Section 3.2),
  - increased prostatic smooth muscle density or activity,
– distal urethral obstruction, eg stricture,
– other, as yet undetermined, abnormalities.

3.2 Benign prostatic hyperplasia

The cause of LUTS has for a long time been directly attributed to benign prostatic hyperplasia (BPH). It was thought that the symptoms arose as a consequence of prostatic urethral obstruction due to the enlargement of the prostate.

The term *benign prostatic hyperplasia* is of itself a source of considerable confusion. The working party’s technical review of the literature revealed that it has been applied as a label for:

- a histological change of hyperplasia within the gland (microscopic);
- clinical enlargement of the prostate gland; and
- the clinical symptom complex of LUTS.

Histological BPH is almost ubiquitous in the ageing male and is said to be as much a part of ageing as grey hair and wrinkles (Simpson et al 1996). Autopsy studies show that it is the most common benign neoplasm in men, with a histological prevalence of 50% in 60 year-old men and 82% in men aged 71–80 (Berry et al 1984). Approximately half of the men with microscopic evidence of BPH will eventually have macroscopic enlargement of the gland (Isaacs 1994).

It is now clear from descriptive studies that there is a poor correlation between urinary symptoms and the degree of prostatic enlargement (Barry et al 1993, Girman et al 1995, Simpson et al 1996). Studies have also demonstrated that the incidence and nature of urinary symptoms for similarly aged samples of men and women is remarkably similar, although women do not have prostate glands to which such symptoms might be attributed (Chancellor and Rivas 1993, Lepor and Machi 1993). The symptoms of urgency, frequency and nocturia increase with age equally in men and women (Homma et al 1994).
3.3 Detrusor hyperactivity

Bladder or detrusor hyperactivity or instability describes the occurrence of detrusor muscle contractions while the patient is trying to inhibit micturition. It is associated with an urge to pass urine when the man does not want to.

While the exact cause of instability of the bladder's detrusor is frequently unclear, it may be:

- a primary or idiopathic (of unknown cause) event, as is frequently seen in women;
- associated with congenital abnormalities;
- related to ageing, or
- secondary to infravesical obstruction (Couillard and Webster 1995).

Outflow obstruction with overdistension of the bladder causes histopathological changes in the bladder wall including changes to the autonomic nerve supply. It leads to a decrease in the density of cholinergic innervation, supersensitivity of the detrusor muscle and fibrosis of the detrusor muscle. The denervation leads to increased smooth muscle excitability and electrical conductivity resulting in a decreased ability to empty efficiently (Gosling et al 1986, Restorick and Mundy 1989).

While detrusor instability is common in men with outflow obstruction it is also found in 25% to 63% of men without obstruction (Abrams 1995). More recent attempts to document the dynamic changes possibly responsible for LUTS have been based on the urodynamic parameters derived from urine flow rates and pressure flow urodynamic studies. As flow is a combination of detrusor function and outflow resistance, values for urine flow alone are unable to provide evidence of the dynamic causes of LUTS. For example, a decrease in flow rate with or without an increase in post-void residual volume (PVR), may be caused by either bladder outlet obstruction or by impaired detrusor contractility (Blaivas 1988).
When detrusor instability and infravesical obstruction are found to coexist on pressure flow testing, it is still not possible to determine whether the detrusor instability is secondary to the obstruction or is a separate primary event. Detrusor instability was reported to disappear in a cohort of men who underwent prostatectomy and were subsequently shown to have a good clinical outcome (Kadow et al 1988). However, this report does not suggest that all men with detrusor instability will revert to normal bladder function after surgery. A 62% incidence of detrusor instability in men undergoing transurethral resection of the prostate (TURP) was found to decrease to 35% postoperatively, suggesting that the cause was not entirely due to outflow obstruction (Abrams et al 1979). It is not yet possible to determine whether the incidence of residual detrusor instability reflects an initially different cause of instability or irreversible permanent change to the detrusor caused by the infravesical obstruction. Also, there are as yet no data to suggest which men with ‘irritative’ symptoms or urodynamically-determined instability will improve after surgery.

Detrusor instability may also be secondary to a number of other conditions including generalised disease processes such as Parkinson's disease or multiple sclerosis, or to regional neurological disturbances. These latter causes of detrusor instability are excluded from the uncomplicated LUTS spectrum to which these guidelines apply (see Section 2.4).

Clinically, detrusor instability is likely to be manifested by ‘irritative’ symptoms such as frequency, urgency and urge incontinence (Neal et al 1987, Speakman et al 1987) although some studies have shown no significant correlation between irritative symptoms and uninhibited detrusor contractions (Cetinel et al 1994, Frimodt-Moller et al 1984). Thus, while it may be possible to suspect detrusor instability on the basis of these symptoms, it is equally possible that the symptoms may be due to other dynamic factors.

Because detrusor instability may result in a small functional bladder capacity and small voided volumes, it can also be responsible for a poor urinary stream and flow rate (Oesterling et al 1994). On the other hand,
frequency can reflect poor bladder emptying either as a result of infravesical obstruction or poor detrusor function. Thus a man may have a poor stream, either because of obstruction in the first instance or small voided urine volumes in the latter.

### 3.4 Detrusor hypoactivity

Deficient detrusor activity (hypoactivity) may arise as a primary event (possibly related to ageing), secondarily to infravesical obstruction, or as a consequence of a variety of neurological abnormalities. It is reported to occur in 20% of men over 75 years (Abrams 1994). It is frequently associated with diminished bladder sensation thereby permitting the man to store a large urine volume without discomfort and can lead to increased PVR and retention.

Although detrusor hypoactivity may be suspected on clinical grounds, definitive urodynamic evidence may be difficult and, at times impossible to obtain. Pressure flow testing may suggest this dynamic abnormality with a finding of an absent detrusor contraction and urine flow induced predominantly by abdominal straining. Where the patient is unable to void it becomes difficult or impossible to determine whether the urinary retention is caused by loss of detrusor muscle tone, infravesical obstruction or both. Thus it may also be impossible to anticipate whether surgical intervention to reverse possible outlet obstruction will be successful, as symptoms are more likely to persist after prostatectomy if there is a weak detrusor muscle (Jensen et al 1988a, Robertson et al 1993).

### 3.5 Infravesical obstruction

The nature of any infravesical abnormality responsible for LUTS has largely been determined by interpreting the outcome of different interventional options or by the results of pressure flow studies. Sound research is still necessary to clarify issues of cause and effect in this field.
Up to 75% of men with sufficiently severe LUTS to warrant surgery are actually obstructed on urodynamic grounds, and these have 76–93% chance of significant improvement in symptoms after surgery (Jensen et al 1988a, Neal et al 1989; Robertson et al 1996) (see Section 6.6.3). These data have been taken to suggest that in these men the cause of their symptoms was a bladder outflow obstruction presumably caused by the enlarged prostate.

Conversely, however, the 25% of men undergoing surgery who have been shown not to be obstructed also have a 65%–78% chance of improvement in symptoms (Jensen et al 1988a, Neal et al 1989, Robertson et al 1996). As these men’s symptoms do not appear to be caused by urodynamically demonstrated obstruction, some other abnormality may account for the original symptoms, which is changed or reversed by the surgery. The nature of this abnormality has not been determined.

Also, when the prostate gland has been estimated to be less than 30 grams, the outcome of surgical management of LUTS is the same using either transurethral incision of the prostate (TUIP) or TURP (Riehmann et al 1995). While TUIP definitively divides the bladder neck fibres it remains unclear why this procedure results in a similar improvement as resection of prostatic lobes. This finding further clouds the traditional perception that most men with LUTS have infravesical obstruction caused by the bulk of the prostate impinging on the prostatic urethra.

Finally, the beneficial effect for some men of the use of α-adrenergic blocking agents suggests that, at least in these men, one of the factors responsible for their LUTS is an increase in smooth muscle activity (Eri and Tveter 1995) either at the bladder neck or in the smooth muscle produced by BPH.

While LUTS in many men may be caused by obstruction due to either the bulk of the prostatic tissue or because of increased smooth muscle activity, obstruction is clearly not the only underlying problem responsible for these symptoms.
4 Clinical assessment of symptoms

4.1 The patient’s perspective

There is evidence from numerous studies that the prevalence of LUTS in men is high, but that they do not seek treatment until a critical level of bother has been reached (Pinnock et al 1996, Ward and Sladden 1994, MacFarlane et al 1995).

A study of urinary symptoms in older men in general practice showed that, while many men reported urinary symptoms, most were not debilitated by their symptoms and their quality of life was not significantly impaired. However, those presenting to a clinician for a consultation about worsening urinary symptoms had high symptom scores, high bother ratings and impaired quality of life, indicating that men seek medical advice when the symptoms become bothersome (Ward and Sladden 1994).

The ‘irritative’ symptoms of frequency, urgency and nocturia are usually cited as the most ‘bothersome’ of the symptoms (du Beau et al 1995). In older men, social embarrassment and increased bother relating to frequency are the most likely reasons for them to seek help (Jacobsen et al 1995).

Key point

Because the causes of LUTS are still uncertain, development of these guidelines has relied on the initial symptoms and the outcomes of evaluation and treatment of these symptoms.
4.2 Degree of ‘bother’

The impact that LUTS has on a man's quality of life is referred to in these guidelines as the ‘degree of bother’ that the symptoms cause him. This terminology is being used increasingly in the literature. There is also evidence that the significance of the term ‘bother’ is well understood by English-speaking men and thus allows them to easily express the impact of their symptoms on their quality of life (Ward and Sladden 1994). The use of this term is recommended in the Australian environment.

By determining the degree of bother caused by the LUTS symptoms, measured either quantitatively or qualitatively, the man and his doctor can:

- determine the man’s perception of the severity of his symptoms;
- decide on the most appropriate management strategy based on the degree of bother; and
- subsequently assess changes in severity as a consequence of the chosen intervention.

It is important to stress that even where there is a discrepancy between the practitioner’s perception of the severity of the man’s symptoms and that expressed by the man, it must be the man himself who eventually decides on the degree to which he is bothered by his symptoms. Exceptionally, there may be a gross incongruity between the man's assessment of his degree of bother and that which, based on the history he gives, the practitioner makes. In these circumstances it may be necessary to consider whether there are other undisclosed issues needing further evaluation (see Section 8.1).

A number of studies have demonstrated that the symptoms that cause the most bother are frequency, urgency, nocturia and urinary incontinence (Sagnier et al 1995, Wasson et al 1995). These reports also found that the bothersome score correlated well with the man's anxiety and the interference with his living activities.
While it is essential to consider the specific symptoms which concern an individual man, the above evidence suggests that the focus of any discussions should be on the degree of ‘bother’ which the symptoms cause. It is the severity of the man’s ‘bother’ which will ultimately determine which management options he will consider.

The degree of bother can be assessed in a number of ways. These are described below.

1. Simply on the basis of a specific question such as, ‘Now that we have discussed your urinary symptoms, how would you rate the extent to which they distress you?’

2. By specifying, using a four-point scale, the answer to, ‘How much are you bothered?’:
   - not at all
   - a little bit
   - moderately
   - severely

3. In answer to the question, ‘If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel?’, using the seven-point scale:
   - delighted
   - pleased
   - mostly satisfied
   - mixed—about equally satisfied and dissatisfied
   - mostly dissatisfied
   - unhappy
   - terrible

More complex quality-of-life scores (Mozes et al 1996) and a BPH Impact Index (Wennberg 1995) have been used for a similar purpose.

In the practical management of the patient, the degree of bother is the most important factor, but in research studies, the use of symptom scores and quality-of-life scores add a degree of precision.
The man's perception of the degree of bother he suffers because of his LUTS is the most important variable which needs to be determined. It is recommended that practitioners should adopt a score for the degree of bother and use this for the initial and subsequent assessment of the severity of the man's symptoms.

### Guideline — degree of bother

<table>
<thead>
<tr>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
</tr>
</tbody>
</table>

#### 4.3 Symptom assessment and urinary symptom scores

The assessment of the man's urinary symptoms permits the patient and his doctor to determine their nature and severity and the impact they are having on his well-being. The assessment may also highlight symptoms that are suggestive of significant pathology underlying the presenting complaint.

Urinary symptom scores are tools to assess the severity of the individual urinary symptoms suffered by a man. By collating the individual answers, a total symptom score can be produced. Although a number of such scores have been published, the most widely used is the American Urological Association (AUA) Symptom Score index. This has subsequently also become known as the International Prostate Symptom Score (IPSS) with the addition of an extra question relating to the impact that the symptoms have on the man's quality of life (Cockett et al 1994).

The AUA symptom score is a self-administered seven-question instrument (see Appendix C). The index has been shown to have a high internal consistency and test–retest reliability (Wennberg 1995). While symptom scores are generally reliable methods of assessing the severity of symptoms, it is possible that there may be some inaccuracy in the
reliability of patient interpretation or recall of the exact symptoms suffered (Lawrence 1996). Actual daytime frequency, intermittence, weakness of stream and nocturia using twenty-four hour home uroflowmetry recordings, were compared to those reported using symptom score questionnaires (Matzkin et al 1996). Reliability was high and the men were able to report nocturia with accuracy. However, they overstated the daytime frequency and there was no correlation between their perception of intermittence or strength of the stream and the scores they subsequently reported.

Symptom scores can be used effectively in men and women (Lawrence 1996, Chancellor and Rivas 1993), but they become less reliable in men over 65 years (Barry et al 1993). Cultural differences have an important impact on the universality of the index and thus the questionnaires need to be linguistically validated before extension of their use to non-American cultures (Sagnier et al 1995).

As individual urinary symptoms or even groupings of symptoms are poor indicators in determining the nature of the pathophysiological and dynamic abnormalities causing LUTS, urinary symptom scores cannot be used for this purpose either. For example, symptom severity does not correlate well with peak flow rate, average flow rate, post-void residual volume, prostate size or urodynamic findings (Barry et al 1993, Chute et al 1993, McConnell et al 1994, Sirls et al 1996).

While symptom scores measure the patient's perception of the severity of their LUTS, this perception can be just as easily assessed using a degree of bother index as discussed above. Symptom scores have their greatest value in the measurement of the change in the severity of symptoms over time without treatment or following some intervention.
Key point

The use of a urinary symptom score, such as the IPSS, is useful to assess change in the severity of symptoms over time or after some form of intervention.

4.4 Men from different cultural backgrounds

Australia is recognised as one of the most culturally diverse societies in the developed world. Increasing numbers of older men with LUTS come from different cultural backgrounds. Interpreter services are mandatory if the patient cannot speak fluent English or give informed consent in English. Further, cultural beliefs are likely to influence a man’s perceptions about his urinary symptoms, their possible link to cancer and their degree of bother. As these should be ascertained on an individual patient basis, the need for interpreters is stressed. It may not always be appropriate to have an interpreter who is a relative of the patient.
5 Patient evaluation

5.1 Detailed medical history

As already discussed the history that specifically relates to the man's LUTS should focus on:

- the reason for his presentation;
- the nature and severity of his symptoms; and
- his anxieties, especially regarding the possible implications of his symptoms.

The general history should include:

- factors aggravating the LUTS, for example, constipation, certain cold/flu medications, diuretics, antidepressants, antihypertensives;

- other relevant urological problems, past or current, including urethral discharge, urinary retention, urological trauma and previous episodes of catheterisation;

- previous surgical procedures;

- other relevant medical problems which might complicate management of the presenting symptoms, such as neurological or psychiatric conditions, diabetes, cardiac disease or poor mobility;

- medications and allergies;

- social, employment and psychological issues relevant to the management of the symptoms; and
• a determination of mental state with specific attention to
  – dementia,
  – anxiety and/or depression.

5.2 Initial physical examination

The specific genitourinary component of the physical examination should include:

• general examination of the abdomen with palpation and percussion of the suprapubic region to detect a distended bladder;

• examination of the penis for conditions such as phimosis, hypospadias, meatal abnormalities;

• digital rectal examination (DRE) to
  – detect gross distortion of the anatomy suggestive of a diagnosis of extensive prostate malignancy, and
  – exclude anal and rectal pathology.

As discussed previously, these guidelines do not specifically address the issue of screening or case-finding for prostate cancer. The NHMRC's position regarding prostate cancer screening is the subject of a recently released Australian Health Technology Advisory Committee report (CDHFS 1996). While DRE is not in this case being advocated as a means of detecting early prostate cancer, it may detect an abnormality suggestive of such a clinical diagnosis. If such a finding is made the management of the man’s condition will fall outside the scope of these guidelines.

Similarly, if other positive findings of genitourinary conditions are found, the man may require further diagnostic testing and once again his management pathway may be quite different to that outlined by these guidelines.
5.3 Size of the prostate

In the past, urological teaching focused on the clinically-determined size of a prostate as an indication for surgical intervention and as a reliable predictor of the outcome of such treatment. Such perceptions have now largely disappeared from the urological literature and from medical teaching.

While it has been traditional to note the ‘size’ of the prostate gland at DRE, such an assessment is not reliable, reproducible or related to the severity of LUTS (McConnell et al 1994). For these reasons it is unnecessary to specifically attempt to evaluate the size of a prostate at the initial presentation of a man with LUTS.

Unfortunately the supposed prognostic significance of prostate size still has considerable credence with many men. It is important that practitioners are aware of this belief and offer reassurance about the significance of prostate size in their discussions with men about LUTS.

Currently the best method of assessing prostate volume is by transrectal ultrasound (TRUS) imaging or magnetic resonance imaging (MRI) studies (al-Rimawi et al 1994). In comparative studies MRI showed a larger volume than TRUS but the variability between visits was 10–12% of the mean volume, regardless of the methods used. Evaluations of prostate volume using DRE and cystoscopy correlate poorly with these forms of imaging (Perrin et al 1991).

Overall, prostatic enlargement is not the critical factor in development of symptoms or outflow obstruction, for example, encroachment of the urethra in the region of the bladder neck.

While prostate size is unrelated to the severity of a man's urinary symptoms its assessment is, however, clinically relevant if a man is considering surgical intervention because there is good evidence that a TUIP offers as good an outcome with less morbidity than TURP for men with small prostate glands. The presence of an extremely large volume prostate gland in a man considering surgical intervention for his LUTS may suggest an open surgical approach as the most appropriate.
As discussed above the assessment of prostate size does not correlate well with the volume determined by imaging methods. Also, cystoscopy can only estimate the length of the prostatic urethra and this also does not correlate very well with prostate volume (determined by imaging). However, such an estimation is usually clinically sufficient to permit the urologist to decide which surgical approach (TURP, TUIP, open prostatectomy) is most appropriate. It is important to note that the RCTs comparing TUIP and TURP all use only DRE and/or cystoscopic findings to determine the ‘size’ of the prostate (Dorflinger et al 1992, Riehmann et al 1995, Soonawalla and Pardanani 1992). Cystourethroscopy (assessment of prostatic urethral length) is routinely carried out. It is not indicated as an independent examination for the assessment of prostate size before surgery.

There is now evidence that the 5-α-reductase inhibitor, finasteride (which is sometimes used to treat LUTS), only provides a statistically significant improvement in symptom scores in men with a prostate volume of greater than 40 mL (measured by TRUS or MRI) (Boyle et al 1996). This suggests that it may be necessary for prostate volume to be assessed by TRUS imaging before considering the use of finasteride (see Section 10.3).

**Key points**

- Prostate size is not important in the initial assessment of a man with uncomplicated LUTS.
- Assessment of prostate size is clinically relevant if a man is considering surgical intervention or treatment with the drug finasteride.
6 Investigations to assess LUTS — their value

6.1 Urine analysis

Urinary tract infections, bladder cancer and general medical conditions such as diabetes can mimic uncomplicated LUTS.

Every man who presents with urinary symptoms should have his urine tested by dipstick or by microscopic examination and culture. If the dipstick test suggests the presence of infection or blood, bacteriological examination of the urine is also necessary.

If the urine test is positive the patient’s initial management is not within the scope of these guidelines.

<table>
<thead>
<tr>
<th>Guideline — urine analysis</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every man with urinary symptoms should have his urine tested.</td>
<td>IV-2</td>
</tr>
</tbody>
</table>

6.2 Voiding diary

A voiding diary is a useful tool for the further assessment of a man's LUTS if he considers his symptoms cause sufficient bother for him to need some form of intervention.
A request to keep such a diary can be made of the patient at the time of the initial consultation in order to document:

- the nature and degree of the urinary frequency;
- if fluid intake is excessive;
- if fluid excretion at night is inappropriately high;
- the voided volumes; and
- the occurrence and timing of any urine incontinence.

The patient is asked to record the time and volume of his fluid intake and voided urine noting any episode of urinary incontinence for a period of 48–72 hours. An appropriately-designed sheet should be provided to the patient (see Appendix D).

### Guideline — voiding diary

| Keeping a voiding diary is a useful tool to assist in the management of a man who thinks that his symptoms cause sufficient bother for him to consider management options for his LUTS. | IV-2 |

### 6.3 Other tests required to assess LUTS

A number of tests have traditionally been performed on men presenting with clinically uncomplicated LUTS. The reason these tests are usually performed is to:

- detect conditions that may pose a serious health threat to the man, if they were to remain undiagnosed and untreated;
- help to better define the nature and severity of his symptoms;
• enable the man to be given an indication of the probable course of his condition, particularly if he decides against immediate intervention; and

• assist in predicting the likely outcome of intervention.

When the tests are performed to exclude a condition that may pose a health threat, the need to undertake them should be determined by the importance a man or his practitioner place on the prevalence of an abnormal test finding in men with uncomplicated LUTS.

In the case of ‘predictive’ tests, their value should be determined by their ability to assist a man in deciding whether the potential benefits of surgery justify such intervention in his particular case. For such tests to be of practical value they need to discriminate between a high probability of a good or poor outcome. Lesser discriminative benefits may not provide the man with clinically useful information.

Despite anecdote there are no published data to demonstrate that combinations of ‘predictive’ tests enhance their value in clinical decision making. Studies to obtain such data using established methodological criteria (Jaeschke et al 1994) are strongly recommended.

**Research recommendation — diagnostic tests**

There should be rigorous appraisal of diagnostic tests using established methodological criteria.

### 6.3.1 Serum creatinine

The prevalence of abnormal renal function in the AHCPR database ranged from 0.3–30% with a mean value of 13.6% (McConnell et al 1994). This prevalence does not however just reflect the incidence of renal function deterioration directly associated with LUTS. Reduced
renal function in elderly men is commonly due to factors not associated with LUTS. There are two reasons why it may be appropriate to detect renal insufficiency in men with uncomplicated LUTS.

First and most importantly is the increased risk that prostatic surgery poses to men with diminished renal function — men who have renal insufficiency and undergo prostatic surgery have an increased risk of postoperative morbidity and mortality. The incidence of morbidity in such men has been estimated to be 50% higher than for those men with normal renal function (Mebust 1990) and they are also reported to have a six-fold increase in mortality (Melchior et al 1974). For this reason a serum creatinine test, if a recent value is not available, should always be performed preoperatively for men considering surgery.

The second commonly proposed reason to detect an abnormal serum creatinine level is that such a finding may predict the presence of asymptomatic chronic urinary retention with a high resting bladder pressure leading to hydronephrosis and silent renal deterioration. That is, renal insufficiency directly attributable to the man's apparently uncomplicated LUTS. It is the prevalence of this finding that should determine the need to undertake a serum creatinine estimation at the initial presentation of a man with uncomplicated LUTS.

Data regarding this prevalence is not immediately and directly available from the literature. It can be derived from studies which report the prevalence of upper urinary tract dilatation directly attributable to uncomplicated LUTS and the prevalence of renal insufficiency in these circumstances. As will be seen from the discussion below the highest reported prevalence of renal insufficiency directly related to LUTS is 1.8% (Koch et al 1996).

These guidelines do not recommend the routine estimation of serum creatinine at the initial assessment of a man with uncomplicated LUTS. The ultimate decision regarding the benefit of this testing should however be determined by the man and his practitioner. Their decision should be based on a 1.8% prevalence of silent renal function deterioration as a consequence of unsuspected pathology underlying the man's LUTS.
Guideline — serum creatinine testing

| The routine estimation of serum creatinine at the time of the initial presentation of a man with uncomplicated LUTS is not recommended. A decision regarding this testing should be determined by the importance the man and his practitioner place on a 1.8% prevalence of detecting a relevant abnormal test finding. | N/A |

6.3.2 Upper urinary tract imaging

The traditional reason for imaging the upper urinary tract of men presenting with clinically uncomplicated LUTS is to detect:

- upper urinary tract dilatation, secondary to chronic urinary retention and a high resting bladder pressure, which may result in progressive silent deterioration of renal function;

- the volume of post-void residual urine (PVR) (the importance and value of this test is discussed in Section 6.5); and

- other unsuspected urinary tract pathology, eg renal or bladder tumours (a form of screening or case-finding for a particular condition; there is no scientifically reported evidence that such screening is justified or appropriate).

While numerous studies report the incidence of abnormalities detected by upper tract imaging, most do not report the impact these findings have on health or on how these findings changed the management of the men's urinary symptoms (McConnell et al 1994).

The AHCPR analysis of this data found an incidence of 6.9% of unilateral or bilateral hydronephrosis in a review of nine studies where
ultrasound was used to evaluate men with LUTS. The incidence of hydronephrosis in a different series of patients given an intravenous urography (IVU) was 3.8% (McConnell et al 1994). It is therefore difficult to deduce from these data the proportion of men with LUTS and abnormal ultrasound findings whose hydronephrosis could be directly attributed to their lower tract pathology.

Recent data is more helpful in defining the prevalence of hydronephrosis directly attributable to apparently uncomplicated LUTS. A prospective study of 128 men scheduled for TURP used abdominal ultrasound and found only one man to have unsuspected upper tract dilatation secondary to the lower tract changes, a prevalence of 0.8% (de Lacey et al 1988). Another study of 556 men with LUTS found a 2.5% prevalence of unilateral or bilateral hydronephrosis. The prevalence of a raised serum creatinine associated with such upper tract dilatation was however only 1.8% (Koch et al 1996).

In summary, where a man presents with apparently uncomplicated LUTS, the prevalence of upper tract dilatation has been estimated to range from 0.8% to 2.5%. The benefits of undertaking an ultrasound examination of the urinary tract in a man with uncomplicated LUTS will be determined by the relevance a man and his practitioner place on this low prevalence of identifying evidence of possible silent renal function deterioration. In most but not all men, this risk would also be identified by serum creatinine testing.

These guidelines do not recommend the routine ultrasound or IVU evaluation of the urinary tract of a man with uncomplicated LUTS. Any benefit of such testing cannot be justified by the estimation of PVR or because of screening.

The very low incidence of hydronephrosis in men with LUTS suggests that it is unnecessary to undertake any upper urinary tract imaging studies in men presenting with LUTS. Indication for such imaging may however include one or more of the following:

- haematuria
- urinary tract infections
• renal insufficiency
• history of urolithiasis
• history of urinary tract surgery

As these conditions lie outside the scope of these guidelines (see Section 2.4) they are not discussed.

<table>
<thead>
<tr>
<th>Guideline — ultrasound imaging</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>The routine ultrasound imaging of the urinary tract at the time of the initial presentation of a man with uncomplicated LUTS is not recommended. A decision regarding this testing should be determined by the importance the man and his practitioner place on a 0.8–2.5% prevalence of detecting a relevant abnormal test finding.</td>
<td>N/A</td>
</tr>
</tbody>
</table>

6.3.3 Endoscopic examination of the lower urinary tract (cystourethroscopy)

Endoscopic examination of the lower urinary tract — cystourethroscopy — allows a visual evaluation of the bladder and urethra. Historically many urologists believed that the visual appearance of the lower urinary tract defined the severity of disease or predicted the outcome of treatment of men with uncomplicated LUTS (McConnell et al 1994). There are no data to support the value of this examination in either of these regards.

Cystourethroscopy is an important part of the evaluation of men with symptoms and signs suggestive of conditions which are excluded from the definition of uncomplicated LUTS.

It has also been proposed that the routine endoscopic assessment of the lower urinary tract may detect the presence of significant pathology.
such as bladder tumours. The prevalence of such conditions in men with uncomplicated LUTS has not been reported. Performing cystourethroscopy for this purpose is a form of screening and there are no data to support the benefits of this.

On the other hand, cystourethroscopy may be used to determine the optimal form of surgery. The presence of a large diverticulum or stone(s) may influence the type of surgical approach as may the endoscopically estimated prostatic urethral length (see Section 5.3). As endoscopy always forms the initial phase of any surgical treatment for LUTS, such an evaluation need not be performed on a separate occasion.

<table>
<thead>
<tr>
<th>Guideline — cystourethroscopy</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystourethroscopy should not form part of the initial evaluation of a man presenting with uncomplicated LUTS. It is an essential part of surgical procedures.</td>
<td>N/A</td>
</tr>
</tbody>
</table>

### 6.3.4 Prostate specific antigen

Prostate specific antigen testing is described in Section 7.2.

### 6.3.5 Post-void residual urine volume

Post-void residual (PVR) urine volume is the volume of urine remaining in the bladder immediately following the end of micturition (Roehrborn et al 1996a). Normal values are reported to range from 0.09 to 12 mL (Hinman and Cox 1967, Di Mare et al 1963). There are, however, reports of considerable intraindividual variation in residual urine values suggesting that the reproducibility of this test is poor. In one study of 30 men assessed by ultrasound for PVR on three separate
occasions, only one-third showed no statistically significant difference in residual volumes across all three measurements (Birch et al 1988).

Further, the magnitude of PVR was not associated with the severity of urinary symptoms in numerous cross-sectional studies and correlated only weakly with urodynamic parameters such as voiding pressures and peak urine flow rate (Cummins 1996). Most importantly, however, pretreatment PVR is at best only weakly associated with treatment outcome. Of five predictive studies on the value of PVR, three studies report no association (Neal et al 1989, Tubaro et al 1995, Bruskewitz 1992) and two report a weak association (Ball and Smith 1982, Lepor and Rigaud 1990). Similarly, two RCTs found no association between pretreatment PVR and treatment outcome (Lepor et al 1992a, Wasson et al 1995).

<table>
<thead>
<tr>
<th>Guideline — post-void residual urine volume</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>The assessment of post-void residual urine volume should not form part of the routine assessment of men presenting with, or considering treatment for, uncomplicated LUTS.</td>
<td>II</td>
</tr>
</tbody>
</table>

### 6.3.6 Urodynamic tests

**Uroflowmetry**

Urinary flow rate recording or uroflowmetry is a noninvasive test where the urinary flow, throughout the course of micturition, is electronically recorded. The uroflow is the product of the pressure generated by the detrusor muscle and urethral resistance. An abnormally low urine flow rate is not necessarily related to obstruction but can be the result of a poor bladder contraction (Poulsen et al 1994). While a number of different parameters of the recording can be analysed, the most commonly reported value is the peak flow rate (PFR...
or $Q_{\text{max}}$ which measures the highest rate of urine flow recorded during the test. A value of greater than 15 mL per second is generally considered normal.

Considerable debate exists on whether PFR can be interpreted without considering the voided volume of urine. While numerous nomograms have been developed to reflect this relationship, there is no universally accepted single volume correction technique and the inaccuracy of flow rates with voided volumes of less than 125–150 mL should be recognised (McConnell et al 1994).

A learning effect has been shown and the use of two flow rates on two separate occasions have been recommended (Roehrborn et al 1996a). Variation in repeat PFR measurements in individual men ranges from 0.1–5.5 mL per second (Barry et al 1995, Golomb et al 1992). However, improvements of greater than 3 mL per second are frequently used as measures of success of treatment in studies analysing efficacy of surgical or medical treatments (Reynard and Abrams 1995).

While it has been suggested that PFR may be helpful in differentiating between those men with LUTS in whom the symptoms are caused by an infravesical obstruction and those where this is not the case, studies do not confirm this. While PFRs of greater than 20 mL per second are unlikely to be associated with urodynamically-defined outflow obstruction (Abrams and Griffiths 1979), a value of less than 15 mL per second does not differentiate between such obstruction and impaired detrusor contractility (Chancellor et al 1991). Thus this parameter is not helpful in making a definitive distinction between those men with urodynamically demonstrated obstruction and those without.

There is conflicting evidence about the predictive value of PFR when looking at outcome after treatment. One study reports that for men who undergo TURP, 71% of those with PFRs over 15 mL per second improved compared to 91% of those between 10 and 15 mL per second and 92% for those less than 10 mL per second (Jensen et al 1988b). However, this study found no difference between improvement in symptom scores between groups, and measured success as a subjective analysis of ‘much better’ or ‘no change’. Pooled data from this and
another similar study shows that there is a relative risk of a poor outcome for men with PFRs above 15 mL per second, compared to those below this value, of 3.8 (Cummins 1996, Jensen et al 1988b, Kuo and Tsain 1988). Several RCTs found that pretreatment PFR values did not predict successful treatment (Wasson et al 1995, Riehmann et al 1995, Jardin et al 1991, Lepor et al 1992a, Gormley et al 1992, Buzelin et al 1993) although high peak flow rates have been associated with more complications after TURP (Wasson et al 1995).

In summary, there is evidence that lower PFRs may be associated with better outcomes after prostatic surgery. However, some men with low PFRs will have a poor outcome and many men with a high PFR will have a good outcome. The only potential benefit of determining the PFR in a man with LUTS is to offer him the odds of a successful outcome of surgical treatment. It is, however, considered inappropriate to deny treatment to men with PFRs over 15 mL per second, on the basis of this test alone.

**Guideline — uroflowmetry**

<table>
<thead>
<tr>
<th>Guideline — uroflowmetry</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>The routine measurement of peak flow rate in the evaluation of the patient is not recommended.</td>
<td>II</td>
</tr>
</tbody>
</table>

**Filling cystometry (cystometrography)**

Filling cystometry is a test that measures changes in bladder pressure during filling of the organ. It requires two catheters to be inserted into the bladder, either transurethrally or suprapubically, and another catheter into the rectum. The former measures total bladder pressure (Pves), and the latter, intra-abdominal pressure. By subtracting one from the other, it is possible to determine the true detrusor pressure (Pdet), (usually recorded in centimetres of water).

This test provides information regarding functional bladder capacity, the presence and threshold of uninhibited detrusor contractions and
bladder compliance (McConnell et al 1994). While these dynamic factors are important in the pathophysiology of LUTS, it is not possible to determine as a consequence of filling cystometrography, whether any individual abnormality, or a combination of them, is a primary event or secondary to other factors. For example, it has been reported that 62% of men who undergo surgery for BPH have unstable detrusor contractions on a preoperative cystometrogram and 26% have such contractions after their surgery (Abrams et al 1979). Thus it might be presumed that, in a large proportion of men, the instability is secondary to some prostatic abnormality such as obstruction, which is corrected by surgery. On the other hand, in a significant proportion of men in whom the dynamic abnormality persists, it may have been a primary event and, for this reason, not influenced by surgical intervention, or it may reflect an irreversible change to the detrusor caused by the infravesical obstruction.

The reliability of conventional cystometry to identify detrusor instability has also been questioned because of a much higher incidence of this dynamic abnormality being identified in ambulatory studies than by the usual laboratory-based investigations (Robertson et al 1996). Thus, while conventional urodynamic studies may identify detrusor instability in men with LUTS, the absence of this finding does not negate its existence.

Cystometrography is an invasive investigation. Because studies have failed to demonstrate that a preoperative finding of detrusor instability will reliably predict the outcome of surgical treatment, the independent use of this test cannot be justified (Kadow et al 1988, McLoughlin et al 1990, Robertson et al 1996).

<table>
<thead>
<tr>
<th>Guideline — filling cystometry (cystometrography)</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>The use of filling cystometrography is not recommended as an independent measure for the evaluation of uncomplicated LUTS.</td>
<td>IV-I</td>
</tr>
</tbody>
</table>
**Pressure flow studies**

The filling cystometrogram is the first part of the pressure flow study. Once voiding is initiated, the pressure generated by the bladder and the urine flow rate are measured synchronously. While the filling portion of the study yields the information discussed above, the voiding part permits an assessment of the pressure generated by the bladder to produce the flow.

It has been proposed that by plotting the bladder pressure against the urine flow rate, it is possible to determine whether or not the man has an infravesical obstruction. The theory is that intervention, either surgically to reduce outlet obstruction or with medication to reduce prostate size or prostate stromal muscular activity, will only be effective in men with bladder outlet obstruction. The corollary is that men without urodynamically demonstrated obstruction should not be treated by these means.

The reproducibility of the test on an individual patient basis has been questioned because of considerable within-patient variation of test results. Twenty-five patients were tested on two or three occasions by pressure flow studies (Madsen et al 1995). While the authors report an intraclass correlation coefficient of 0.84 for detrusor pressure and 0.71 for maximum flow rate in 26% of the men, the maximum flow rates changed by more than 3 mL per second or the detrusor pressure by more than 20 cm of water, during the repeated tests (Cummins 1996). The authors recommend that assessment of multiple consecutive tests is necessary to eliminate this variation.

Much of the argument about the value of pressure flow studies involves pathophysiological reasoning as to why, or why not, pressure flow studies might be useful. However the value of the test can only be determined by answering the question: do men who have the test have a better outcome after intervention than those who do not? Outcome must be defined in terms that matter to men, not in pathophysiological terms. Thus, the fact that treatment has not affected a man's pressure flow parameters is of no relevance to him, if his urinary symptoms improve after treatment. Naturally, the converse is also true.
The literature review on which these guideline recommendations are based attempted to identify all published studies that assessed the value of pretreatment pressure flow studies in predicting post-treatment patient-centred outcomes. It was disappointing to find only ten such predictive studies. The quality of these publications were then further assessed using the following three main criteria.

- Was the decision to treat independent of the findings of pressure flow studies?
- Was outcome data reported on all subjects who had had pretreatment studies?
- Was outcome assessed ‘blind’ to findings of pressure flow studies?

On the basis of quality and sample size, the best studies were those by Jensen et al (1988a), Neal et al (1989) and Robertson et al (1996). Unfortunately, the study by Jensen failed to clearly identify the nature of the symptom assessment, making an assessment of the reported outcomes more difficult than in the other two studies. While the other two papers were the most valuable, these studies also suffered from methodological problems including different definitions of obstruction and relatively short follow-up periods.

The probability of good symptomatic outcomes of surgery, for each of the three studies when the preoperative pressure flow findings demonstrated obstruction or where they were equivocal or showed no obstruction are shown in Table 1.
<table>
<thead>
<tr>
<th>Study</th>
<th>Total number of men</th>
<th>No. with obstructed urodynamic finding (%</th>
<th>No. obstructed with good outcome/total number obstructed (%)</th>
<th>No. unobstructed or equivocal with good outcome/total number unobstructed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jensen et al 1988a</td>
<td>123</td>
<td>87 (71%)</td>
<td>81/87 (93%)</td>
<td>28/36 (79%)</td>
</tr>
<tr>
<td>Neal et al 1989</td>
<td>214</td>
<td>92 (43%)</td>
<td>74/91 (81%)</td>
<td>82/123 (67%)</td>
</tr>
<tr>
<td>Robertson et al 1996</td>
<td>99</td>
<td>80 (80%)</td>
<td>60/79 (76%)</td>
<td>13/20 (65%)</td>
</tr>
</tbody>
</table>

There are a number of disparities between these studies. It would seem that the cohort of men in the studies was dissimilar, as the percentage of men having an obstructed urodynamic finding was 71%, 43% and 80%, respectively. Further the outcome of treatment was significantly better for both groups of men in the study by Jensen et al, than in the other two studies where the results were remarkably similar. Despite these disparities, a number of important conclusions can be drawn from these study findings.

- While there is always a better outcome for men with urodynamically demonstrated obstruction, the difference between this group and those unobstructed or with an equivocal result is relatively small.

- It is questionable that such differences would have any clinical meaning for a man trying to decide the advisability of surgery, based on the probability of a good outcome.
• Taking as an example the most recent and the most methodologically sound paper (Robertson et al 1996), it is apparent that:

– when the urodynamic findings suggested obstruction, 19% of the men still had a poor outcome;

– if it had been recommended that surgery not be undertaken because the findings were equivocal or suggested no obstruction, 13% of the men would have been inappropriately denied the benefits of successful surgery;

– if, as the urodynamacists suggest, the purpose of pressure flow studies was to define those men who were not obstructed and would therefore possibly have an unsuccessful outcome, then 99 men had to undergo these invasive tests to identify just seven men who were unobstructed and would have a poor outcome from surgery.

<table>
<thead>
<tr>
<th>Guideline — pressure flow studies</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on the studies available and the absence of any other compelling evidence for the benefit of pressure flow studies in predicting clinically significant outcomes of treatment, it is recommended that pressure flow studies should not form part of the routine evaluation of a man before pharmacological or surgical intervention. Where it is thought that a man may still find the difference in predicted outcomes for surgery helpful in assisting him to make a management decision, such a study could be offered to him for this purpose.</td>
<td>III-2</td>
</tr>
</tbody>
</table>
7 Concerns about prostate cancer

7.1 Anxiety regarding prostate cancer

Anxiety regarding prostate cancer can be the principal reason why a man consults his doctor about urinary symptoms. The anxiety may be his alone or may be shared with, or even initiated by, others close to him, such as his partner, family or friends, and perhaps the media.

Most men over 50 will note changes in their urinary function with or without high levels of bother. If they also harbour an anxiety about prostate cancer, this may focus their attention on specific symptoms of LUTS and reinforce their fear. They may present to their practitioner expressing a concern about LUTS, while in reality it is their anxiety about prostate cancer that underlies their presentation. In some men such concerns can only be highlighted by direct questioning. The incidence in Australia of men presenting with LUTS because their principal concern is anxiety about prostate cancer, has not been reported.

Key point

It is important to establish if the man's concern about prostate cancer is the principal or an important reason for his presentation so that this anxiety can be addressed in its own right.
The man’s anxiety may be due to:

- a belief that prostate cancer causes urinary symptoms;
- the knowledge that prostate cancer is common;
- a cross-over effect from the considerable publicity regarding the benefits of early detection, through screening, for breast and cervical cancer; and/or
- extrapolation that screening for prostate cancer must also be beneficial.

It is important that the practitioner is able to present the appropriate information to the man so that he can be fully informed regarding the risks of prostate cancer in his specific circumstance and the need for further evaluation.

As these guidelines only relate to the management of LUTS and are not intended to provide specific advice regarding screening for, or the management of, prostate cancer, further discussion will be confined to the relationship between LUTS and prostate cancer. Specific information on screening for prostate cancer is given in the recent Australian Health Technology Advisory Committee (AHTAC) report on the subject (CDHFS 1996).

An association between LUTS and prostate cancer is difficult to investigate. The ideal study to address this question is one of men screened for prostate cancer independently of their LUTS symptom experience. Studies that have investigated men with LUTS symptoms more readily than those without such symptoms are confounded and the results of such studies that show an apparent association of LUTS with prostate cancer must be considered an artefact.

Four studies have been identified in which prostate cancer screening was performed independently of LUTS symptoms (Babaian et al 1991, Catalona et al 1994, Mettlin et al 1996, Rietbergen et al 1997). These four studies involved a total of 19,142 men enrolled from the
community at large (Catalona et al 1994, Mettlin et al 1996, Rietbergen et al 1997) and 362 men from a clinic setting (Babaian et al 1991). All men were tested for the possible presence of prostate cancer by DRE plus serum prostate specific antigen (PSA) estimation with (Babaian et al 1991, Mettlin et al 1996, Rietbergen et al 1997) or without (Catalona 1994) transurethral ultrasound (TRUS). The results are shown in Table 2.

Table 2: Acceptable studies of the association between prostate cancer and lower urinary tract symptoms in men (and proportion of cancers among men with and without lower urinary tract symptoms)

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Biopsy rate (%)</th>
<th>Cancer (%)</th>
<th>With LUTs (cancers/total)</th>
<th>No LUTs (cancers/total)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catalona et al 1994</td>
<td>6630</td>
<td>18</td>
<td>4.0</td>
<td>144/3500 (4.1%)</td>
<td>120/3130 (3.8%)</td>
<td>1.07 (0.57 – 2.0)</td>
</tr>
<tr>
<td>Mettlin et al 1996</td>
<td>2999</td>
<td>16</td>
<td>2.8</td>
<td>36/1482 (2.4%)</td>
<td>26/1511 (1.7%)</td>
<td>1.4 (0.66 – 3.0)</td>
</tr>
<tr>
<td>Babaian et al 1991</td>
<td>362</td>
<td>30</td>
<td>10.0</td>
<td>27/165 (15%)</td>
<td>10/197 (5%)</td>
<td>3.2 (1.3 – 8.0)</td>
</tr>
<tr>
<td>Rietbergen et al 1997</td>
<td>9513</td>
<td>21</td>
<td>4.3</td>
<td>109/565 (19%)</td>
<td>255/1229 (20%)</td>
<td>0.93 (0.50 – 1.7)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>19,504</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>1.27 (0.90 – 1.8)</strong></td>
</tr>
</tbody>
</table>

*RR = relative risk; CI = confidence interval

b Unadjusted for age

As shown in Table 2, the combined results, unadjusted for age indicate a nonsignificant trend to a small increase. However, as the 95% confidence interval crosses unity in all of the larger studies, this trend is likely to be due to chance. Also, if symptoms increase with age, this would be an overestimate as the apparent increase in prostate cancer
with LUTS symptoms may be due to the simultaneous increase with age both of LUTS symptoms and the incidence of prostate cancer. As there are not sufficient data to allow adjustment for age, a definitive conclusion between LUTS symptoms and prostate cancer cannot be made. Overall, LUTS appears to be a very poor predictor of cancer of the prostate.

It is therefore appropriate for a man who presents with LUTS and who has no specific clinical findings suggestive of prostate malignancy (such as an abnormal DRE), to be reassured that:

- just because he has LUTS does not suggest that he may have prostate cancer; and
- he has little or no increased risk of developing such a malignancy than men without these symptoms.

Conversely, it is also not possible to guarantee that he does not actually have prostate cancer.

Despite this reassurance some men will continue to express concern regarding the possibility they may have prostate cancer. Some may also specifically request that they have further tests to see if they have the disease.

<table>
<thead>
<tr>
<th>Guideline — prostate cancer</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men with uncomplicated LUTS should be advised that current data suggest that they have little or no increased risk of prostate cancer. NOTE WORDING</td>
<td>IV-I</td>
</tr>
</tbody>
</table>

60  Management of LUTS
7.2 Serum prostate specific antigen

Prostate specific antigen (PSA) is a glycoprotein produced by the glandular component of the prostate. Its serum concentration is correlated to prostate size, as measured by TRUS, and patient age (Oesterling et al 1993).

Serum PSA levels increase as a consequence of benign prostatic enlargement, prostatic inflammation (prostatitis), prostatic instrumentation, or because of the development of prostate cancer.

The only reason for estimating a man's PSA level when he presents with LUTS, is to test for the possible presence of prostate cancer. The issues concerning the possible association between LUTS and prostate cancer have been discussed above (Section 7.1). Undertaking a serum PSA test on a man with LUTS and no clinical evidence of prostate cancer is a form of screening for prostate cancer known as ‘case-finding’. The recent report of AHTAC on prostate cancer screening has recommended that screening for prostate cancer is not justified at this time (CDHFS 1996).
<table>
<thead>
<tr>
<th>Guideline — PSA testing</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is not recommended to estimate serum PSA as part of the normal evaluation of a man with LUTS. Serum PSA testing should only be done after a man with LUTS has been fully informed of the consequences of such testing. It is important that he understand that there is no scientific evidence of a relationship between LUTS and presence of early prostate cancer.</td>
<td>IV-2</td>
</tr>
</tbody>
</table>
8 Management options — general issues

8.1 Decision making

It is a central tenet of these guidelines that ‘the patient should be at the centre of the decision making process regarding the management [of his LUTS]’ (Wennberg 1995). The depth of information needed by an individual man in order for him to make an informed decision regarding his most appropriate management, will vary greatly from man to man.

Because of the significance placed on the patient making his own decisions, it is important for the patient and his practitioner to be able to communicate openly and freely. Where a language barrier exists, an interpreter should be used. Cultural issues are important as some men may not wish to have a female interpreter or a member of his family acting in this capacity.

The first issue to resolve is the reason for the man's initial visit to his doctor. If his only or principal reason was an anxiety about prostate cancer, then this can hopefully be resolved with advice and reassurance in line with the information provided above. Where he wishes to be tested for prostate cancer and gives informed consent, then a PSA estimation should be offered to him.

Where the man consults his doctor because of his LUTS, then he should be advised that his decision regarding further management will be based principally on the degree of bother his symptoms are causing him. It should be stressed that although the man's practitioner should at all times assist the man in his decision-making, it must be ultimately the man who determines how bothered he is by his symptoms. While there
may be an incongruity in the practitioner's mind between the severity of the man's symptoms and the degree of bother he is ascribing to them, it can only be the patient who can finally assess the degree of bother it causes him.

Exceptionally, there may be a gross incongruity between the man's assessment of his degree of bother and that which the practitioner makes, based on the history he gives. In these circumstances it may be necessary to consider whether there are other undisclosed issues needing further evaluation.

Management options fall into three distinct categories:

- reassurance and advice;
- pharmacological intervention; or
- surgical treatment.

The patient should understand that one form of management does not preclude a change to another if there is a change in the severity of the symptoms or a lack of success with one particular management strategy (see the decision tree in Figure 1; pages 68–69).

Research recommendation — patient information

Research is required to develop and evaluate patient information that reduces anxiety about prostate cancer; supports clinical decision-making for LUTS and enhances clinician and patient satisfaction with care.

8.2 Degree of bother — its role in treatment selection

Each man must judge for himself the severity of his LUTS — the degree of bother it causes him — and must then decide whether he
wishes intervention to relieve symptoms, and the nature of such intervention. While individuals may have an intrinsic preference for one form of intervention above others, many men may wish to judge the evidence purely on merits. Thus the man should be advised of the pros and cons of the various forms of intervention available, both pharmacological and surgical.

While men with a mild degree of bother usually accept reassurance and do not opt for intervention, those with moderate or severe bother will generally wish to assess the active treatment options in a discussion with their doctor. This should permit the man and his doctor to decide on a preferred form of intervention and will also allow them to consider other alternatives, if the initial one provides insufficient relief or is completely unsuccessful.

A man with severe bother may select surgery as his preferred management option because the more severe the bother caused by LUTS, the more likely there will significant improvement after surgery (Wasson et al 1995). Conversely, he may request a trial of pharmacological intervention before considering surgery.

Just as men severely bothered by their LUTS have the best outcome from surgery, those only moderately bothered may have a less favourable outcome (Wasson et al 1995). Therefore, in these cases, consideration can be given to a trial of pharmacological intervention after likely benefits and side effects have been discussed. If this fails to improve the condition, they can assess the surgical option while realising that the outcome may not be quite as optimal as for those men with severe bother.

The doctor should assist the man in this decision-making process by detailing the benefits, side effects and disadvantages of each form of intervention and the time to maximum potential benefit. A consumer booklet companion to these guidelines has been designed to assist in this process (see Section 1.5).
Guideline — selection of treatment

| Men whose LUTS cause a moderate degree of bother requiring intervention may, in the first instance, consider a trial of pharmacological intervention. | IV-2 |

Research recommendation — pharmacological intervention

Randomised controlled trials to assess durability of treatment are required using ‘bother’ as an outcome measure of pharmacological interventions for men severely bothered by urinary symptoms.

8.3 The placebo effect

As in other areas of clinical practice, the placebo effect plays a prominent role in the management of LUTS. Pooled placebo data from drug trials on men with LUTS show an improvement of symptom scores for periods of from 3 to 6 months and there are reports that the impact may persist for up to two years (Fitzpatrick and Lynch 1995). Short-term placebo controlled studies of between 8 and 24 weeks, also show significant increases in peak urine flow rates and improvement in symptom scores in the placebo-treated men.

The response to placebo may be due to release of endogenous endorphins (Isaacs 1990). The expectation of relief could spontaneously decrease the sympathetic stimulation of the smooth muscle. A review of 12 clinical trials showed that the percentage of patients who got better over time was the same in placebo-treated and untreated patients, but the proportion who got worse was lower in the placebo group (Isaacs 1990). The untreated group was followed for 2.6–5 years and the placebo group for up to six months. Approximately half the placebo group had no change in symptoms within six months.
(which he concluded was enough time to know if the placebo patients were likely to improve spontaneously or deteriorate). A similar effect was shown by finasteride trials where there were marked effects of placebo for 6 months, but the positive effects of the drug were only found later (Tammela and Kontturi 1993, Andersen et al 1995).

The placebo effect must always be considered when assessing the outcome of any intervention study. For this reason, only randomised placebo controlled studies can provide a true reflection of the impact of a particular form of intervention.

### 8.4 The expectation effect

While difficult to distinguish from the placebo effect, positive expectations lead patients to assess their outcomes in a more positive light. As part of a study of outcomes following prostatectomy, men were asked by how much they expected their symptoms to be improved by the surgery. Symptoms and post-treatment health (three months after surgery) were compared to preoperative health status. The investigators found a short and long-term influence of positive expectations on patient's assessment of improvement. Positive expectations led patients to report greater subjective improvement, while the actual symptom frequency and overall health status was not affected by their expectations (Flood et al 1993).

The study findings suggest that either the men distort recall of their presurgical health status, or the more optimistic patients experience improvement as more significant than those patients with less positive expectations. It could be concluded that assessments of outcomes based on patient recall or direct questions which ask them to assess their level of improvement may be biased by the patient's previous expectations.

Similarly, patients who have undergone a stressful treatment are more likely to exaggerate its benefits. Retrospective reports of change in health give much more positive results than prospective measures of change. In a study of prostatectomy, Aseltine and co-workers (1995) showed from questionnaires that 62% of men reported retrospective
improvement, whereas only one-third reported improvement when a postoperative symptom score was compared to their preoperation score. These data suggest that clinicians, who might rely on retrospective assessment strategies (for example, ‘Are you feeling better after treatment?’), will receive a response that exaggerates the benefits of treatment because of this effect, particularly if there is a strong nonverbal disincentive for the patient to say ‘no’ conveyed by the doctor’s body language.

Figure 1  Decision tree for the management of uncomplicated LUTS
Figure 1  Decision tree for the management of uncomplicated LUTS (contd)
9 Conservative management

9.1 Reassurance and advice

In other guidelines and much of the literature, reassurance is known as watchful waiting. This term implies that something may happen to the man if there is no intervention. The term, reassurance, as used in these guidelines, does not imply this. It is used in the same context as the word is defined by the Oxford dictionary: to restore confidence.

Reassuring the man therefore should encompass a discussion regarding:

- the natural history of LUTS;
- the potential impact of this condition on his quality and length of life;
- the nature of possible changes in symptoms which may suggest that he should seek further advice; and
- advice regarding various conservative measures that may improve his degree of bother.

9.1.1 Natural history of LUTS

As in all aspects of clinical medicine, it is impossible to predict with 100% accuracy the course of uncomplicated LUTS in an individual man. Instead, clinicians rely on previous research to present data based on probability and risk. Thus, the man should be informed that, based on currently available information, the natural history of the condition
(Section 2.5) is very variable over time. Many men actually notice a spontaneous improvement in their symptoms (Isaacs 1990).

In the context of the variable natural history of LUTS, it is also relevant to discuss the small risk of acute urinary retention, as this is frequently a specific cause of concern for men.

9.1.2 Quality and quantity-of-life issues

The patient can and should be reassured that the existence of LUTS does not suggest he has any condition which is likely to pose a significant health threat to him, now or at any time in the future. Reassurance is a viable option for all men with LUTS (Cockett et al. 1994).

To minimise the impact of LUTS, reassurance may, where appropriate, be accompanied by advice regarding:

- modification of various lifestyle factors (see Section 9.2); and
- bladder training (see Section 9.3).

A concern which might be expressed by patients who are considering no active intervention is that, by delaying, they will become ‘too old’ for surgery. They, therefore, suggest that it may be better to undergo surgery while they are in their current state of health rather than later when they may be less so. Although the surgical management of LUTS results in a slight increase in morbidity with age, this change is not sufficiently significant to alter the decision to have surgery. These issues deserve a full discussion between the man and his doctor.

9.1.3 The need for review

The man should be counselled that a further review of his condition may be indicated if there is:
• a change in the symptom complex; and/or

• an increase in the man's perception of the degree of bother caused by his symptoms.

9.1.4 Reassurance as definitive management

The individual man must be at the centre of the decision-making process regarding his specific management. Generally, however, reassurance will be used where the man considers that his LUTS is causing him only mild bother or none at all. Some men with a greater degree of bother may also feel that reassurance, with no other intervention, is the appropriate management for them.

Key point

Men with LUTS can be reassured that the existence of these symptoms do not suggest they have a condition which is likely to pose a significant health threat to them now or without warning in the future.

9.2 Lifestyle modification

Minor modifications to lifestyle or behaviour can have a beneficial effect on the degree of bother a man's LUTS causes (Palmer 1996). Such changes include:

• the reduction of fluid intake at specific times to reduce urinary frequency at times of greatest inconvenience, for example, at night or when going out in public (the recommended total daily fluid intake should not be reduced);

• avoidance or moderation of the quantity ingested of specific beverages such as tea, coffee or alcohol, which may have a diuretic
Management of LUTS

Effect thereby increasing fluid output and enhancing frequency, urgency and possibly urgency incontinence;

- urethral stripping — this describes the digital stripping of urine from the bulbous urethra at the end of micturition to speed up urethral emptying of urine and prevent postmicturition dribble;

- distraction techniques such as penile squeeze, breathing exercises, perineal pressure, mental ‘tricks’ to take the mind off the bladder and toilet;

- toilet scheduling, where the man is encouraged to use the toilet or bedpan every 2–4 hours, the aim being to empty the bladder regularly to avoid incontinent episodes;

- reviewing a man’s medication and changing the time of administration or substituting drugs for others that have fewer urinary effects;

- modification of physical, social and environmental factors;

- providing necessary assistance where there is impairment of dexterity, mobility or mental state; and

- other conservative options
  – treatment of constipation,
  – reversal, where possible, of polyuria,
  – arranging for a diuretic to be given, where it is required, at a time of convenience.

9.3 Bladder training

Bladder training, known also as bladder drill, can be used to improve the sensory components of LUTS. That is, the desire to void frequently due to a sensory hypersensitivity rather than detrusor instability (Palmer 1996, AHCPR 1996).
The elements of this approach include:

- an explanation of the nature of sensory urgency so that the man understands the problem and is able to accept the purpose of this approach to his management;

- the use of a voiding diary so the man can appreciate the small volumes of urine that he is passing (see Section 6.2);

- maintenance of a normal fluid intake;

- recording the time of first desire to void and requiring that he ‘hold on’ for a specified period of time; eg 20–30 minutes, then record the time he actually voids;

- recording the time and volumes of urine voided; and

- setting a goal for the man to comfortably store 400 mL in his bladder.

The effectiveness of bladder training will be determined by the nature of the man's LUTS, the rigour of his application to the program and the level of encouragement he receives from his doctor or other supporters.

Many of these measures require regular reinforcement, encouragement, evaluation and monitoring if they are to be successful. There are other health professionals who may be able to help in this conservative management. These include physiotherapists, nurses and continence advisers. These professionals provide advice on bladder training, pelvic floor exercises and continence management.
Key point

Conservative management of LUTS needs to focus on the urinary symptoms as well as the general health and functional ability of the patient. In some circumstances this may be more effectively implemented by using a multidisciplinary approach involving different health professionals.

Guideline — conservative management

<table>
<thead>
<tr>
<th>Guideline — conservative management</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reassurance and advice regarding conservative measures to minimise the degree of bother is a viable option for all men with uncomplicated LUTS. It is most appropriate for those men with a mild degree of bother or who are only anxious about their symptoms.</td>
<td>IV-2</td>
</tr>
</tbody>
</table>
10 Pharmacological management

Key point

Any medical practitioner contemplating prescription of any of the drugs mentioned in this section should consult the most recent publications listing drug side effects and prescribing information. This chapter is not intended to replace such sources. It is strongly recommended that the patient be informed of the side effects of any medication being prescribed.

10.1 Introduction

Most studies of pharmacological interventions for LUTS that were reviewed had inclusion criteria requiring a healthy cohort of men, usually described as being in good physical and mental health. This requirement may create a bias in the studies regarding patient compliance. Further, the cohort of men in the studies may not be representative of men with LUTS in the general population, whose symptoms may be less bothersome and compliance lower. It is difficult to compare the results of pharmacological intervention studies with those of men treated surgically because of the difference in the inclusion criteria between the two groups. The use of standard selection criteria is encouraged in future studies (Aso et al 1996).

All of the placebo controlled studies showed a variable but significant placebo effect and studies without a placebo arm are compromised as a result.
Numerous trials have indicated that there are subgroups of patients that respond to pharmacological treatment and those that do not. For some drugs there are as yet no data that permit identification of such responders prospectively.

Many studies have low follow-up rates. Long-term data may typically represent men who had a positive response to treatment initially and are prepared to stay in the study. This may represent a bias within the study cohort.

There are several distinct groups of pharmacological agents and each will be considered separately.

### 10.2 Alpha-adrenergic blocking agents

#### 10.2.1 Introduction

Contraction of the prostate smooth muscle and an increase in urethral pressure is mediated by α-adrenoceptors (Yamada et al. 1994). Alpha-adrenoceptor antagonists act on the stromal smooth muscle to decrease the prostate tone and the urethral resistance, and are postulated to improve symptom score and urine flow by acting on the dynamic component of LUTS (Eri and Tveter 1995).

There are several subtypes of these receptors with different tissue specificities. Ligand binding and molecular biological studies indicate that the α 1c subtype is the main type in the prostatic stroma, and this is not found in the systemic vasculature. In theory, it would be preferable therefore to use selective blockers where cardiovascular effects are not required (Eri and Tveter 1995).

The peripheral vascular effects of α-adrenoceptors can have adverse effects, such as fatigue, dizziness and headache, mainly due to their effects on the cardiovascular system (Kirby 1994). These antagonists may also act on the central nervous system and produce side effects such as tiredness and sedation (Andersson 1995). Long-acting blockers
include terazosin, doxazosin and tamsulosin, and can be given once a day at bedtime to decrease the impact and severity of dizziness and tiredness (Lepor 1995).

It appears that there is one patient population that responds to alpha blockade and one that does not. Approximately 30% of patients show no initial response to the drug. This may reflect a higher response in those men with a higher stromal to glandular ratio. Morphometric studies of prostate tissue demonstrate a marked increase in the ratio of stromal to glandular component in cases of hyperplasia (Bartsch et al 1979, Shapiro et al 1992).

As the only way of establishing the stromal to glandular component is by biopsy, and this is considered to be inappropriately intrusive in the context of pharmacological intervention, it may be appropriate to offer an initial course of treatment to assess a man’s response. If an improvement is not seen, then treatment should be discontinued.

Some studies have indicated an initial significant increase in maximum urinary flow rate which then decreased with time, presumably due to development of tolerance or to a dynamic re-balancing of pressure flow relationships (Chapple 1995). Other studies showed a maintenance of improved urinary flow rate for up to 24 and 42 months (Lepor et al 1992a).

10.2.2 Terazosin

Terazosin is a long-acting $\alpha_1$-adrenergic blocking agent used to treat hypertension and LUTS.

In a 12-month RCT with 976 patients on terazosin and 973 on placebo, there was a mean improvement in symptom scores of 7.6 for terazosin (20.1 reduced to 12.5 — a 37.8% improvement) and 3.7 for placebo (20.1 reduced to 16.4 — an 18.4% improvement), and a similar improvement in the quality-of-life scores (Roehrborn et al 1996b). Peak flow rate was only measured in a subset of the patients but there was an improvement of 2.2 mL per second after terazosin and 0.8 mL
per second after placebo \( (P<0.05) \). Statistically significant improvements were seen in all outcome measures by four weeks.

In a further 12-month randomised controlled study, where 1229 men were treated with either placebo, finasteride, terazosin or a combination of terazosin and finasteride, 82% completed the 12-month evaluation (Lepor et al 1996). Using the AUA symptom score, the one-year decrease in scores were 2.6, 3.2, 6.1 and 6.2 respectively. The changes for terazosin and the combination were statistically significantly different from placebo and finasteride alone. Of the men on the active agents, 4.8% to 7.8% discontinued medication because of adverse effects.

Eligibility criteria included a symptom score of at least 8 and a PFR of 4–15 mL per second. The mean prostate volume at baseline, determined by TRUS, ranged from 36.2 mL to 38.4 mL. Although the lowest symptom score was only reached at 13 weeks after starting terazosin and combination treatment, all responders had demonstrated a significant symptom score improvement by four weeks.

This study suggests that in the cohort of men in this study, there was no benefit from combining terazosin with finasteride over using terazosin alone. It should be emphasised that the mean prostatic volume in this study was considerably less than in the finasteride studies reporting symptom improvement (see Section 10.3). More data are required regarding the efficacy of terazosin, singly or in combination with finasteride in men with larger volume prostates.

The findings of these two studies suggest that the magnitude of mean symptom score improvement for men taking terazosin is both statistically and clinically significant. Barry et al (1995) reported that a 3-point change in AUA symptom index was perceived by patients as subjectively apparent improvement.

These studies do not identify the necessary duration of terazosin therapy. It has been assumed that the duration of any pharmacological therapy should be indefinite in order to maintain optimal benefit. This does not however take into account the natural history of
uncomplicated LUTS (Section 2.5) with 30% of men showing improvement in symptoms over time without treatment. Taking the potential for improvement into account, it may be appropriate to discontinue medication after a period of time to see if the severe bother recurs. This aspect of pharmacological therapy requires further investigation.

Although there have been no studies randomising men with LUTS to terazosin therapy or surgery, the magnitude of symptom score improvement with this drug therapy is much less than for men with a successful outcome following surgery. Many men who have successful surgical intervention consider that they have no residual symptoms. That is, that they are completely cured. On the other hand, most men taking pharmacological therapy continue to have some, albeit less severe, symptoms. While this does not minimise the potential benefits of terazosin therapy, only an individual man can judge whether the degree of symptom and bother improvement is likely to be adequate for his circumstance. Thus it is likely that a man with moderate bother will derive more benefit from terazosin therapy than one who is severely bothered.

A number of other studies have been reported regarding terazosin (Jackson 1996). None have the length of follow-up or large numbers of the two studies quoted above.

Dosage for terazosin

Tablets: 2 mg, 5 mg or 10 mg

The dose is adjusted according to the individual response. Initially 1 mg is given at bedtime for four days to minimise the potential for severe hypotensive effects. Then 1 mg in the morning for the next three days followed by 2 mg every morning for the next seven days, 5 mg every morning for seven days and 5–10 mg in the mornings.

Side effects

Reported side effects include:
Dizziness (reported in 1.6–19% of patients), headaches (reported in up to 13% of patients), postural hypotension, palpitations, oedema (0.8%), tachycardia (0.6%), weight gain (0.6%), asthenia (2.8%), nausea, dry mouth, lack of energy and weakness, erectile dysfunction, drowsiness and syncope (Lepor 1995, Brawer et al 1993, Fabricius et al 1990, Roehrborn et al 1996b).

Approximately 10% of patients have been shown to stop treatment because of side effects (Lepor et al 1992a). The mean probability of mild adverse effects from terazosin is 13.7% compared to 11.6% for placebo. For severe effects the probability is 5.2% for terazosin compared to 5% for placebo (McConnell et al 1994).

**Key points — terazosin**

- The data suggest that changes in the degree of bother and symptom index should be assessable by four weeks of treatment although maximum response may take up to 13 weeks. Men who demonstrate no significant improvement in these indices should have their treatment discontinued.
- The symptomatic impact of terazosin is not as great as surgical measures. Only an individual man can judge whether the degree of symptom and bother improvement is likely to be adequate for his circumstance. LUTS is usually not completely eradicated.

**Guideline — terazosin**

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Terazosin has been shown to be a moderately effective agent in reducing the degree of bother caused by uncomplicated LUTS.</th>
</tr>
</thead>
</table>
10.2.3 Prazosin

Prazosin is an $\alpha_1$-adrenergic blocker which causes a decrease in total peripheral resistance. It has a short half-life of 2–3 hours so must be given at least twice during the day. There are no long-term RCTs demonstrating a beneficial effect of prazosin on LUTS, and short-term trials have few patients and report contradictory outcomes. Support for its use is based on the RCTs for terazosin and the similarity of the two drugs.

Early trials were of 2–4 weeks duration and had between 8 and 55 patients enrolled (reviewed by McConnell 1994, Chapple 1995, Eri and Tveter 1995). The overall short-term response suggested an improvement in symptoms but the statistical significance varied between papers. There was a small change in PFR.

A 12-week RCT with a double-blind parallel group found that the maximum flow rate improved and that there was a 19% reduction in micturition pressure but no improvement in diary card data or subjective assessment of urinary frequency (Chapple et al 1992). The study reports that the investigators evaluated the overall efficacy of the treatment as being significantly better than with placebo, although the methods used are not specified. The patients’ and the clinicians’ assessment of the efficacy seem to contradict each other.

The same group compared TURP and medication with prazosin directly (Chapple et al 1993). Fifty-eight normotensive males on a 12-week double-blind placebo controlled trial were given 2 mg prazosin twice daily. At the end of this time 40 elected to undergo TURP. Pre- and postoperative symptom scores were available for 14 placebo-treated and 14 prazosin-treated patients. There was no difference in flow rates between the placebo or prazosin groups. There was a significant improvement in flow rates, and particularly in symptom scores after TURP. The patients’ assessment suggested that more than 95% favoured the results of surgery.

Similarly, a study aimed at general practice patients studied prazosin for 4, 8 and 12 weeks (Steven et al 1993). Patients were given screening
questions as well as an analogue rating scale ranging from ‘no problems at all’ to ‘total blockage’. They found a small improvement in symptom scores at four weeks only and no statistically significant differences at 8 or 12 weeks, but an improvement as shown by the analogue rating scale at all time-points. The authors assume that this scale has greater validity in providing an indication of response to treatment.

**Dosage for prazosin**

Tablets: 2 mg or 5 mg

It is recommended that 0.5 mg be given twice daily for 3–7 days, then the dose adjusted according to clinical response up to 2 mg twice daily.

**Side effects**

Reported side effects include:

- Dizziness, headaches (reported in up to 13% of patients), postural hypotension, palpitations, oedema, nausea, dry mouth, lack of energy and weakness, erectile dysfunction and drowsiness (Chapple et al 1992).

Standing and lying blood pressure should be carefully monitored during starting and adjustment of doses, and assessed monthly, as it may cause syncope and sudden loss of consciousness. It may exacerbate angina.

It is recommended that the dosage be gradually increased from minimal levels, to minimise the cardiovascular side effects, and that assessment of bother and symptom index be performed at three and six weeks after commencing the drug. If there is no improvement in these indices by six weeks, the treatment should be discontinued.
Key point — prazosin

While there is considerable anecdotal evidence that prazosin can have a symptomatic benefit for men with uncomplicated LUTS, there is no convincing scientific evidence to support this.

Guideline — prazosin

Before starting a course of prazosin medication, men should be fully informed of the lack of evidence supporting the efficacy of this drug.

<table>
<thead>
<tr>
<th>Guideline — prazosin</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before starting a course of prazosin medication, men should be fully informed of the lack of evidence supporting the efficacy of this drug.</td>
<td>IV-2</td>
</tr>
</tbody>
</table>

10.3 Alpha-reductase inhibitor — finasteride

The enzyme 5-α-reductase converts testosterone to dihydroxytestosterone (DHT), its active form in the prostate, essential for prostate growth and differentiation (Imperato-McGinley 1994). 5-α-reductase inhibitors block this conversion resulting in decreased levels of DHT in the prostate. The rationale for treatment is that lowering the DHT leads to a reduction in the volume of the prostate and so reduces the mechanical factors of urethral outflow resistance.

RCTs show a slight but statistically significant improvement in symptom scores with finasteride compared to placebo (Stoner 1993, Nacey et al 1995, Andersen et al 1995). Subsequent 24 and 36-month extension studies showed a maintenance of the effect, although only 55% and 45% of the original treated patients were followed up (Stoner 1994a). Randomised controlled trials have shown that the effect of finasteride on symptom scores is not seen until at least 6–9 months after starting treatment (Stoner 1994b, Andersen et al 1995). Short-term studies, looking at 19 finasteride and 17 placebo patients for six months, found no significant differences in symptom scores partly because there was a 27% improvement in the placebo arm (Tammela
and Kontturi 1993). It is likely that the maximum effect of the drug may occur beyond one year of treatment as the symptom scores continue to improve in some studies (Kirby et al 1992, Stoner 1994b). Similarly, PSA levels decrease following finasteride treatment and continue to decline after 12 months of treatment.

It is apparent that symptom improvement as a result of finasteride treatment can only be expected in 25–33% of the men enrolled in RCTs (Nacey et al 1995). This may explain the relatively high drop-out rate seen in many of the study extensions.

Studies of 12 months or longer demonstrate a symptom score improvement of between 13–21% following finasteride and 1.5–13.5% following placebo (Stoner 1994b, Nacey et al 1995, Andersen et al 1995). Patients on finasteride showed up to a 30% drop in prostate volume and a 6% drop with placebo. Improvements in PFR for men on finasteride range from 1.4 to 2.7 mL per second after 6–24 months treatment and 2.3–5.2 mL per second in studies of 36 months or more. The placebo response ranges from a drop of 1.1 mL per second to a rise of 1.1 mL per second. The open extension studies which are assumed to follow responders only, show an improvement of 30–45% in symptom scores (Kirby et al 1993, Geller 1995).

The two studies most relevant to an assessment of the benefits of finasteride are those by Lepor et al 1996 and Boyle et al 1996.

The data from the study by Lepor et al has been discussed above (Section 10.2.2). There was no statistically significant improvement in symptom scores for the men on finasteride when compared with placebo. Similarly there was no difference in benefit between the men on terazosin alone and those on a combination of terazosin and finasteride. In this study, finasteride did not appear to be an effective agent in the management of LUTS. It should be noted however that the mean baseline volume of the prostates in this study ranged from 36.2 mL to 38.4 mL.

More recently Boyle et al (1996) have published a meta-analysis of three published randomised controlled trials and three as yet
unpublished trials data provided by Merck, Sharp and Dohme. The meta-analysis involves 2601 men randomised to placebo or finasteride with a minimum follow-up of 12 months. Symptom score assessment was using a quasi-IPSS index with a maximum score of 30 which compares to a maximum score of 36 for the AUA symptom score index.

Analysis was undertaken in subsets based on the initial prostate size determined by transrectal ultrasound or MRI studies (paper quotes size in grams). While there was always a benefit from finasteride therapy against placebo only men with an initial prostate size greater than 40 grams had a statistically significant improvement when compared to placebo. Using the quasi-IPSS score, the mean benefits range from 2.52 points for baseline prostate volumes of 40–49 mL to 2.82 for prostate larger than 60 grams (or 60 mL in terms of these guidelines). Similar placebo improvements were 1.14 and 1.06 respectively.

The authors pointed out that Barry et al (1995) found that three AUA symptom score points were perceived by men to be subjectively perceptible. As the quasi-IPSS index has a 30-point maximum and the AUA score a 35-point maximum, they stated that the 2.82 point mean score improvement for prostate size greater than 60 grams was clinically perceptible to the man.

The working party acknowledges that a Level I study has demonstrated that finasteride can produce a statistically significant improvement in symptom scores when it is used to treat men with a prostate volume of greater than 40 grams (or 40 mL). Whether the improvement in symptom scores translates into a clinically appreciable improvement can only be assessed on the basis of the data presented above. Only an individual man can decide whether the potential benefits, as outlined, justify a trial of the medication.

It seems clear from the data that a minimum six-month period of therapy is necessary before the potential benefits can be assessed. It is still unclear when the lowest symptom score is actually reached. Current recommendations state that therapy needs to be continued long term for the benefit to be maintained. As already discussed for terazosin (Section 10.2.2), these recommendations do not take into
account the natural history of LUTS. Thus the need for continuous long-term therapy remains unproven.

It would therefore seem that finasteride is an active agent in the treatment of LUTS but the magnitude of the clinical benefit is still the subject of debate. The current data suggest, however, that it should only be used in men with a prostate size of greater than 40 grams. Neither DRE nor cystoscopic estimation of prostate urethral length is sufficiently precise to estimate prostate size (see Section 5.3). These guidelines recommend that it would be necessary to perform a transrectal ultrasound (TRUS) or MRI for estimation of prostate volume to advise men whether they are likely to benefit from finasteride therapy.

**Dosage for finasteride**

Tablets: 5 mg

One 5 mg tablet daily.

**Side effects**

Reported side effects include:

Sexual dysfunction including impotence, decreased libido or decreased volume of ejaculate in up to 19% of patients (Stoner 1993, 1994a,b; Andersen et al 1995). Impotence has been reported in 3–9% of patients on finasteride and 1–5% of patients on placebo (Stoner 1994a,b; Lepor et al 1996).

The prescribing literature states that when the patient’s sexual partner is or may become pregnant, the patient should avoid exposure of his semen to her, or discontinue finasteride, because of the possibility of causing abnormalities of the external genitalia of a male fetus (MIMS 1996).
Key points — finasteride

- The data suggest that compared to placebo treatment there is only a statistically significant change in the degree of bother and symptom index after six months of therapy. It is not known when the maximum benefit will be achieved. Men who demonstrate no significant improvement in these indices after 6–9 months of treatment should have their treatment discontinued.

- The working party draws attention to the question of whether the statistically significantly improved symptom scores reported by the two major studies discussed in this section, necessarily equates to a clinically significant improvement in the severity of bother, which is the fundamental outcome sought by a man.

- The symptomatic impact of finasteride is not as great as interventional measures. Only an individual man can judge whether the degree of symptom and bother improvement is likely to be adequate for his circumstance. LUTS is usually not completely eradicated by this treatment with finasteride.

<table>
<thead>
<tr>
<th>Guideline — finasteride</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finasteride only has a statistically significant beneficial impact on the severity of LUTS if the prostate volume is greater than 40 mL. It is likely that a clinically perceptible benefit will only occur if the prostate volume is greater than 60 mL.</td>
<td>I</td>
</tr>
</tbody>
</table>

10.4 Anticholinergic medication

Most nerves in the bladder are cholinergic (ie release acetylcholine as the neurotransmitter). Bladder contraction and a rise in infravesical pressure can be produced by cholinergic agonists acting on muscarinic (visceral) receptors. Symptoms that may be associated with detrusor hyperactivity or instability, such as urge incontinence, urinary
Anecdotal evidence suggests that it is usually possible to anticipate the benefits of treatment within two to three weeks of starting medication.

There are no long-term randomised clinical trials to assess the effects of anticholinergic medication in men with LUTS. Reported studies have included small numbers of both women and men, often with detrusor hyperactivity secondary to a neuropathic bladder dysfunction, and have been designed to look for a short-term response only.

In some cases these drugs do not have any effect. Further studies are required to determine whether the failure of these agents is due to altered receptors, altered nerve function or the involvement of neurotransmitters other than anticholinergics.

Anticholinergic drugs reduce the severity and amplitude of unstable detrusor contractions. Where detrusor instability is one element underlying LUTS these drugs may permit a man’s bladder to store a greater volume of urine thereby reducing the frequency of his need to void.

If the contractility of the bladder is decreased, anticholinergic medication may result in acute urinary retention. As it is not possible to definitively identify the dynamic abnormalities which may predispose a bladder to this problem, men being offered anticholinergic medication should be warned of this potential complication and accept the risk that it may occur.

Further randomised controlled trials are needed to evaluate the effectiveness of anticholinergics in the management of men with LUTS, providing better information about dosage, side effects and duration of treatment effectiveness. Because of the possible detrimental impact of anticholinergic agents in men with acute angle glaucoma it may be inappropriate to prescribe these drugs for men with this
condition. Advice should be sought from the man’s ophthalmologist, where appropriate.

### 10.4.1 Propantheline bromide

Propantheline bromide is a quaternary amine and an antagonist of muscarinic (visceral) cholinergic receptors. The site of action of this drug is thought to be directly at the detrusor or its local innervation. It needs to be administered on an empty stomach, but even then it is difficult to predict the relationship between the oral dosage and subsequent serum levels. Its clinical effect is thus unpredictable. After an oral dose, peak levels are reached in six hours but there is considerable individual variation (Finkbeiner et al 1977, Atala and Amin 1991).

**Dosage**

Tablets: 15 mg

The usual daily dosage is 15–30 mg four times a day on an empty stomach, but the most appropriate dose is the lowest dose that is clinically effective. The maximum daily dose should not exceed 120 mg.

**Side effects**

Reported side effects include:

- Dry mouth, decreased sweating, blurred vision, heat stroke, nervousness, drowsiness, weakness, insomnia, headache, tachycardia, loss of taste, nausea, vomiting, constipation, urinary hesitancy and retention, impotence, allergic effects and ophthalmic effects.
10.4.2 Oxybutynin chloride

Oxybutynin is a tertiary amine with anticholinergic and antispasmodic action. It has a similar action to that of propantheline bromide although it is more reliably absorbed and thus its clinical efficacy is higher, with a peak plasma concentration within one hour.

Because the natural history of LUTS is variable, as discussed above, it may be appropriate to reduce the dosage of the medication or discontinue it after a period of stabilisation of the symptoms. Where the degree of bother of the symptoms increase again, the medication can be continued on a long-term basis.

Dosage

Tablets: 5 mg, scored

Usual daily dosage is 5 mg three times a day. The smallest effective dose should be used as this minimises the side effects of the drug. As it develops its clinical effect within one hour of ingestion, it can be used on an ‘as required basis’ where increased urinary frequency can be anticipated in a particular situation or at a particular time. Similarly the dosage can be scheduled at times of maximal symptomatology.

Side effects

Reported side effects include:

- Palpitations, tachycardia, vasodilation, decreased sweating, rash, constipation, decreased gastrointestinal motility, dry mouth, nausea, urinary hesitancy or retention, asthenia, dizziness, drowsiness, hallucinations, insomnia, restlessness, ophthalmic effects and impotence.

92 Management of LUTS
10.4.3 Tricyclic antidepressant agents

The tricyclic antidepressant agents have a multivalent action which includes an anticholinergic effect. The exact site of action of these drugs is unclear and it is suggested that they may act both centrally and peripherally.

The most commonly used agents are:

- imipramine
- nortriptyline
- amitriptyline

The dose should be increased slowly to minimise and to predict the development of side effects and to allow a determination of the lowest dose which is effective for the particular patient. While these drugs are usually prescribed as a once daily dosage when used for their psychotrophic action, it is unclear whether they are as effective in their role as an anticholinergic with this dosage schedule or whether they should be given through the day in divided doses. If nocturia is the principal bothersome complaint, then it may be appropriate to prescribe only a night time dosage.

**Dosage**

Tablets: 10 mg and 25 mg

The starting dose should be determined by the nature of the symptoms and the age and health of the patient. Maximum daily dose is usually 75 mg but may be exceeded depending on the clinical circumstances.

**Side effects**

Side effects that have been noted include:

- Palpitations, tachycardia, vasodilation, hypo or hypertension, myocardial infarctions, arrhythmias, heart block, stroke, confusional states, hallucinations, anxiety, dry mouth, nausea,
vomiting, constipation, blurred vision and dry eyes, difficulty voiding and acute retention, impotence, allergic reactions, bone marrow depression, gynaecomastia, impotence or libido changes, testicular swelling and altered hepatic function.

**Key point — anticholinergic agents**

While there are no studies specifically addressing the use of anticholinergic agents to treat irritative or other symptoms of LUTS, there is Level II and III evidence that these agents are effective in treating detrusor instability. Most of these studies have been conducted on women or patients with neuropathic bladders.

<table>
<thead>
<tr>
<th>Guideline — anticholinergic agents</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men with predominantly irritative symptoms, and who request pharmacological intervention, can be offered a trial of an anticholinergic agent. Such men should be informed that there is no definitive evidence that the treatment will be of benefit.</td>
<td>IV-3</td>
</tr>
</tbody>
</table>

### 10.5 Phytotherapy

Phytotherapeutic agents (plant extracts) are reported to have few side effects and provide high patient satisfaction (Fitzpatrick and Lynch 1995, Krzeski et al 1993). However, there are few randomised clinical trials and the toxicological effects are unknown (Lowe and Ku 1996).

More rigorous randomised controlled trials are needed to evaluate the effectiveness of phytotherapeutic and other over-the-counter agents in the management of men with LUTS, particularly with larger sample
sizes and independent documentation of toxicity and duration of treatment effect.

10.5.1 Serenoa repens

The agent is a purified lipid sterol extract of *Serenoa repens* produced by a patented extraction process. It appears to lower DHT levels and competitively inhibit the binding of DHT to its receptors (Carilla et al 1984).

There are several clinical papers describing the effects of extract of *S. repens*, including double-blind placebo controlled trials, but the numbers of patients range from 22 to 168 and the lengths of study range only from 28 to 90 days (Cukier et al 1985, Champault et al 1984). These are mainly non-English journals and the data have not been reviewed here (see Buck 1996).

A double-blind placebo controlled trial compared *S. repens* to placebo for three months and found a significant improvement in frequency using their own three-point scale (Descotes et al 1995). They also showed improvement in flow rates in the treatment group compared to placebo, but no difference in global efficacy, and considered that the symptom improvement was not clinically significant.

**Dosage**

Tablets: 80 mg purified standardised *S. repens* extract

Two tablets to be taken twice a day with a meal.

10.5.2 Certinin

Efficacy of certinin pollen extract was studied in 79 patients for 12 weeks (Yasumoto et al 1995). Improvement in symptom scores was from 9.6 down to 6, peak flow improved from 9.3 mL per second to 11 mL per second and PVR fell from 54.2 to 30 mL. The authors noted a
marked decrease in prostate size as measured by TRUS. Twenty-eight respondents continued for one year and had further improvements in PFR and symptom scores. No adverse reactions were identified. An RCT showed a 69% improvement in symptom scores for the active agent with only 30% improvement for placebo (Buck et al 1990).

10.5.3 *Pygeum africanum*

The agent is a bark extract from the *Pygeum africanum* tree. It has been used in clinical trials, but at varying doses (Andro and Riffaud 1995).

There are no randomised placebo controlled trials to demonstrate efficacy.

10.5.4 Beta-sitosterol

An RCT of beta-sitosterol looked at 200 patients (Berges et al 1995). After six months, symptom scores fell by 7.4 points in the treatment group and 2.1 in the placebo group. There were no severe adverse reactions and no treatment effects were seen until after 4 weeks of treatment. The authors note that the magnitude of the therapeutic benefit is equivalent to that seen after finasteride, but without the reduction in prostate volume.

10.5.5 Toxicity of phytotherapeutic agents

While all conventional pharmaceutical agents are subjected to stringent toxicological assessment, this is infrequently the case for phytotherapeutic agents. Possibly because these products are available through a different marketing outlet than conventional pharmaceuticals, they do not appear to be subjected to the same therapeutic assessment standards that are required of pharmaceutical products.

While this is not to imply that any specific phytotherapeutic agent poses a health hazard to those who use it, the absence of high level
toxicological data should make consumers cautious regarding their use. Although short-term usage without significant side effects may suggest that the agents are safe, it is not possible to anticipate whether the same safety will pertain with longer-term use.

**Key point — phytotherapeutic agents**

Short-term studies with few patients demonstrate that certainin pollen extract, *Serenoa repens*, and β-sitosterol may have a beneficial impact on symptom scores and flow rates. Toxicity and side effects have not been well established.

<table>
<thead>
<tr>
<th>Guideline — phytotherapeutic agents</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>The use of phytotherapeutic agents is not recommended because of the absence of long-term randomly controlled trials and the absence of reliable toxicological and safety data.</td>
<td>IV-2</td>
</tr>
</tbody>
</table>
11 Standard surgical intervention

11.1 Introduction

It has been traditionally accepted that LUTS can be due to an enlarged, hence obstructing, prostate and with surgical removal, symptoms should improve (Campbell 1996). This concept derived considerable credence from the success of prostatectomy in the treatment of urinary retention. It is now clear that there is no relationship between the degree of prostatic enlargement and the severity of LUTS or the bother it causes (Simpson et al 1996).

The relationship between LUTS and infravesical obstruction is also less convincing than was previously thought. Pressure flow studies have shown that of the men with LUTS sufficiently severe to undergo prostatectomy, only a proportion are actually obstructed (urodynamically defined). The actual incidence of such obstruction relates to the nature of the cohort of men under consideration. The three studies which were considered in Section 6.6.3 had an incidence ranging from 43% to 80% (Jensen et al 1988a, Neal et al 1989, Robertson et al 1996). Further, the nature of the symptoms (eg ‘obstructive’) do not correlate well with urodynamically defined obstruction. Urodynamically-defined obstruction is not the only cause of significantly bothersome LUTS.

A review of the ability of pressure flow studies to predict the outcome of the surgical treatment of LUTS (see Section 6.6.3) has also found the predictive value of the test result particularly wanting.
This suggests that the beneficial effect of surgery for LUTS may be achieved, in some cases at least, because of a change in factors other than the removal of prostatic tissues that may be obstructive. Similar questions are raised as to why transurethral incision of the prostate (TUIP) results in a beneficial outcome in the treatment of LUTS.

11.2 Assessing surgical data

One of the difficulties encountered in assessing studies of surgical procedures is the inability to determine the exact nature of the procedures being evaluated. While it may at first glance seem that evaluating the outcome of different studies addressing a specific operation, say TURP, should be little different than undertaking a similar evaluation of a pharmaceutical agent, in practice this is not necessarily so. Drugs have specific well-determined composition and dosage but, while the descriptive term of an operation (eg TURP, TUIP, open prostatectomy) may generically cover the usually accepted operative steps, there are many variations to the way an operation can be performed. In any event, a number of different surgeons usually contribute cases to a particular series and this makes it very unlikely that the technique used across the series is identical. As few surgical studies reported standardised or replicable procedures, many of the identified studies were unhelpful in developing these guidelines. Attempts to standardise, document and describe in detail surgical interventions are recommended in future research.

The issue of whether variations in technique have an impact on outcome remains unresolved by the current literature. One study which considered variation in technique and compared the outcome of extensive TURP compared to minimal resection, is discussed in Section 11.4, below (Aagaard et al 1994).
11.3 Indications for surgery

The variables which most reliably predict outcome of TURP are the severity of the symptoms and the degree of bother the LUTS cause the patient at presentation (Wasson et al 1995, Bruskewitz et al 1996). The relationship between these two variables and the outcome following open prostatectomy or TUIP, has not been reported. Because the outcome of TURP and TUIP is similar, at least in glands evaluated to be less than 30 grams, it is presumed that the variables of severity of symptoms and the degree of bother also predict the outcome of TUIP. While there are no data to support this contention, there is anecdotal evidence for this.

Thus surgical success is usually greatest in those patients with moderate to severe symptom levels. A significant improvement in quality-of-life measures was only found if the symptom scores were severe (Fowler et al 1988). As a consequence some authors do not advise a surgical approach for men with a mild degree of bother (Mozes et al 1996).
Guideline — indications for surgical intervention

<table>
<thead>
<tr>
<th>Surgery should only be considered for:</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• men severely bothered by their symptoms;</td>
<td>II</td>
</tr>
<tr>
<td>• men who are moderately bothered but do not improve after pharmacological management; or</td>
<td></td>
</tr>
<tr>
<td>• men who do not wish drug therapy and yet request active intervention for their LUTS.</td>
<td></td>
</tr>
</tbody>
</table>

11.4 Transurethral resection of the prostate

Transurethral resection of the prostate (TURP) is the longest-established endoscopic surgical treatment for LUTS and has, by general consensus, been considered the ‘gold standard’ of surgical management. Probably because of its historic position it has rarely been subjected to the intensive scientific scrutiny which is now demanded of newer interventional modalities. A number of studies have randomised TURP against other forms of intervention and they are discussed below.

There has been only one recent RCT comparing TURP to ‘watchful waiting’ (reassurance) and this showed that TURP offers a greater benefit with a 66% decrease in symptom scores following TURP and 38% decrease following ‘watchful waiting’ (Wasson et al 1995). Peak urinary flow (6.2 mL/second compared to 0.2 mL/second), residual urinary volume (58 mL compared to 41 mL) and bother and interference with daily living were all significantly improved. There were no differences between the two groups in sexual performance, general well-being or social activities. The numbers lost to follow-up were similar in each group but 24% of the men in the ‘watchful waiting’ group required surgery during the three-year period of the study.
The variables which best predicted the outcome of TURP were the severity of symptoms and the degree of bother suffered by patients at presentation. This was well demonstrated by a subset analysis of the men undergoing surgery in the previous study. Men with the highest symptom scores were most likely to have symptom improvement and those most bothered by their symptoms had the greatest improvement in quality of life (Bruskewitz et al 1996). This important finding has been confirmed by other authors who noted that men with mild symptoms stand little chance of benefiting from surgery. The largest decrease in bother is noted if they are severely affected to start with even though they may still be bothered after treatment (Mozes et al 1996, Doll et al 1994).

While it has been thought that men with ‘obstructive’ symptoms may have a better outcome from TURP than those with ‘irritative’ symptoms, such symptom groupings have not proved to be predictive of outcome (Flood et al 1993). No objective tests measuring physiological parameters make clinically significant contributions toward predicting the outcome of TURP (Bruskewitz et al 1996) (see Chapter 6).

Recently there has been discussion regarding the benefits of ‘full’ as compared to ‘minimal’ resection of the prostate. Full TURP gave better symptoms relief at 6–12 months follow-up than minimal TURP, but at ten years, resulted in more strictures (Aagaard et al 1994).

The AHCPR review (McConnell et al 1994) of the literature noted mean improvements in symptom scores of 85% and an increase in PFR of 9.8 mL per second following TURP. A review of papers published subsequent to the AHCPR literature analysis (McConneil et al 1994) show an improvement of 67% (range 59–87%) for symptom scores and 9.3 mL per second (range 6.2–12.2) for PFR (Jackson 1996).

Most benefits of TURP are achieved by three months and the improvement is sustained over one year (Flood et al 1993).
11.5 Transurethral incision of the prostate

Transurethral incision of the prostate (TUIP) is also referred to in the literature as bladder neck incision. There are a number of variations in surgical technique reported including two incisions at the five o’clock and seven o’clock position or one incision at the six o’clock position. The incision is usually described as being made from just proximal to the bladder neck to about the midprostatic urethra distally and through the tissues posteriorly until fat tissue is seen. These guidelines are based on the generic description of TUIP or bladder neck incision and do not account for variations in surgical technique. There are no RCTs to compare the outcomes of different techniques.

There have been a number of randomised controlled studies comparing the outcome of TURP and TUIP. All have excluded prostate glands assessed to be larger than 30 grams and some excluded glands larger than 20 grams. Some also excluded men with a middle lobe. It is important to note that the assessment of prostate size in all of these studies used either a DRE evaluation alone, or this in combination with the cystoscopic assessment of prostatic urethral length. As has previously been discussed in Section 5.3 neither of these methods of evaluation is particularly accurate or reproducible.

This suggests that there may have been considerable variation in the actual size of the prostate glands in the series discussed below. Possibly the accurate sizing of the prostate is not as essential as might be interpreted by the selection criteria of some of these studies.

These RCTs show that TURP and TUIP cause an equivalent improvement in symptom scores. The mean improvement was 75% after TURP and 70.3 after TUIP. There were no significant differences between the improvement in PFR of 8.14 mL per second (range 4–11.9 mL/sec) after TUIP and 9.17 mL per second (range 7–12 mL/sec) after TURP (Nielsen 1988, Hellstrom et al 1993, Dorflinger et al 1992, Soonawalla and Pardanani 1992, Riehmann et al 1995, Orandi 1987).

A descriptive paper of TUIP reported that 97% of patients with urinary retention recovered spontaneous micturition and 93% of patients
showed an improvement in symptom score suggesting that urinary retention is not a contraindication for TUIP (Cerruti and Tani 1994). An RCT to compare bladder neck incision (TUIP) and TURP in patients with a preoperative catheter due to acute urinary retention found a significant difference in blood transfusion and operating time in favour of TUIP, but no differences in clinical outcome (Li and Ng 1987).

There is a wide variation reported in the optimal interval between operation and the removal of the catheter. This has been studied in a prospective RCT to compare systematic removal of the catheter at the discretion of the surgeon (voiding of clear urine without irrigation) or at 24 hours after TUIP or 48 hours after TURP (Irani et al 1995). No statistically significant differences were found between the different groups.

The AHCPR guidelines noted that TUIP produced a 73% improvement in symptom scores, and a 7.2 mL per second improvement in PFR (McConnell et al 1994). A review of papers published subsequent to the AHCPR literature analysis show that the overall symptom improvement rate ranged from 45–82% and PFR improvement ranged from 3–12 mL per second.

In a study which assessed the long-term outcome of TURP and TUIP there was no difference in patient opinion of either operation ten years after the operation although there was a decline in approval after five years, for both surgical interventions (Miller et al 1992).

**Key point**

There are significant advantages for small glands of TUIP over TURP in terms of operative time, intraoperative bleeding, duration of catheter drainage, postoperative complications and hospital stay (Dorflinger et al 1992, Riehmann et al 1995).
11.6 Open prostatectomy

Current surgical dictum suggests that a TURP should remove most, if not all, of the adenomatous tissue of the prostate, using the identification of the ‘prostatic capsule’ as the peripheral limit of the resection. Thus, if this dictum is accepted, then the size of the prostate gland, and consequently the volume of the tissue to be resected, becomes a potential limiting factor in the use of TURP for these large volume glands.

One of the complications of TURP is intravenous absorption of the irrigant fluid. The volume of fluid absorbed is determined by, amongst other factors, the duration of the procedure which, in turn, relates to the volume of tissue to be resected. Further, the volume of tissue resected is also related to intraoperative blood loss and the need for transfusion (Agarwal et al 1993).

It is thus apparent that a limitation to the use of TURP is the size of the gland. While there is no absolute value of prostate volume at which TURP becomes an unacceptably hazardous procedure, very large glands with volumes of greater than 100–150 mL, and specifically where the resection is likely to take longer than 75 minutes, are usually considered best managed by open prostatectomy because of a lower mortality and morbidity rate with the open approach (Agarwal et al 1993).

Outcomes and side effects of open prostatectomy have been reviewed in detail (McConnell et al 1994). The AHCPR meta-analysis found that the median probability for symptom improvement after open prostatectomy was 98%. However, the only symptom score data was that gathered from 12 patients using a scoring system that the authors devised themselves (Castro et al 1971). The studies on open prostatectomy are significantly older than those for other surgical techniques, so that the improvements in surgical and anaesthetic technique since these data were collected should be taken into account when considering outcomes and side effects of this procedure.
One study reported a comparison of TURP and open prostatectomy based on the size of the prostate (Servadio 1992). They followed 262 TURP patients and 710 open prostatectomies and found that operating time was ten to fifteen minutes longer and hospital stay 2–3 days longer in patients having the open operation. Patients from the open prostatectomy group (3.8%) and from the TURP group (4.6%) needed re-admission for acute medical complications. Repeat surgery was needed in 2.6% of patients who had undergone open prostatectomies and 14.5% patients who had undergone TURP. The study reports that with a larger gland the total operating time for the open procedure is shorter because of the rapid enucleation of the gland.

11.7 Complications of surgery

Although there are numerous reports regarding specific complication rates following surgical intervention, most do not quote rates for all commonly occurring complications. Because of this, it is not possible to know whether the subjects in the study did not experience the particular complication or whether the investigators neither measured or reported it.

It is very likely that the incidence of specific complications will be related to the:

- selection criteria for the procedure;
- operative techniques employed;
- nature of the patient follow-up; and
- time when the study was undertaken — older series may not have had the benefit of current technology, and so on.

If a study has been prospectively designed to specifically address complication rates, the validity of the data is considerably greater.

It is also difficult to compare data that is analysed in different ways. The AHCPR guidelines quote a calculated median or mean probability for a complication to occur with 90% confidence intervals (90% CI) (McConnell et al 1994) (see Table 3).
Table 3: Complication rates following surgical management (calculated median or mean probability)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Open prostatectomy (90% CI)</th>
<th>TURP (90% CI)</th>
<th>TUIP (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrograde ejaculation</td>
<td>77.2% (46.4–95.2%)</td>
<td>73.4% (30.4–96.9%)</td>
<td>24.9% (6.1–55.1%)</td>
</tr>
<tr>
<td>Impotence</td>
<td>32.3% (17.3–50.4%)</td>
<td>13.6% (3.4–32.4%)</td>
<td>11.7% (4.0–24.4%)</td>
</tr>
<tr>
<td>Stress incontinence</td>
<td>1.9% (0.4–5.2%)</td>
<td>2.1% (1.75–2.5%)</td>
<td>1.75% (1.4–2.2%)</td>
</tr>
<tr>
<td>Total incontinence</td>
<td>0.5% (0.35–0.75%)</td>
<td>1.0% (0.7–14%)</td>
<td>0.1% (0.02–0.5%)</td>
</tr>
<tr>
<td>Urethral stricture</td>
<td>2.6% (2.8–9.4%)</td>
<td>3.1% (0.5–9.7%)</td>
<td>2.65% (1.85–9.1%)</td>
</tr>
<tr>
<td>Bladder neck contracture</td>
<td>1.8% (0.2–6.1%)</td>
<td>1.7% (1.3–2.1%)</td>
<td>0.4% (0.1–1.0%)</td>
</tr>
<tr>
<td>Mean probability mortality ≤90 days</td>
<td>2.4% (1.0–4.6%)</td>
<td>1.5% (0.5–3.3%)</td>
<td>0.7% (0.2–1.5%)</td>
</tr>
</tbody>
</table>

Notes: CI – confidence interval; TURP – transurethral resection of the prostate; TUIP – transurethral incision of the prostate.

Source: McConnell et al 1994

Data from studies published since the completion of the AHCPR literature review and evaluated for these guidelines, use the complication rates and ranges as reported by the original authors.

There is evidence to suggest that a number of factors, including surgical experience and the medical condition of the man, has an impact on the incidence of early complications. An independent audit of 12 United Kingdom hospital sites reported a statistically significant increase in the mortality rate and early complication rate in hospitals treating less than 100 patients per year compared to hospitals with more than 100 patients. Elective admissions had a lower complication rate than emergency admissions, and elderly men admitted as emergencies (especially if they had prostate cancer), were at most risk (Thorpe et al 1994).
Postoperative urinary retention has been reported in 0.5–6% of patients after TURP or TUIP (Orandi 1987, Wasson et al 1995).

There are very wide variations in the reported rates of blood transfusion during or following TURP, partly due to the lower transfusion rates since the onset of the AIDS epidemic and to improvements in technique. Rates from 2.4% (Thorpe et al 1994) to 32.4% (Koshiba et al 1995) have been reported. The latter study, however, followed up the patients for 22 years and reported that the transfusion rate fell to 3.6% once improved equipment came into use.

The intravenous absorption of isotonic glycine during TURP, may result in the ‘TURP syndrome’. This includes hyponatraemia (reduced blood sodium level), cardiorespiratory depression, confusion and occasionally coma and temporary blindness. The reported incidence is 6% (McConnell et al 1994, Soonawalla and Pardanani 1992). The risk is higher in large or very vascular glands, or those with long resection times with a reported incidence of up to 28% (Agarwal et al 1993, Mebust et al 1989). This complication has not been reported following TUIP. Recent data report the accurate monitoring of fluid absorption during TURP using ethanol-tagged irrigation fluid and the measuring of expired breath (Hahn 1991, Hulten et al 1991).

The incidence of stress incontinence or involuntary loss of urine is difficult to quantitate as most studies which actually report such an incidence do not specifically report at what time-point during follow-up the patient was assessed for this symptom.

Urgency and urgency incontinence are part of the LUTS complex. While they may be caused by an underlying outflow obstruction, it is also possible that they reflect a primary detrusor instability and this may therefore persist or become worse after surgery. Few reports are available regarding the incidence of this type of incontinence and it is therefore not possible to specify a value for this.

Total incontinence is the complete loss of voluntary control over micturition and is considered one of the most important complications influencing a treatment decision (McConnell et al 1994). Leach et al
(1987) showed that in 60.5% of a group of patients referred for management of postoperative incontinence, the major factor was bladder dysfunction.

Recently reported rates of total incontinence following TURP range from 1–38%. In one study, 38% of patients reported incontinence after TURP while 20% of the men still had some degree of incontinence at three months (Doll et al 1992). It is important to note, however, that incontinence was not included on the list of ‘surgeon reported’ complications, suggesting a significant discrepancy between the perceptions of the surgeon and the man. This also makes comparisons between studies difficult.

Surgery may cause damage to the urethra, leading to stricture formation, or of the bladder neck with consequent contracture. These complications frequently cause a deterioration in urinary symptoms and may require further surgical intervention. Recent studies report an incidence of 1–14% following TURP. One study has shown a much higher incidence of bladder neck contractures and urethral strictures following low weight TURP (Trapasso and Irwin 1994).

As noted above, the AHCPR guidelines (McConnell et al 1994) report a wide variation in the incidence of impotence following all conventional forms of surgery for LUTS. The median probability values are substantial. It is stressed that many of the studies reviewed to determine these values were undertaken a number of years ago. More recent studies, published since the AHCPR guidelines, report a low incidence of impotence following TURP.

One study used the objective parameter of a snap gauge test result to measure potency pre and postoperatively and reported an 8.3% impotence rate in men potent before surgery (Tscholli et al 1995) while a further study found that, in men less than 65 years, the risk of impotence following the resection of a small gland (<10 grams resected weight) was 7.1% but fell to 0% for larger glands (Wasson et al 1995). Another study noted that the risk of impotence was 28.1% if the capsule was breached but only 10% if this did not occur. This study also reported that men who were only partially potent before surgery
were at a great risk of becoming impotent afterwards (Hanbury and Sethia 1995).

The AHCPR guidelines reported a median probability of impotence following TUIP of 11.7% (McConnell et al 1994). It should be noted that these data were based on a meta-analysis of the incidence of impotence following surgery on only 144 men. It is also not clear in how many of the studies the preoperative potency of the men was adequately assessed. There is no reported incidence of impotence in any of the recent studies involving TUIP.

It is difficult to estimate retreatment rates because of the differences in the definition of this complication and the lengths of time men were followed in different studies. More recent reports indicate treatment failure rates at one year of 0–1.5% (Anson et al 1995, Doll et al 1992). A much higher incidence of retreatment rates of 12.9% was found in a study of prostatectomies with mean resected weights of 8 grams (Dorflinger et al 1992).

A study evaluating the incidence and mortality in men undergoing a TURP compared to age-matched controls found that neither a diagnosis of BPH nor the fact they had prostatic surgery led to an increased risk of developing carcinoma in the subsequent ten years (Hammarsten et al 1994).

11.8 Mortality rates following surgery

It has been estimated that the risk of death at age 67 within the next three months is 0.8% (US Decennial Life Tables 1990), so mortality rates of surgery for LUTS need to be higher than this to be significant.

A study using insurance claim data found a substantially higher mortality rate in TURP patients compared to those following open prostatectomy in the eight years subsequent to surgery (Roos et al 1989). This report generated an enormous amount of interest in the literature and there are now numerous studies also reporting on this specific issue.
A subsequent report that reviewed the Roos paper has suggested that concomitant heart disease may have led to the decision to perform TURPs, rather than open prostatectomies, in these patients, and that the TURP patients were older and more ill at the time of operation (Concato et al 1992).

Recent studies suggest that there is no difference in the mortality rate between TURP and open prostatectomy (Lewis et al 1992, Crowley et al 1995). Further reports found no difference between the long-term mortality for men undergoing TURP and a similar cohort of men in the general population (Fuglsig et al 1994, Koshiba et al 1995).

Mortality rates following TURP were highest in high-risk patients and the elderly (Doll et al 1992, Lewis et al 1992, Agarwal et al 1993). A raised serum creatinine (>1.6 mg/dL) was also a risk factor for a higher mortality rate (Koshiba et al 1995). Conversely, patients with no previous medical conditions had a better survival following TURP than men undergoing open prostatic procedures (Crowley et al 1995).

A medical record study of 13,815 men, analysed specifically for co-morbidity, suggested that mortality rates after TURP were close to that expected from background population rates and lower than that for open prostatectomy cases. The study presumed that open prostatectomy was only performed on fitter patients (Seagroatt 1995).

Reviews of the literature subsequent to the AHCPR report show an early mortality rate for TURP (less than 30 days) ranging from 0–3.8% and late mortality rates ranging from 1.7–8.2% (Thorpe et al 1994, Seagroatt 1995, Jackson 1996). A similar review for open prostatectomy report a 30-day mortality rate of 1.9% and 7.4% at one year (Seagroatt 1995).

### 11.9 Selection of surgical procedure

As discussed in Section 5.3, the volume of the prostate gland is one factor which determines a decision regarding open or endoscopic approach to surgery.
Key point

It is apparent that a limitation to the use of TURP is the size of the gland. While there is no absolute value of prostate volume at which TURP becomes an unacceptably hazardous procedure, very large glands with volumes of greater than 100–150 mL and where the operative time is expected to exceed 75 minutes, are usually considered best managed by open prostatectomy. The use of this approach may, however, need to be modified on the basis of the patient’s medical condition or other factors.

The guideline recommendations regarding the selection of endoscopic surgical procedures between TUIP and TURP are based on the following assumptions:

- the scientific literature reports the mean resected weight of tissue in TURP series is 27 grams (Thorpe et al 1994);

- a review of the Level II studies, comparing TURP and TUIP for glands estimated to be less than 30 grams, shows that there is no significant difference in outcome between the two procedures;

- there is some suggestion that TUIP is inappropriate where a middle lobe is present;

- there is evidence that complications after TURP are greater in glands less than 10 grams resected weight (Dorflinger et al 1992);

- there are no RCTs to determine whether TUIP on glands greater than 30 grams would offer a similar outcome to that for TURP, although there are descriptions of successful TUIPs on larger glands;

- TUIP has been demonstrated to have a shorter duration of catheterisation and hospital stay and a lower complication rate than TURP; and
• TUIP is less expensive, in health care terms, than TURP (see Chapter 14).

While TURP is currently considered the ‘gold standard’ for the surgical treatment of LUTS, there are data to suggest that TUIP should be considered the standard procedure for small prostate glands.

Where there is a middle lobe component associated with such a small gland, TUIP with a concomitant resection of this lobe may be an appropriate procedure, although there is no scientific evidence that this provides a better or worse outcome than TURP.

As there are no specific RCTs regarding the outcome of TUIP on moderate or large glands, and based on current evidence, it is considered appropriate to undertake a TURP in these men, although descriptive studies note successful outcome after TUIP of such sized glands.

<table>
<thead>
<tr>
<th>Guideline — selection of surgical procedures</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Based on currently available evidence, TUIP is an appropriate operative procedure for men with small glands (&lt;30 grams estimated weight).</td>
<td>II</td>
</tr>
<tr>
<td>• For men with glands estimated to be larger than 30 grams, or those with a middle lobe component, the current evidence favours the performance of a TURP. While it may be appropriate to offer such men a TUIP, they should be informed that there are no reports of data comparing outcomes of TUIP to TURP in such conditions.</td>
<td>II</td>
</tr>
<tr>
<td>• Open prostatectomy should be considered the procedure of choice where operative time for TURP is expected to exceed 75 minutes and where the gland is estimated to be larger than 100–150 grams.</td>
<td>III-2</td>
</tr>
</tbody>
</table>
Long-term randomised clinical trials are recommended which should be appropriately funded and designed to compare TURP and TUIP using clear and standardised eligibility criteria based on bother, standardised surgical procedures and serial outcome measures.
12 Alternative forms of treatment

12.1 Introduction

Many of the techniques directed at finding the most effective alternative surgical intervention for the management of LUTS are based on similar principles, that is, the use of heating of the prostatic tissue to varying temperatures, as follows:

**Moderate heating** (<45°C):
- produces an inflammatory reaction with lymphocyte infiltration, but no immediate cell death;
- generally produced by microwaves.

**Higher temperature heating** (>45°C):
- causes coagulative necrosis and irreversible changes to the prostate;
- results in a progressive sloughing of tissue over a period of time and subsequent cavitation of the prostate;
- may be produced by
  - microwaves,
  - laser,
  - radiofrequency, or
  - high intensity focused ultrasound (HIFU).
Evaporation of the prostatic tissue (TUEP):

- results in the most significant cavitation although there is associated coagulative necrosis and subsequent slough of tissue;
- are produced by
  - contact lasers, or
  - modifications of the standard resectoscope loop.

Other therapies involve dilatation of the prostatic urethra using a balloon dilator and the placing of stents in the prostatic urethra.

Most of the therapies use acronyms to describe the specific modality and this sometimes makes it difficult to define the exact technique being used. This also makes meaningful comparison of different therapies difficult.

The papers on which this discussion are based are RCTs or studies with a follow-up of greater than three months, in which more than 50% of the patients were available at follow-up.

### 12.2 Laser prostatectomy

The use of lasers in medicine has been popularised by the lay press as being ‘state of the art’. This encourages patients to have a similar perception and might precipitate a specific request for this form of treatment.

Numerous laser techniques are in the investigational or developmental stage and specific long-term clinical data is limited. Most use a neodymium YAG laser but because the different techniques use different probes, systems and laser doses, comparison between varying techniques is difficult (Dixon 1995a). While most papers include detailed methodology, there is frequently little information regarding the inclusion or exclusion criteria.

Laser coagulation techniques produce heating and consequent coagulation by one of two methods. The most commonly used is a
noncontact technique using side firing fibres, with 80–90 degree divergent beams at low power. Alternatively, probes can be used to heat the prostate by direct contact or by being placed in the prostate (interstitial laser therapy) (Dixon 1995b).

Laser treatment is reported to have nearly the same efficacy as TURP and its proponents described it as having a lower morbidity, especially in regard to bleeding, during and after the procedure.

### 12.2.1 Morbidity

Because laser heating of the prostate causes a coagulation effect on the tissue, the affected prostate then undergoes necrosis and this dead tissue may remain *in situ* for up to four months. The necrotic tissue is gradually passed through the urethra but during this period the majority of patients have bothersome, ‘irritative’ symptoms that are frequently not mentioned in the literature possibly because many of the reports start their post-treatment assessment at three months (Dixon 1995a).

The need for catheterisation after laser therapy is greater than that for patients treated by TURP or TUIP probably because there is no instant removal of tissue but rather swelling of the coagulated prostate. Attempts are being made to reduce both the duration of the catheterisation and the severity and duration of the irritative symptoms by the use of biodegradable stents.

The more recent use of laser treatment to vaporise the prostate tissue may result in an improvement in these parameters. Unfortunately there appears to be concomitant coagulation of the adjacent tissue resulting in some continued necrosis and persistent sloughing of material over time.

Endoscopic examination six months after treatment shows residual prostatic tissue with contiguous lateral and apical lobes in 40% of patients. There is a wide variation in tissue cavitation between studies and this appears, at least in part, to relate to the specific type of laser apparatus used. Optimisation is required for wattage settings, laser
wavelength, location of laser applications and duration of the applications (Cowles et al 1995).

12.2.2 Transurethral ultrasound guided laser prostatectomy

Transurethral ultrasound guided laser prostatectomy (TULIP) was the first laser system devised. The laser is delivered under ultrasound guidance with the probe moved distally from the bladder neck. It causes deep coagulation necrosis. Urinary drainage is usually provided by a suprapubic catheter. As TULIP can be done under analgesic sedation it is said to be especially useful for the high-risk patient. It takes a considerable time to get a subjective and objective improvement because of the prolonged period of irritative symptoms in the postoperative phase (Schulze et al 1995). Studies report low rates of blood loss and 4–25% retrograde ejaculation (Schulze et al 1995, McCulloch and Schulze 1994).

The mechanism of action is probably due to cell damage as there is a minimal change in prostate volume 24 hours after treatment but a 14-fold increase in serum PSA (Bosch et al 1994).

None of the reviewed studies followed patients for more than one year. While there is a reported overall symptom score improvement of 65.3–70.6%, there is also evidence that the early good response has only a short durability. Bosch and co-workers showed improvement for up to six months but most of the men in the study had a significant decrease in their urinary stream at or after 12 months (Bosch et al 1994).

There is a wide range of side effects reported in the literature. Side effects include 0.01% perforation of bladder wall, 0.04% epididymitis, 0.03% clot retention, 4–25% retrograde ejaculation, 1.7% impotence, 13.8% improved potency, 1% bladder neck contraction, 29% urinary tract infection and up to 5% reoperation rates.

One study quoted ‘irritative’ symptoms of urgency, dysuria and mild haematuria due to urethral oedema for 2–3 weeks (McCullough
et al 1993). Bosch noted that the ‘irritative’ symptom of urgency did not improve until six months after treatment (Bosch et al 1994).

<table>
<thead>
<tr>
<th>Guideline — transurethral ultrasound guided laser prostatectomy</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>TULiP is not recommended at present because of the lack of long-term randomised controlled trials.</td>
<td>IV-2</td>
</tr>
</tbody>
</table>

**12.2.3 Visual or endoscopic laser assisted prostatectomy**

Visual or endoscopic laser assisted prostatectomy (VLAP or ELAP) is the most widely used of the alternative therapies and has been compared directly to TURP in randomised controlled trials with follow-up periods of 12 months.

Two studies (60–75 in each arm) have reported symptom score improvement ranges from 50–66% at three months to 52–78% at 12 months (Anson et al 1995, Cowles et al 1995). Both studies reported significantly greater improvements with TURP compared to VLAP.

A more recent RCT again showed that there was no significant difference in improvement in symptom scores or PFR six months after treatment when comparing TURP and VLAP (Sengor et al 1996). This study reported early postoperative morbidity of dysuria, voiding difficulties and urinary retention, which however resolved in time.

The incidence of irritative symptoms is reported to be 41% at 4 weeks and 15% at 3 months. Other reported side effects include strictures 1.8–10%, ‘prostatism’ 2.6%, and postoperative retention between 1.2 and 30.4%. Urinary tract infection had occurred in 3–16% of patients and impotence in 5.4%. Retrograde ejaculation was reported to be 27% in one study. Reoperation rates are said to ranged from 4–18% at 12 months.
While a number of RCTs have shown similar medium-term outcomes for VLAP and TURP, there remain a number of unanswered questions.

Some of the benefits attributed to VLAP are — the short hospital stay, minimal morbidity (advantage for men on anticoagulants) and lower overall cost when compared to TURP. While the laser therapies can be used for larger glands, they have been used principally in smaller glands, just as is also seen for the TUIP cohort of patients.

Given the equivalence of TUIP to TURP in small glands, it seems more appropriate for VLAP to be compared in randomised studies to TUIP. As yet there are no such data available.

### Key points

- It is important to stress that adequate follow-up data in RCTs does not extend beyond 12 months. Any recommendation for the use of endoscopic laser assisted prostatectomy needs to include clear advice that long-term follow-up data is still lacking.

- The paucity of data in most series regarding the early morbidity following VLAP is disappointing and of concern. While most publications allude to a *significant* incidence of irritative symptoms most neglect to comment specifically on this incidence. Despite the lack of a well-documented incidence of troublesome complications, it is essential that men consider this morbidity carefully when they consider the potential benefits of VLAP over conventional surgical interventions.
There is now sufficient data to permit the use of VLAP in a clinical rather than experimental setting. It is important that men considering this form of therapy clearly understand:

- the absence of data regarding long-term efficacy (beyond 12 months);
- an undefined but significant incidence of early morbidity; and
- the probability that this therapy offers similar results to TURP and, where the gland is small, TUIP, the latter also having a low morbidity profile.

### 12.2.4 Transurethral evaporation of the prostate

Laser evaporation techniques involve contact of the laser fibre tip with the tissue and much higher power settings to evaporate and desiccate the tissue.

Transurethral electroevaporation of the prostate (TUEP) has been described as a separate entity that removes the tissue by evaporation rather than causing coagulation (Narayan et al 1994, 1995). The amount of bleeding was less with laser treatment than reported for TURP, but once the catheter was removed, 28% failed to void. The authors noted that the current delivery systems for lasers are still being developed and that only small glands should be treated.

Narayan et al (1995) compared VLAP with TUEP directly in an RCT. They found that there was little difference between the improvement in either group except that PFR improved significantly more after evaporation. VLAP had much higher reoperation rates (16% versus 0%) and higher urinary retention rates (25% versus 6.3%).
12.2.5 Transurethral balloon laser thermotherapy

Transurethral balloon laser thermotherapy (TUBAL-T) involves a urethral cooling system, a balloon catheter and an irradiating laser moving through 360 degrees. It causes deep necrosis and coagulation of the prostate but preserves the urethral mucosa. One study reports that 88% of patients had a 50% or more improvement in symptom scores (Furuya et al 1995).

12.3 Microwaves

12.3.1 Transrectal or transurethral hyperthermia

Hyperthermia involves temperatures of above body temperature but less than 45°C. It produces an inflammatory reaction with lymphocyte infiltration, but no immediate cell death. The microwaves may be delivered either transrectally or via the transurethral route.
Transurethral hyperthermia is performed under sedation and the urethra is cooled with water to reduce pain. It involves a single treatment. Transrectal hyperthermia involves multiple sessions often over several weeks.

Most trials report clinical benefit for symptomatic relief but no change in urodynamic parameters. The reported studies have largely been nonrandomised and uncontrolled.

A study that compared hyperthermia to sham treatment where the microwave was not activated, showed a subjective improvement in 33% of the sham-treated patients but with no improvement in objective parameters at three months (Zerbib et al 1992). Sixty eight (68%) of the treated patients reported improvement (subjective). Of these, an objective improvement could be demonstrated for 53%. There was a subjective improvement in 68% of treated patients and an objective improvement in 53%.

Another study compared the transrectal and transurethral routes with their respective sham controls and found little significant difference in response between groups (Abbou et al 1994, 1995). Withdrawals caused by worsening symptoms were 17–23% for the treatment groups and 17–38% in the sham groups.

<table>
<thead>
<tr>
<th>Guideline — transrectal or transurethral hyperthermia</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>The use of transrectal or transurethral hyperthermia is not recommended at present because of the lack of data from long-term randomised controlled trials.</td>
<td>IV-3</td>
</tr>
</tbody>
</table>

### 12.3.2 Transurethral microwave thermotherapy

Transurethral microwave thermotherapy (TUMT) results in coagulative necrosis and irreversible changes to the prostate and uses temperatures...
above 45°C (Goldfarb et al 1995). Treatment can be performed on an outpatient basis with little or no sedation or analgesia making it a potentially attractive alternative to other forms of intervention.

The mechanisms of microwave action is unknown as there is no change in the overall size of the prostate and little evidence of decrease in periurethral tissue. Cavitation does not occur with lower power settings (Carter et al 1991) but a recent report using higher settings have found cavitation to occur (de la Rosette et al 1996). It is postulated that microwave therapy acts by destroying the $\alpha_1$-adrenoceptors in the bladder neck and prostatic urethra, causing an increased elasticity in the prostatic urethra. Urethral and rectal temperatures need to be monitored for safety and the position of the probe monitored using TRUS.

TUMT has been compared to sham treatments (where the equipment is not activated) in a number of studies, most showing a 40–70% improvement in symptom scores for the active treatment compared to 10–20% for the sham treatment (Bdesha et al 1993, Ogden et al 1993, de Wildt et al 1996). Two studies which compared TUMT to placebo treatment did, however, unexpectedly show a greater improvement for the inactive management ranging from 32% to 54% (de la Rosette et al 1994, Mulvin et al 1994).

In an RCT comparing TUMT with TURP, 37 men were treated with TUMT and 32 by TURP and followed to 24 months. Mean symptom score reduction (improvement) at 24 months was 12.1–2.6 for TUMT and from 13.6–1.1 for TURP. Clearly there is no difference although it should be recognised that the initial severity of the symptoms was only mild to moderate (Dahlstrand et al 1995).

A recent multicentre case-series of 116 men treated with TUMT attempted to correlate pretreatment urodynamic parameters with similar observations after treatment. While such findings are not considered particularly relevant to these guidelines, the study reports an improvement in IPSS from a mean baseline value of 17.5 to 7.9 at six months and 7.1 at one year. At six months 90% of men were assessable and 58% at one year. Irritative voiding complaints were noted in a
‘large number’ (incidence not reported) of patients for up to 2–4 weeks (de la Rosette et al 1996).

While the data regarding outcome of treatment with TUMT are limited in number there does appear to be a significant improvement in symptoms when compared to sham treatments. The impact on symptom scores is similar to TURP in one study.

**Key point**

While TUMT treatment shows promise, there is yet insufficient data from large RCTs to permit strong endorsement of this intervention. Because of the ease of administration it may be appropriate for men to consider this form of therapy (having been informed of the limited data available regarding long-term efficacy and short and medium-term morbidity).

<table>
<thead>
<tr>
<th>Guideline — transurethral microwave thermotherapy</th>
<th>Level of evidence</th>
</tr>
</thead>
</table>
| There is now sufficient data to permit the use of TUMT in a clinical rather than experimental setting. It is important, however, that men considering this form of therapy clearly understand:  
  • the absence of large studies showing a long-term efficacy; and  
  • an undefined but 'significant' incidence of early morbidity. | II |

**12.4 Transurethral vaporisation of prostate**

The transurethral vaporisation of the prostate (TUVP) involves the use of a standard resectoscope but with a modified electrical loop and
diathermy power settings which deliver 30–50% higher power than in a routine TURP. The tissue is vaporised as the loop passes through the tissue in a similar mechanism to laser TUEP. A study to compare TUVP and TUEP showed an improvement in both groups compared to baseline, but no difference between them. Postoperative symptoms were found in 83% of TUEP patients but in only 6.9% of the TUVP group (Kaplan and Te 1995).

More data will be important as there are potential hazards, such as burns, nerve and muscle stimulation and urethral strictures, from using high frequency power. There are now data that reveal that the power used by TUVP may be ten times greater than that needed for TURP. Whether this will result in a greater incidence of complications remains to be determined.

<table>
<thead>
<tr>
<th>Guideline — transurethral vaporisation of prostate</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>The use of TUVP is not recommended at present because of the lack of long-term RCTs. More data will be important as there are potential hazards from using high frequency power, such as burns, nerve and muscle stimulation and urethral strictures.</td>
<td>IV-3</td>
</tr>
</tbody>
</table>

### 12.5 Transurethral needle ablation

Transurethral needle ablation (TUNA) involves the transmission of low frequency radio waves through needles placed directly into the prostatic lobes. It produces well-defined necrotic lesions and spares the urethra (Dixon 1995b). There are only as yet preliminary reports available for review. These are based on few patients with very short follow-up periods and high attrition rates but the data suggests minimal complications. Further RCTs are presently under way to assess the value of this therapy.
12.6 High intensity focused ultrasound

High intensity focused ultrasound (HIFU) uses a focused beam of ultrasound to produce temperatures of between 80–200°C at selected depths in the prostate leaving intervening tissues undamaged. It is positioned using ultrasound.

Phase II clinical trials (still experimental) on limited numbers of patients have been performed using this technique (Devonec et al 1993, Madersbacher et al 1994, Bührle et al 1994). Symptom scores and PFR are reported to be reduced by 55% and 47% respectively after one year. A catheter is required for at least six days postoperatively as otherwise all patients develop retention. The procedure requires a general anaesthetic but no manipulation of the urethra or prostate.

12.7 Prostatic stents

Stents function by holding the prostatic lobes apart. Many different devices exist such as the Urolume endoprosthesis, the Titan
intraprostatic stent, the Prostakath and the Urospiral (Smith et al 1996). Some are intended for permanent implantation with the urethral mucosa overgrowing the material of the stent (Uroleum, Titan stent). Others are considered to be temporary devices such as the Prostakath or Urospiral. These do not become incorporated into the urethral wall and may be either removable or biodegradable (Kletscher and Oesterling 1995).

Voiding problems persist in approximately 30% of patients with stents. The stents can be difficult to put in place, can migrate and 20% will require removal (Smith et al 1996). They are used for patients who would need permanent catheter drainage because they are unsuitable for surgery, refuse long-term catheterisation or decline operations even when medical therapy has failed.

<table>
<thead>
<tr>
<th>Guideline — prostatic stents</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stents may have a role in the management of patients with urinary retention or with severe LUTS who are in poor general health and may not tolerate any form of surgical intervention.</td>
<td>IV-2</td>
</tr>
</tbody>
</table>

12.8 Balloon dilatation

Balloon dilatation involves stretching the prostatic urethra by the inflation of a balloon. Tears or splits are produced through the stroma along the length of the prostate but not through the bladder neck. Some patients in early series had effects only lasting six weeks, and it was proposed that the commissures of the prostate need to be ruptured for the effect to be maintained.

Short-term trials show an initial improvement in symptom scores but there is evidence that the effect may not be long lasting. One study of patients with prostates of less than 40 mL measured by TRUS, reported that 87% of patients had a 50% or greater decrease in symptom scores
and 49% had a 50% or greater improvement in PFR. Only 56% of patients were available for follow-up (Moseley 1992).

Another study compared balloon dilatation with TUIP and found equivalent early effects on symptom scores. Of the men treated with the balloon, 75% of those available for evaluation had recurrences of symptoms while 20% of those who had a TUIP developed recurrent symptoms 44 months after treatment (Chiou et al 1994). Similar effects were seen in a study which compared balloon dilatation to TURP (Donatucci et al 1993). Both procedures improved symptom scores although only TURP improved flow rates. The balloon-treated patients all had a return of symptoms to preoperative levels. The study concluded that balloon dilatation only produces temporary relief of symptoms. Lepor found that there was no difference between the effects of balloon dilatation and the diagnostic test of cystoscopy (Lepor et al 1992b).

<table>
<thead>
<tr>
<th>Guideline — balloon dilatation</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>The use of balloon dilatation is not recommended. Trials have been of short duration with few patients but suggest that there is little response and this is not maintained.</td>
<td>II</td>
</tr>
</tbody>
</table>
### 12.9 Summary of alternative treatments

**Key point**

The extensive literature review demonstrated that some of the outcomes of alternative therapies are promising. However, there remain many unanswered questions regarding their long-term benefit when they are compared to the established and conventional surgical interventions. The review confirms that most of these procedures should continue to be considered experimental and should be evaluated using randomised controlled trials comparing sham and conventional surgical interventions.

**Research recommendation — alternative treatments**

Further randomly controlled trials are needed to evaluate the more promising of these procedures. They should be compared to conventional surgery and sham interventions.

Design of these trials should involve larger sample sizes and consider comparison with conventional surgery, standardised interventions, validated outcome measures and duration of treatment effectiveness.
13 Economic aspects

13.1 Introduction

Little research has been undertaken on the economic impact of LUTS in men. Lowe et al (1995, p 478) state that:

More than 1100 articles on BPH and its treatment have appeared in the peer-reviewed medical literature since 1989, but fewer than ten have dealt with the economic impact of the various interventions. No reports compared the costs of medical and surgical interventions for BPH despite the recent explosion of cost-effectiveness research in medicine.

In view of this situation, it is not surprising that the Australian literature on the economics of LUTS in men and its management is virtually nonexistent.

13.2 Unit costs of therapy

13.2.1 Transurethral resection of the prostate

The cost of a transurethral resection of the prostate (TURP) in the United States has been variously estimated at between US$6000 to US$10 000 depending upon the relevant Australian national diagnostic-related group (AN-DRG) and the region of the country in which the operation is performed (Holtgrewe et al 1989, Metropolitan Life Insurance Company 1993, Kabalin and Butler 1995). Studies in Europe, the United Kingdom, Sweden and Australia have estimated the cost of a TURP generally to be in the range $2000–$3500 (Australian
dollars, 1991 prices) (Ellis 1991, Holtgrewe et al 1992, Cuckow 1992, Gordon 1994, Hugosson et al 1993). Taken together, the results suggest that the unit cost of a TURP in the United States may be two to three times higher than in Australia or Europe.

These unit cost estimates do not include the cost of managing any complications associated with the procedure or the cost of reoperation in a proportion of patients. Within one year of the initial operation, the costs of complications or reoperation have been found to be about 5% of the initial cost of the TURP (Weis et al 1993).

In the third version of the AN-DRGs, there are three specific DRGs for TURP (DRGs 604–606). The difference between them relates to the age of the patient and the presence or otherwise of any complications or co-morbidities. In public acute hospitals in Australia in 1993–94, the weighted average cost per hospital discharge across these three DRGs was $3400 and the average length of stay was six days (Commonwealth Department of Health and Family Services 1996, p 129). As this cost is based on public hospital data, it includes all hospital and medical charges; a man opting to be treated as a public patient in a public hospital receives treatment at no charge.

The average fee charged by private medical practitioners for TURPs funded under Medicare in 1994–95 (item number 37203) was $992. The current Medicare Benefits Schedule fee is $850. In addition to bearing some out-of-pocket expense for the surgeon’s fee, a man choosing to be treated as a private patient would also face expenses associated with other medical fees (for example, for the anaesthetist) and hospital and pharmaceutical charges. The exact out-of-pocket expense incurred will depend upon the level of private insurance cover held.

**13.2.2 Open prostatectomy**

Open prostatectomy is a much less common procedure than TURP for the management of LUTS and it is more difficult to find evidence on the cost of this procedure. Weis et al (1993) report that, in a sample of
14 480 men who underwent TURP or open prostatectomy under United States Medicare in 1986 or 1987, only 5.2% had open prostatectomy and the average charge for the procedure (including hospital and professional charges) was US$10 223. This compared with the average charge for a TURP in that group of men of US$6501. The cost of complications or reoperation within one year of the initial open prostatectomy amounted to 2.5% of the cost of the initial procedure.

In the AN-DRGs (ver. 3.0), there are no DRGs which are unique to open prostatectomy. DRGs 558–559, which cover prostatectomy with or without complications or co-morbidities, include not only open prostatectomy but also radical prostatectomy and perineal prostatectomy. The weighted average cost per hospital discharge in public acute hospitals in Australia in 1993–94 across these two DRGs was $4492 with an average length of stay of nine days.

The average fee charged by private medical practitioners for open prostatectomy funded under Medicare in 1994–95 (item number 37200) was $928. The current Medicare Benefits Schedule fee is $746. As with TURP, for those who choose to be treated as private patients, out-of-pocket expenses will also be incurred for other medical, hospital and pharmaceutical charges. The exact out-of-pocket expense will depend upon the level of private insurance cover held.

**13.2.3 Transurethral incision of the prostate**

Comparisons of the cost of transurethral incision of the prostate (TUIP) to the cost of TURP and other surgical interventions is scant. Hugosson et al (1993) reported the costs of TUIP in 30 cases treated as outpatients under local anaesthesia, finding that it was less than one quarter as expensive as TURP in the same hospital. However, the subsequent cost of management of treatment failures was not included.

In the AN-DRGs (ver. 3.0), there is no specific DRG for TUIP. DRGs 556–557 encompass a range of minor bladder procedures including TUIP, but TUIP is also included in a number of other DRGs. The average length of stay for TUIPs provided within these two DRGs in
public acute hospitals in 1993–94 was three days. As the average cost per day for these two DRGs was $674, this suggests that the unit cost of this procedure in public hospitals is around $2000.

The average fee charged by private medical practitioners for TUIP funded under Medicare in 1994–95 (item number 36854) was $408. The current Medicare Benefits Schedule fee is $343. The average fee charged is considerably lower than for TURP and open prostatectomy. When combined with a potentially lower length of stay in hospital, this suggests that TUIP should be a considerably less expensive procedure in Australia than TURP or open prostatectomy.

13.2.4 Pharmacotherapy

While the unit cost of drugs used in the management of LUTS can be obtained, the cost of a course of therapy will depend upon how long a patient remains on that therapy. In Australia, the $\alpha$-adrenergic blocker, prazosin (see Section 10.2.3), is listed on the Pharmaceutical Benefits Scheme. The annual cost of this drug when used as a continuing therapy for LUTS is about $135. Finasteride and terazosin are not listed on the Pharmaceutical Benefits Schedule. The annual cost of finasteride is approximately $1400 and for terazosin from $600 to $1400 depending on the dose used.

13.3 Economic burden of illness

Cost-of-illness studies attempt to estimate the economic burden of illness on society. The costs included are usually categorised according to whether they are direct costs (the costs of managing or treating the illness), indirect costs (the lost output or earnings as a result of lost productivity due to the illness) and intangible costs (the pain and suffering caused by the illness).

Several cost-of-illness studies of BPH have been undertaken overseas (Drummond et al 1993 for the United Kingdom; Scott and Scott 1993 for New Zealand; and Ahlstrand et al 1995 for Sweden). An
unpublished study is also available for Australia (Butler et al 1993). All of these studies provide estimates of the direct and indirect costs of BPH in one year in the respective countries. Indirect costs generally account for 15–25% of the total cost of the illness. Within the direct costs, the cost of hospital care is the largest component ranging from 54% to 82% of total direct costs. The Australian study found a total direct and indirect cost of illness of $95.8 million based on data in the late 1980s. This is not a large cost-of-illness estimate in comparison with the cost of treatments for other diseases. However, further research undertaken in the course of developing the present guidelines (discussed later in this chapter) suggests that the cost of LUTS in Australia is now substantially higher than previously estimated.

All the cost-of-illness studies relate to treated BPH and hence are influenced by the extent to which men seek treatment for their condition. This may explain the wide variation in the per capita cost-of-illness estimates from these studies, which range from $2.47 per head of population (UK) to $6.19 per head (Sweden) (Australian dollars, 1991 prices).

13.4 Economic evaluations of treatment options

Evaluative studies are concerned with comparing the costs and health outcomes of two or more interventions for an illness. As such, the quality of these studies is heavily dependent on the quality of the evidence on the effectiveness of the interventions under consideration.

An additional complication in evaluating interventions for LUTS is that men not uncommonly change between therapies, depending upon the symptom improvement experienced with a particular therapy. A man may commence with reassurance/advice (‘watchful waiting’) from his medical practitioner, switch to pharmacotherapy after six months if symptom improvement is not forthcoming, and finally opt for surgery if drug therapy is also unsuccessful.
The few economic evaluations of therapy in this area have attempted to incorporate this behaviour into the estimates of costs and outcomes associated with various choices of initial therapy. The results reported on the costs of treatment in these studies then include not only the cost of that initial therapy but also subsequent therapies which have been chosen if the initial therapy failed. The AHCPR guidelines, for example, report costs of therapy over a two-year time-frame, estimating that the cost associated with choice of reassurance as initial therapy was US$1802, finasteride US$2114, α-adrenergic blockers US$2240, TURP US$8966 and open prostatectomy US$12 857 (McConnell et al 1994, Table 26). These cost estimates include the cost of complications, reoperation and cross-over to other therapies. No conclusion can be drawn from these estimates, however, as to the appropriate choice of therapy on economic grounds, as comparative data on the effectiveness of the different therapies over the two-year time-frame are not included in the analysis.

Using an approach similar to that employed in the AHCPR guidelines, Lowe et al (1995) have undertaken a cost-effectiveness analysis of terazosin, finasteride and TURP for men with moderate to severe BPH. The time-frame for this analysis was two years. Cross-over between therapies was built into their model in terms of both the costs and effectiveness of therapy. Health outcome was measured in terms of the average number of months of successful treatment and the number of days of work or other customary activity lost due to side effects. They found a cost advantage in favour of initial drug therapy with all therapies showing similar treatment effects but initial TURP having a larger number of days lost due to side effects. The limitations of this study are that it does not distinguish between degrees of symptom improvement, that success rates are measured in terms of symptom scores rather than degree of bother to the patient, and that a two-year time-frame may bias costs in favour of drug therapy (which has lower costs in earlier years relative to TURP but which must be continued through time in order to sustain success).

More recently, the Canadian Coordinating Office of Health Technology Assessment (CCOHTA) undertook a cost-utility analysis of finasteride compared with watchful waiting and TURP (CCOHTA 1996, Baladi
et al 1996). As in cost-effectiveness analysis, cost–utility analysis assesses the costs and health outcomes of the interventions but, in addition, it attaches quality-of-life weights to the various possible health outcomes. The CCOHTA analysis distinguishes between men with mild, moderate and severe symptoms. The time-frame for the analysis is 15 years. The cost–utility results for any particular pairwise comparison of alternatives (finasteride vs watchful waiting, finasteride vs TURP, TURP vs watchful waiting) generally depend upon the life expectancy of the patient and the severity of symptoms. For patients with mild symptoms, commencing therapy with watchful waiting was found to be the most appropriate treatment strategy regardless of life expectancy. For patients with moderate symptoms, finasteride was found to be dominant over watchful waiting and TURP for men with a life expectancy of less than three years (‘dominant’ meaning that it was both less costly and resulted in more quality-adjusted life-years). Finasteride was also found to be dominant over TURP in the management of moderate symptoms for men with a life expectancy of less than 15 years. For men with severe symptoms, TURP was dominant over finasteride for men with a life expectancy greater than 14 years, and was more costly but resulted in more quality-adjusted life-years for men with a life expectancy less than 15 years.

In summary, this study found that, on economic grounds, the choice of finasteride as initial therapy depends upon two factors: life expectancy and severity of symptoms. The greater the life expectancy and the more severe the symptoms, the less likely it is that finasteride would be economically superior to TURP. This is because, for those who remain on finasteride, there is a recurring annual cost for the drug, and because TURP can achieve a greater degree of symptom improvement in patients with severe symptoms than is attainable with finasteride. Conversely, the lower the life expectancy and the milder the symptoms, the more likely it is that finasteride would be first-line therapy on economic grounds.

A significant limitation of this study is that long-term effectiveness data on finasteride are lacking. Consequently, the authors rely on extrapolation of short and medium-term effectiveness data in extending the time-frame to 15 years. This illustrates an important limitation in
conducting economic evaluations in this area. If a short-term time perspective is adopted in the analysis, more reliable effectiveness data are available but a bias may be created in favour of drug therapy which must be continued through time to sustain any beneficial effect. If a long-term time perspective is adopted, the cost bias is addressed but long-term effectiveness data are lacking.

The absence of long-term effectiveness data is also a problem in a cost–utility analysis undertaken by Bisonni et al (1993) where balloon dilatation is compared with TURP. The time-frame for this analysis was 11.8 years. Using a relapse rate of 43% for balloon dilatation, the authors find that balloon dilatation is less costly and results in more quality-adjusted life-years lived than TURP. The superior health outcome achieved with balloon dilatation arises because it has no associated mortality while there is a small mortality risk associated with TURP. However, the analysis also found that TURP would be economically superior if the relapse rate for balloon dilatation over 11.8 years was 83% or higher. As discussed in Section 12.8 of these guidelines, trials have been of short duration with few patients but suggest that there is little response and that this is not maintained.

13.5 Potential economic impact of guidelines

Virtually no research on economic aspects of LUTS in men has been undertaken in Australia. In an attempt to provide some estimates of the potential economic impact of these guidelines for the management of LUTS in men in Australia, a prevalence-based economic model of the management of this condition in Australia for men aged 45 years and over was developed (Butler 1996). This model is based on the management pathway for men with LUTS in Australia (illustrated in Figure 2).

This pathway describes the various treatment options facing men with LUTS who seek medical advice regarding their condition. Of all men with LUTS in the community, some will visit a GP about their condition. The GP may provide reassurance and advice which in this economic model is intended to suggest that the patient is reassured but
advised to return for a further subsequent visit. Alternatively the GP may commence pharmacotherapy or refer the patient immediately to a specialist. Pharmacotherapy comprises either prazosin hydrochloride (95%) or imipramine (5%), with 75% of the patients receiving prazosin completing a full course.

If reassurance/advice or pharmacotherapy is chosen, some men will subsequently opt for no additional treatment either because the therapy was a success or because it failed and they decided not to continue with any other treatment. If initial treatment fails and further therapy is desired, cross-over to another therapy occurs. Such cross-over to other therapies may also occur following immediate referral to a specialist. However, the model assumes that reassurance/advice, drugs and surgery are hierarchical in that, if reassurance/advice is to be employed as a therapy, for example, it will always be chosen before drugs or surgery are selected.

For men who reach surgery as an end-point in Figure 2, the surgical options considered in the model are shown in Figure 3. The initial choice is between TURP, TUIP and open prostatectomy. Complications (bladder neck contracture, urethral stricture and urinary incontinence) following each option are included in the model, as is reoperation following TURP and the possibility that some patients will elect to have a TURP following TUIP.

The proportions of patients proceeding along each treatment pathway are also shown in Figures 2 and 3. These proportions are based on a combination of Australian evidence, overseas evidence, calibration of the projected numbers of surgical procedures and nonsurgical hospitalisations against Australian data, and consensus among members of the working party.
Figure 2  Management pathway used in model for LUTS in Australia

Notes: The figures show the proportions of patients that proceed along each pathway. For more details on 'surgery' option, see Figure 3. RA = reassurance/advice.
Source: Butler 1996
Notes: The figures show the proportions of patients that proceed along each pathway.
Source: Butcher 1996

Figure 3 Management pathway for the surgical treatment of uncomplicated LUTS, Australia
The proportion of men with LUTS who visit a GP (18%) is based on estimates of the community-based prevalence of LUTS and the number of such men who visit a GP in a year. The community-based prevalence of LUTS is derived from a recent survey of 3016 individuals in South Australia which found that 37.1% of men aged 45 years and over experienced troublesome urinary symptoms (Pinnock and Marshall 1997). Applying this survey proportion to the population of Australian men aged over 45 years as at June 1994 suggests that approximately 1 022 000 men in this age group have LUTS. The estimated proportion of these men who visit a GP is based on this prevalence estimate together with diagnosis data collected from 113 468 GP consultations in a national survey of morbidity and treatment in general practice (Bridges-Webb et al 1992). In this survey, BPH or a relevant urinary symptom was managed at 210 (0.185%) encounters. This survey proportion was then applied to the total number of GP attendances in 1993–94 to provide an estimate of the total number of men who visited a GP in that year concerning the relevant urinary symptoms (178 813). This number was then expressed as a proportion of the community-based prevalence of LUTS to give the GP visit rate among men with LUTS.

The national survey of morbidity and treatment in general practice also provides the basis for estimating the proportions of men choosing the three initial treatment options in Figure 2:

- reassurance/advice,
- pharmacotherapy (predominantly prazosin), or
- immediate referral to a specialist.

Of the 210 encounters in the survey for men aged 45 and over at which BPH or a relevant urinary symptom was diagnosed, a drug for the management of that diagnosis was prescribed at 49 (23.3%) of those encounters, while referral to a specialist occurred at 72 (34.2%) of those encounters. These proportions provide the basis for the relevant probabilities in the model in Figure 2, with the proportion opting for reassurance as initial therapy (43%) being derived as the remainder.
From this point on, it is difficult to find Australian data to inform the choice of probabilities to attach to the various branches of the management pathways in Figures 2 and 3. In their model, CCOHTA (1996) used a success rate of reassurance of 42% and further assumed that this therapy failed in another 20% of patients who did not seek further treatment. This implies 62% of patients who receive reassurance/advice will have no further treatment. This proportion has been used in the ‘no further treatment’ branches following GP-supervised reassurance in Figure 2.

The AHCPR guidelines reported a success rate for alpha blockers of 74% (McConnell et al 1994, Table 13). In the model in Figure 2, the proportion of patients opting for no additional treatment following drug therapy ranges from 70% to 90%. (Recall that ‘no additional treatment’ includes both treatment successes and treatment failures who opt not to have any additional treatment). For the surgical options (Figure 3), the complication rates used in the model for TURP and TUIP are based on those reported in Section 11.7, Table 3. The complication rates used for the three surgical options are summarised in Table 4.

<table>
<thead>
<tr>
<th>Complication</th>
<th>TURP</th>
<th>TUIP</th>
<th>Open prostatectomy(a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder neck contracture</td>
<td>1.7</td>
<td>0.4</td>
<td>1.8</td>
</tr>
<tr>
<td>Urethral stricture</td>
<td>3.1</td>
<td>2.7</td>
<td>2.6</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>3.1</td>
<td>1.9</td>
<td>2.4</td>
</tr>
<tr>
<td>TOTAL</td>
<td>7.9</td>
<td>5.0</td>
<td>6.8</td>
</tr>
</tbody>
</table>

Notes: (a) Any method. For urinary incontinence, the median for total urinary incontinence is reported.
Source: TURP and TUIP: Consensus estimates from the working party; Open prostatectomy: AHCPR guidelines (McConnell et al 1994, Tables 20 and 21).

The remaining probabilities in Figures 2 and 3 have been estimated taking into account the numbers of TURPs, TUIPs and open prostatectomies performed in Australia in 1993–94, the number of nonsurgical hospitalisations for BPH in that year, and the consensus view of the working party.
For each treatment choice in Figures 2 and 3, unit cost estimates have also been developed based upon the costs of management in Australia. In developing these estimates, the absence of data on the practice patterns of urologists was problematic. To assist in reaching consensus on these values, the working party arranged for a short questionnaire concerning urologists’ practice patterns to be distributed to urologists attending the annual meeting of the Urological Society of Australasia in Canberra in March 1996. This survey provided some useful information on the tests and investigations used by urologists in their evaluation of men with LUTS. The unit costs for each treatment option in the model are summarised in Table 5. Further details on the unit cost estimates are available in the relevant technical report on economic aspects of LUTS prepared for the working party (Butler 1996).

The estimated direct health care costs of LUTS in Australia in 1994–95 obtained from the model are summarised in Table 6. In aggregate, the direct costs are estimated to be $176.8 million, of which $115.7 million are for inpatient treatment and $61 million are for outpatient treatment. The direct costs of treatment amount to $173 per man with LUTS aged 45 years and over in the community, or $961 per man with LUTS who visits a GP. Among those who visit a GP, the cost per man is higher if immediate specialist referral occurs ($1835) than if reassurance/advice or drugs are chosen as initial therapy ($486 and $557 respectively).
Table 5: Unit cost estimates for treatment options

<table>
<thead>
<tr>
<th>Treatment option</th>
<th>Unit cost $A(a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP visit</td>
<td>58</td>
</tr>
<tr>
<td>Urological investigations</td>
<td>349</td>
</tr>
<tr>
<td>Reassurance:</td>
<td></td>
</tr>
<tr>
<td>GP-supervised</td>
<td>24</td>
</tr>
<tr>
<td>specialist-supervised</td>
<td>33</td>
</tr>
<tr>
<td>Pharmacotherapy (including medical fees):</td>
<td></td>
</tr>
<tr>
<td>GP-supervised</td>
<td>170</td>
</tr>
<tr>
<td>specialist-supervised</td>
<td>197</td>
</tr>
<tr>
<td>Surgery:</td>
<td></td>
</tr>
<tr>
<td>TURP</td>
<td>3400</td>
</tr>
<tr>
<td>TUIP</td>
<td>2034</td>
</tr>
<tr>
<td>Open prostatectomy</td>
<td>7441</td>
</tr>
<tr>
<td>Complications of surgery:</td>
<td></td>
</tr>
<tr>
<td>TURP</td>
<td>1000</td>
</tr>
<tr>
<td>TUIP</td>
<td>745</td>
</tr>
<tr>
<td>open prostatectomy</td>
<td>1052</td>
</tr>
<tr>
<td>Hospitalisation without surgery</td>
<td>1113</td>
</tr>
</tbody>
</table>

**Notes:** (a) Australian $, 1994–95 prices.

**Source:** See Butler (1996) for a detailed discussion of the sources of these estimates.
Table 6: Estimated health care costs of uncomplicated LUTS in Australia, 1994–95

<table>
<thead>
<tr>
<th>Aggregate costs</th>
<th>$A (million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total health care costs for LUTS in men</td>
<td>176.8</td>
</tr>
<tr>
<td>– for inpatient treatment</td>
<td>115.7</td>
</tr>
<tr>
<td>– for outpatient treatment</td>
<td>61.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Costs per individual</th>
<th>$A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of treatment per man with LUTS aged 45+ in the community</td>
<td>173</td>
</tr>
<tr>
<td>Cost of treatment per man with LUTS who visits a GP</td>
<td>961</td>
</tr>
<tr>
<td>– if reassurance/advice is chosen initially</td>
<td>486</td>
</tr>
<tr>
<td>– if drugs are chosen as initial therapy</td>
<td>557</td>
</tr>
<tr>
<td>– if immediate specialist referral occurs</td>
<td>1835</td>
</tr>
</tbody>
</table>

Source: Butler (1996)

The model was then used to estimate the economic impact of a number of changes in clinical practice or patient behaviour which may occur as a result of effective implementation of these guidelines. Specifically, the following are the alternative scenarios which were considered.

**Reduction in GP visit rate**

Under this scenario, additional reassurance provided to men with mild LUTS is assumed to result in a reduction in the proportion of men with LUTS visiting a GP from 18% to 17%. This scenario is coupled with two alternative responses in terms of the number of men going to surgery.

(a) The first response assumes that the proportions of men going to hospital with or without surgery in the model remain unchanged. Under this response, the cost savings in one year amount to $9.8 million, of which $6.4 million arise from a reduction in inpatient costs and $3.4 million from a reduction in non-inpatient costs.

(b) The second response assumes that the men who no longer visit their GP for LUTS are men with mild symptoms who would not have been hospitalised or had surgery anyway. Consequently there is a
compensating increase in the proportions of men hospitalised and going to surgery in the model. Under this response, the estimated cost savings amount to $3.5 million, all of which are non-inpatient costs.

**Reduction in immediate referral rate to specialists**

Under this scenario, GPs are assumed to refer fewer men with mild LUTS to specialists before providing reassurance/advice or drug therapy. A reduction in the referral rate from 34% to 32% is assumed, with a consequent increase of one percentage point each in the proportion of men choosing GP-provided reassurance/advice and GP-supervised drug therapy. Referral rates to specialists following failure of these therapies are assumed to remain unchanged. The estimated cost savings under this scenario amount to $4.8 million, of which $4.0 million arise from a reduction in inpatient costs.

**Increased use of TUIP in surgical patients**

This scenario assumes that there is a change away from TURP in favour of TUIP in men with small prostates who also satisfy the other criteria required for the use of TUIP. The proportion of surgical patients electing to have a TURP as their first operation is assumed to fall from 82% to 60%, with the proportion of men electing to have a TUIP increasing from 16% to 38%. The cost savings estimated to arise from this change amount to $7.6 million, all of which represent savings in inpatient costs.

**Reduction in the use of ultrasound and cystoscopy in managing LUTS**

In the baseline scenario, it was assumed that 5% of men visiting a GP and 37% of men visiting a specialist had ultrasound. Further, it was assumed that 20% of men going to a specialist would have a cystoscopy as part of their urological investigation. Under this alternative scenario, these weights are reduced by 75%. Two projections are considered.
(a) The first projection is based upon a 75% reduction in the use of ultrasound in the management of LUTS by GPs only. This is estimated to provide outpatient cost savings of $0.7 million.

(b) The second projection then includes this change in clinical practice along with 75% reduction in the use of ultrasound and cystoscopy by specialists. The cost savings under this projection are estimated to be $5.1 million, all of which arises from a reduction in outpatient costs.

These predicted treatment cost savings arise through reductions in health service use by men with LUTS, or by a change in service use in favour of less expensive but potentially equally effective therapies. It is perhaps worth stressing that this model does not consider any consequential changes in health outcomes, or health service use related to these possible changes in health outcomes. It might be argued, for example, that the treatment cost savings derived from the model are being ‘purchased’ at the expense of increased complications in men with LUTS further into the future as a result of their having fewer services or no treatment in the present. The quantitative importance of this would depend on the natural history and aetiology of LUTS, which is not well understood.

Obtaining treatment cost savings through changes in clinical practice or patient behaviour does not necessarily imply a reduction in the quality of health care which patients receive. Indeed, such cost savings could be committed to further research into the management of LUTS in Australia so as to bring about an improvement in the quality of care received.
14 Where to from here?

14.1 Guideline dissemination and implementation

Overseas (Field and Lohr 1992, Grimshaw and Russell 1993b, Hayward and Laupacis 1993) and local (NHMRC 1995) authorities have promoted the development of evidence-based clinical practice guidelines to promote more effective health care and enhance patient outcomes.

However, it also has been recognised that publication of guidelines is insufficient in itself to ensure changes in clinical practice (Gupta et al 1997a,b). There now is general acceptance that ‘dissemination’ and ‘implementation’ are distinguishable phases which must follow guideline development and publication if patient outcomes are to improve (Grimshaw and Russell 1994). ‘Dissemination’ refers to those activities that ensure a specific guideline is available to all relevant ‘end-users’, encourage positive attitudes towards the guideline and address identified or perceived gaps in knowledge or clinical skills.

Examples of effective dissemination strategies include publication in professional journals, continuing medical education and endorsement by recognised peers. Further, ‘implementation’ refers to those activities that aim to achieve changes in actual clinical behaviour, whether within the context of individual patient-provider consultations or outside it as a system-wide initiative (Grimshaw and Russell 1994). Overseas research suggests that effective implementation strategies include giving clinicians feedback about current practice compared to guideline recommendations, providing financial incentives for clinical practice consistent with guideline recommendations, withdrawing payments for practice outside the guidelines as well as providing information,
checklists or prompts directly to patients or consumers at the time of their consultation (Grimshaw and Russell 1993a, Davis et al 1995).

While there is evidence of increased activity in the development of evidence-based guidelines in Australia, dissemination and implementation have received less emphasis (Holt et al 1996). Despite the importance of this challenge for improved health and better health care, few Australian studies have been conducted to identify effective strategies to disseminate guidelines and to change practice. Of those few which have, intensive strategies involving academic detailing (visits to general practitioners in their own practices by trained staff to discuss the content and implementation of the guidelines), workshops based on adult learning principles and practice-based prompts have been the most effective. Cost-effectiveness remains poorly studied. Financial incentives through changes to Medicare rebates or conditional pathology test-ordering are regarded as being effective although controlled trials have never been performed.

The Working Party on Voiding Dysfunction in Men is keen to ensure these guidelines are disseminated effectively and implemented. The emerging interest in men's health creates a timely climate for research to identify effective ways to improve outcomes for men, including a rigorous study to evaluate strategies to disseminate and implement the guidelines. Five baseline studies are in progress as follows:

1. A qualitative study of men's experiences of LUTS and impact on quality of life.

2. An assessment of general practitioners' current management of men with LUTS and preferred strategies for guideline dissemination and implementation.

3. A quantitative community survey of men's urinary symptoms, perceptions of risk of prostate cancer and utilisation of health services for urinary symptoms.

4. An identical study in an ageing ethnic community.

152 Management of LUTS
5. An assessment of consultation content using a representative sample of video tapes of Victorian general practitioners at work.

A larger intervention study building on the findings of these baseline studies would have substantial potential to improve outcomes for men. Such a study should be designed to meet the following aims:

- achieve significant changes in men's attitudes, intentions and utilisation of health services for uncomplicated LUTS;
- achieve significant changes in clinical behaviour and patient outcomes in general practice;
- monitor the process of dissemination and implementation and evaluate its reach and acceptability;
- evaluate the impact on clinical behaviour and patient outcomes of tested strategies; and
- calculate the most cost-effective strategies for national implementation.

Such a study could usefully employ a quasi-experimental design whereby matched localities or divisions of general practice are randomly allocated to different innovative dissemination and implementation strategies. At least two interventions should be designed, each sufficiently different to the other and responsive to the preferences of the surveyed groups yet grounded in the theoretical dissemination frameworks of others (eg Lomas 1994).

At least one intervention arm should include a direct public education strategy. The potential of local ‘opinion leaders’ and small groups to apply the guidelines locally, as well as quality assurance programs and internet technology could be evaluated. The protocol for the dissemination trial including baseline measures, interventions and follow-up measures should be submitted to appropriate institutional ethics review committees.
Without this study, the working party has insufficient information to identify a cost-effective program to implement the guidelines on a national basis. Without a cost-effective dissemination and implementation plan, men's health is likely to remain compromised and savings to be gained from the consistent application of the recommendations contained within the guidelines will not eventuate.

Key performance indicators for guideline dissemination include:

- 80% of general practitioners are aware of the LUTS guidelines within a year of publication; and
- 40% of men aged 50 years or over with bothersome urinary symptoms are aware of the consumer guidelines within a year of publication.

Similarly, key performance indicators for guideline implementation include:

- reduction of attendance at a general practice by men not bothered by their urinary symptoms;
- reduction of PSA test-ordering for screening purposes;
- reduction of referral to urologists for investigation and management of men not bothered by urinary symptoms;
- increase of reassurance/advice as a management plan for men not severely bothered by urinary symptoms; and
- decrease in TURPS performed on men ‘not at all’ or only ‘mildly’ bothered by uncomplicated urinary symptoms.

The working party recommends further consideration be given to the development of additional performance indicators for dissemination and implementation phases. Further, the degree of expected reductions or increases as a result of effective implementation should be estimated.
in order to inform sample size calculations and other methodological aspects of the proposed evaluation study.

14.2 Research

The working party recommends that researchers be invited to tender for research projects in the following critical issues that have emerged from its deliberations:

1. Development and psychometric testing of measures of ‘bother’ and quality of life which are valid, reliable, responsive to changes in health status and practical for serial measurement in clinical trials conducted in Australia, while also addressing the need for culturally appropriate outcome measures.

2. Epidemiological studies of urinary symptoms, degree of bother and quality of life to determine the natural history of LUTS in ageing Australian men.

3. Rigorous appraisal of diagnostic tests using established methodological criteria (Jaeschke et al 1994).

4. Replication in Australia of epidemiological studies to determine the association between urinary symptoms and early prostate cancer.

5. Development and evaluation of patient information which reduces anxiety about prostate cancer; supports clinical decision-making for LUTS and enhances clinician and patient satisfaction with care.

7. Randomised controlled trial of TUIP versus TURP, using clear and standardised eligibility criteria based on degree of bother, standardised surgical procedures and serial outcome measures.

8. Further randomly controlled trials to evaluate the more promising of the alternative procedures, which should be compared with conventional surgery and sham interventions. Design of these trials should involve larger sample sizes and consider comparison with conventional surgery, standardised interventions, validated outcome measures and duration of treatment effectiveness.

Tenders for these projects could be sought through the NHMRC Strategic Health Research Committee proposed for the 1997–9 triennium. Submissions should be subjected to peer review and transparent evaluation using published criteria. Funds obtained through reductions in unwarranted test-ordering and intervention in general practice could be used as a dedicated resource for urological research. More critically, findings need to be available before the scheduled date of revision of the guideline (in 1999).
Appendixes

A: Working party terms of reference and membership

B: The guideline development process

C: American Urological Association seven-point symptom score

D: Voiding diary
A Working party terms of reference and membership

Terms of reference

• Undertake the development and implementation of clinical practice guidelines which will facilitate the identification and care of men with voiding dysfunction.

• In fulfilling this task, review key literature and follow the procedures recommended by the Quality of Care and Health Outcomes Committee's draft first edition of Guidelines for the Development and Implementation of Clinical Practice Guidelines, that is:
  
  – identify
    - questions to be addressed by the guidelines;
    - target groups; and
    - health outcomes;
  
  – assess existing guidelines and relevance of overseas guidelines to Australian circumstances;
  
  – review and evaluate the extent and strength of scientific evidence relating to the effectiveness and appropriateness of the relevant interventions;
  
  – write evidence-based guideline documents;
  
  – undertake wider consultation;
– report on the guideline development process, including
  - a strategy for dissemination and implementation; and
  - a plan for evaluating and updating the guideline documents in response to new evidence.

• Provide advice and present clinical practice guidelines to the Quality of Care and Health Outcomes Committee.

**Membership**

Dr Geoffrey Hirst  
(Urologist  
(Chair)

Dr James Butler  
(Health economist

Dr Veronique Lajoie  
(General practitioner

Dr Peter Maher  
(Urologist

Professor Villis  
(Urologist

Marshall

Dr Michael Sladden  
(General practitioner

Mr Anthony Walsh  
(Consumer representative

Dr Jeanette Ward  
(Methodologist/health services representative

**Consultants**

Dr Anne Jackson  
(Freelance researcher/writer

Ms Ann Burgess  
(Freelance researcher/writer

**Secretary**

Mrs Cathy Clutton
B The guideline development process

Background

The need for procedures which ensure effective clinical practice, and focus the health system more directly on health outcomes, had been identified as part of the national health strategy (Harvey 1991) and by the Australian Health Ministers' Advisory Council.

The National Health and Medical Research Council (NHMRC) subsequently established a Standing Committee of the National Health Advisory Committee (formerly the Health Care Committee) to undertake the task. Initially named the Quality of Health Care Committee, the standing committee was later re-named the Quality of Care and Health Outcomes Committee (QCHOC) to reflect its emphasis on outcomes of care. QCHOC was given the task of:

- establishing a recommended national approach to the development of clinical practice guidelines which are focused on improving patient health outcomes; and

- working with the clinical colleges and other expert groups to encourage and facilitate the development of such guidelines and outcome measures by these groups.

Having drafted guidelines for the development of clinical practice guidelines, the standing committee then established a number of pilot working parties with the dual role of developing clinical practice guidelines in selected areas and trialing the proposed methodology for developing guidelines. The standing committee agreed on the following criteria when selecting pilot projects:
• high health burden imposed by the disease;
• high cost of treatment interventions;
• the existence of significant variation in current practice for similar conditions;
• a reasonable expectation that guidelines would lead to an improvement in the quality of care and health outcomes;
• the existence of a receptive group interested in taking on the development of guidelines for a particular issue of concern;
• pilot projects should represent the four focus areas under the Commonwealth Department of Human Services and Health's national health goals and targets (then cardiovascular health; cancer control; injury prevention and control; and mental health) (Nutbeam et al 1993);
• guidelines should be achievable (in some areas, guidelines cannot be developed; in others, guidelines are not required); and
• given the rising costs of health care, the area chosen for guideline development should offer some degree of potential for achieving cost-effectiveness in treatment.

The management of uncomplicated lower urinary tract symptoms in men was selected for guideline development because, as well as meeting the above criteria, there were concerns that knowledge of the scope of symptoms, their impact on patient health, and the management options available were not well understood among health professionals. It was also felt that not all men with voiding dysfunction were being presented with the range of appropriate treatment options, and that guidelines would help patients make informed choices.

Membership of the working party reflected the multidisciplinary nature of the management of urinary tract symptoms, with representatives from specialist clinical practice, general practice, health services, health
economics, and consumer groups. Membership details are provided at Appendix A, together with the working party's terms of reference. Throughout guideline development the working party maintained links with the Urological Society of Australasia as well as international and Australian experts in the field of urology.

**Purpose and scope of the guidelines**

Concern about increasing costs and practice variations in the management of men with lower urinary tract symptoms contributed to the development and publication of the Agency for Health Care Policy and Research (AHCPR) *Clinical Practice Guidelines for Benign Prostatic Hyperplasia* in 1994. Sponsored by the United States government, the recommendations contained in those guidelines were based on a review and, where possible, meta-analysis of all available English language literature to 1990.

By 1995, the emergence in Australia of similar activity to that which prompted the development of the AHCPR guidelines, was revealed by general practice statistics, prescription patterns and surgical data, thus identifying a need for local guidelines.

Early in the development of the Australian guidelines however, a circular argument about the clinical problem being considered by the working party, became evident. The argument arose because of a lack of knowledge about important aspects of the clinical problem, particularly natural history and outcome evaluation. This required a redefinition of the subject of the guidelines.

For the purpose of these guidelines, urinary symptoms refers to a group of lower urinary tract symptoms that occur commonly in men. They have become known in the literature by their acronym LUTS (lower urinary tract symptoms). While these symptoms may cause the man some bother they only rarely progress to pose a serious health threat to him. Thus, impact, ie quality of life, is outcome.

The guidelines contain explicit recommendations regarding the evaluation, investigation and treatment of men over the age of 50 years.
presenting with uncomplicated (ie not complex) urinary tract symptoms. The strength of the evidence on which the recommendations have been made is presented so that the patient, with guidance from his medical practitioner, can make informed decisions regarding the management of the condition.

The central tenet of these recommendations is the

...consideration of how the patient weighs the likely consequences of his choice. There are substantial differences in the risks and benefits associated with different management choices; in order to make the right decision, men must be fully informed and empowered to base their decisions on their own values and expectations. (Wennberg 1995)

The guidelines are based on the following key principles which form the basis of QCHOC's approach to guideline development and implementation:

- a systematic evaluation of the latest scientific evidence;
- a focus on the improvement of patient outcomes; and
- the adoption of a multi-disciplinary approach which involves all stakeholders, including consumers.

Processes employed

The working party approached the development of the guidelines by way of the following key tasks:

Task 1 Identification of the known clinical problems and areas of uncertainty.

Task 2 Collection and review of scientific evidence to identify best and most appropriate practice for the various interventions in the management of simple urinary tract symptoms in men.

164 Management of LUTS
Task 3  Collection and review of literature on best practice from the patient's perspective.

Task 4  Development of a glossary of technical terms for incorporation in both the clinical practice guideline and the consumer guide.

Task 5  Public consultation.

Most of the work of the working party was conducted out of session, with meetings used primarily to identify the direction to follow, and to review out-of-session activity. Technical experts were contracted to conduct systematic reviews of the scientific literature and prepare critical analyses. The clinical practice guidelines were then prepared by drawing all the information together, in consultation with the working party. The tasks were addressed as follows:

- At initial working party meetings, various individuals and groups identified known clinical problems or issues in their respective fields.

- Systematic reviews of the scientific literature were conducted in all areas covered by the guidelines, namely risk factors, natural history, pharmacological and surgical interventions, alternative therapies, and cost-effectiveness of treatment.

The findings from these reviews were incorporated into the guidelines.

The working party decided that it was important to give a clear indication in the guidelines as to the strength of the evidence for key statements, and provide references where appropriate. The modified level of evidence ratings system is discussed in detail at Section 1.4. The technical reports are available upon request.

- The working party commissioned a search of the professional and consumer literature. The review of the literature showed that there was very little information on the consumer perspective. As a
result the consumer guide was shaped with input and feedback from direct consultations with consumers.

- All members of the working party contributed to the compilation of a glossary of terms, which is included in both the clinical practice guidelines and the consumer guide.

- In accordance with the requirements of the NHMRC Act 1992 two stages of public consultation were conducted:
  - late 1995 — the issue of LUTS was identified as an area of interest and priority for NHMRC; and
  - August/September 1996 — draft guidelines circulated for public consideration.

**Costing issues**

A review of the existing literature on the economic evaluation of treatment was undertaken. The review was not exhaustive, and focused only on those articles that considered options for treatment discussed in the guidelines. Statistical information was obtained which detailed the numbers of men presenting for particular interventions (by Medicare number) and it was, thus, possible to cost current treatment practices.

A decision tree based on the recommendations of the guidelines was developed and costs applied to key points. As a result of this process, cost effectiveness issues have been identified within the clinical practice guidelines.

**Consultation/feedback**

Since acceptability of the guidelines by relevant stakeholders is a critical first step towards their implementation, consultation is an integral part of the development process. The availability of the draft guidelines, and an invitation to make submissions, was forwarded to all members of the Urological Society of Australasia, university faculties of general practice, all branches of the Royal Australian College of General Practitioners, and all divisions of general practice.
In addition, overseas review by recognised experts in the field was sought in order to draw to the fullest extent on expertise on this topic.

Consultations with consumers, through the Continence Foundation of Australia Inc, provided essential feedback from consumers.

Fifty-eight submissions were received as a result of the consultation process (see list at the end of this appendix). The working party considered these submissions and made adjustments to the clinical practice guidelines where evidence was presented for such a change.

**Distribution**

As well as general practitioners and urologists, it is recommended that the guidelines be forwarded to:

- allied health organisations;
- the State/Territory health authorities;
- public policy makers;
- hospitals;
- consumer and patient groups;
- health economists; and
- professional journals.

Computer technology also presents possibilities for ready access and dissemination.

**Dissemination and implementation**

The working party developed a plan for dissemination and implementation, including performance indicators.
Preliminary data collection is under way and includes:

- a survey of general practitioner knowledge and practice patterns;
- a survey of men's knowledge; and
- attitudes, and patterns of approaches to health professionals.

The latter survey is being replicated in a non-English speaking community.

Following implementation of the guidelines, it will be possible to evaluate the impact of the guidelines by repeating surveys and comparing both clinical practice patterns and men's patterns of seeking assistance.

**Evaluation**

An essential part of the guideline development and implementation process is an evaluation of their effectiveness. Evaluation of the effectiveness of the guidelines has been written into a draft implementation research strategy. This research project has proposed the collection of data to determine the impact of the guidelines on clinician behaviour and patient health outcomes. Such evaluation would also identify data for certain target groups identified in the guidelines, eg frail aged men.

**Updating**

The guidelines reflect existing knowledge at the time of publication. However as new evidence emerges from new work and systematic reviews, the guidelines will require revision in order to maintain validity. It is recommended that the Urological Society of Australasia and the Royal Australian College of General Practitioners cooperate on a review of the guidelines no later than two years from publication.

**2000 Review**

In 1999, following the raising of a number of concerns, a review team was engaged to investigate the predictive power of lower urinary tract...
symptoms in men for the diagnosis of prostate cancer. Their findings were considered by the original working party and the Health Advisory Committee. In February 2000, the NHMRC agreed to three minor amendments to Chapter 7 of the report to reflect the relationship between lower urinary tract symptoms and early prostate cancer.
List of submissions received

1. Dr S. Wisniewski, Urologist, WA
2. Professor D. Neal, Head, Department of Surgery, University of Newcastle, UK
3. Dr B. McGregor, Chair, ANZ Association of Urological Surgeons, WA
4. Mr J.C. Smith, President UK Medical Defence Society, UK
5. Mr P.S. Lawson, Urologist, VIC
6. Mr A.J. Andrew, NSW
7. Mr J. Holman, NSW
8. Tasmanian Rural Divisions Co-ordinating Unit, TAS
9. Dandenong District Division of General Practice, VIC
10. Mr J. Wheelahan, VIC
11. Dr L.C. Thompson, Urologist, QLD
12. Dr C. McRae, Urologist, New Zealand
13. Division of General Practice, Fairfield Health Service Inc., NSW
14. Mr L.M. Harewood, Urologist, VIC
15. Public & Environmental Health Service, South Australian Health Commission, SA
16. Mr T. Low, President, Urological Society of Australasia
17. Rhone-Poulenc Rorer, NSW
18. Mr G. Joyce, Urologist, VIC
19. NSW Section, Urological Society of Australasia, NSW
20. Dr H. Logan Holtgrewe, Chairman, Health Policy Council, American Urological Association, USA
21. Dr C. Pinnock, SA
22. Victorian Section, Urological Society of Australasia
23. Mr W.H. Bowles, NSW
24. NSW Central West Division of General Practice Ltd, NSW
25. Mr P. Robertson, VidaMed Australia Pty Ltd, NSW
26. Mr W.G.E. Straffon, Urologist, VIC
27. Mr P.M. Katelaris, Urologist, NSW
28. Mr D. Golovsky, Vice-President, Urological Society of Australasia, NSW
29. Mr A.N. James, Urologist, QLD
30. Mr D. Gunter, VIC
31. Australian Nursing Services, SA
32. Merck Sharp & Dohme, NSW
33. Mr P McTaggart, Urologist, QLD
34. Mr A. Crosthwaite, Urologist, VIC
35. Dr P Heathcote, Chairman, Northern Section, Urological Society of Australasia, QLD
36. Royal College of Nursing, Australia, ACT
37. Dr R.J. Millard, A/Prof Urology, NSW
38. Mr G.S. Reisner, Urologist, VIC
39. Mr A.S. Wood, Urologist, VIC
40. Mr L.K. Cleeve, Urologist, VIC
41. Dr J. Rogers, Consultant urologist, NSW
42. Dr H. Wu, NSW
43. Border Urology Clinic, NSW
44. Royal Australian College of General Practitioners, VIC
45. Ms H. O'Connell, Urological surgeon, VIC
46. Mr D. Ellis, Urological surgeon, VIC
47. Mr K.G. Braslis, Urologist, VIC
48. Mr J.S. Peters, Urologist, VIC
49. Mr D. Webb, Urologist, VIC
50. Mr M. Frydenberg, Urological surgeon, VIC
51. Mr S. Stening, Urologist, Qld
52. Dr G.J. Buckham, Urologist, Qld
53. Mr P McTaggart, Urologist, QLD
54. Mr D. Golovsky, Vice-President, Urological Society of Australasia, NSW
55. Dr R.J. Millard, A/Prof Urology, NSW
56. Dr L.C. Thompson, Urologist, QLD
57. Dr M.R. Jones, Director Medical Services, VIC
58. Dr P Heathcote, Chairman, Northern Section, Urological Society of Australasia, QLD
### American Urological Association seven-point symptom score

<table>
<thead>
<tr>
<th>Questions to be answered</th>
<th>AUA symptom score (circle 1 number on each line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the past month how often have you -</td>
<td>Not at all</td>
</tr>
<tr>
<td>1. had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
</tr>
<tr>
<td>2. had to urinate again less than 2 hours after you finished urinating?</td>
<td>0</td>
</tr>
<tr>
<td>3. found you stopped and started again several times when urinating?</td>
<td>0</td>
</tr>
<tr>
<td>4. found it difficult to postpone urination?</td>
<td>0</td>
</tr>
<tr>
<td>5. had a weak urinary stream?</td>
<td>0</td>
</tr>
<tr>
<td>6. had to push or strain to begin urination?</td>
<td>0</td>
</tr>
<tr>
<td>7. most typically, got up at night to urinate (bedtime — morning)?</td>
<td>0</td>
</tr>
</tbody>
</table>

**Sum of 7 circled numbers (AUA symptom score):** _______  

Source: Barry et al (1992)
D Voiding diary

Sample diary

<table>
<thead>
<tr>
<th>TIME &amp; VOLUME CHART</th>
<th>NAME:</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLUID INTAKE</td>
<td>URINE OUTPUT</td>
</tr>
<tr>
<td>Date</td>
<td>Time</td>
</tr>
<tr>
<td>2 Jan</td>
<td>7.30 am</td>
</tr>
<tr>
<td>8.00 am</td>
<td>Tea</td>
</tr>
<tr>
<td>10.00 am</td>
<td>Juice</td>
</tr>
<tr>
<td>12.30 pm</td>
<td>Coffee</td>
</tr>
<tr>
<td>2.00 pm</td>
<td>Beer</td>
</tr>
</tbody>
</table>

Adapted from voiding diary supplied by the Continence Foundation of Australia. A blank chart for reproduction is shown on the next page.
<table>
<thead>
<tr>
<th>TIME &amp; VOLUME CHART</th>
<th>NAME:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FLUID INTAKE</strong></td>
<td><strong>URINE OUTPUT</strong></td>
</tr>
<tr>
<td>Date</td>
<td>Time</td>
</tr>
<tr>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHCPR</td>
<td>Agency for Health Care Policy and Research (United States)</td>
</tr>
<tr>
<td>AHTAC</td>
<td>Australian Health Technology Advisory Committee</td>
</tr>
<tr>
<td>AN-DRG</td>
<td>Australian national diagnostic-related group</td>
</tr>
<tr>
<td>AUA</td>
<td>American Urological Association</td>
</tr>
<tr>
<td>BPH</td>
<td>benign prostatic hyperplasia</td>
</tr>
<tr>
<td>CCOHTA</td>
<td>Canadian Coordinating Office of Health Technology Assessment</td>
</tr>
<tr>
<td>DHT</td>
<td>dihydroxytestosterone</td>
</tr>
<tr>
<td>DRE</td>
<td>digital rectal examination</td>
</tr>
<tr>
<td>DRG</td>
<td>diagnostic-related group</td>
</tr>
<tr>
<td>GP</td>
<td>general practitioner</td>
</tr>
<tr>
<td>HIFU</td>
<td>high intensity focused ultrasound</td>
</tr>
<tr>
<td>IPSS</td>
<td>International Prostate Symptom Score</td>
</tr>
<tr>
<td>IVU</td>
<td>intravenous urography</td>
</tr>
<tr>
<td>LUTS</td>
<td>lower urinary tract symptoms</td>
</tr>
<tr>
<td>mg</td>
<td>milligrams</td>
</tr>
<tr>
<td>mL</td>
<td>millilitres</td>
</tr>
<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
<tr>
<td>NHMRC</td>
<td>National Health and Medical Research Council</td>
</tr>
<tr>
<td>PFR</td>
<td>peak flow rate (urine) or Qmax</td>
</tr>
<tr>
<td>PSA</td>
<td>prostate specific antigen</td>
</tr>
<tr>
<td>PVR</td>
<td>post-void residual (urinary volume)</td>
</tr>
<tr>
<td>QCHOC</td>
<td>Quality of Care and Health Outcomes Committee</td>
</tr>
<tr>
<td>RACGP</td>
<td>Royal Australian College of General Practitioners</td>
</tr>
<tr>
<td>RCT</td>
<td>randomised controlled trial</td>
</tr>
<tr>
<td>TRUS</td>
<td>transrectal ultrasound</td>
</tr>
<tr>
<td>TUBAL-T</td>
<td>transurethral balloon laser thermotherapy</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>TUEP</td>
<td>transurethral electroevaporation of the prostate tissue</td>
</tr>
<tr>
<td>TUIP</td>
<td>transurethral incision of the prostate (bladder neck incision)</td>
</tr>
<tr>
<td>TULIP</td>
<td>transurethral ultrasound guided laser prostatectomy</td>
</tr>
<tr>
<td>TUMT</td>
<td>transurethral microwave thermotherapy</td>
</tr>
<tr>
<td>TUNA</td>
<td>transurethral needle ablation</td>
</tr>
<tr>
<td>TURP</td>
<td>transurethral resection of the prostate</td>
</tr>
<tr>
<td>TUVP</td>
<td>transurethral vaporisation of the prostate</td>
</tr>
<tr>
<td>VLAP</td>
<td>visual laser assisted prostatectomy</td>
</tr>
</tbody>
</table>
Glossary

Adrenergic

An adjective used to refer to: substances that have effects similar to epinephrine (adrenaline); nerves that release nor-epinephrine to pass impulses to other nerves or to muscle fibres; and to receptors for epinephrine/nor-epinephrine.

Alpha (α)-adrenergic receptors

Receptors in smooth muscle muscle innervated by adrenergic fibres of the sympathetic nervous system. They respond to nor-epinephrine and to certain stimulating or blocking agents. Blocking agents for α₁-adrenergic receptors, such as the drugs, doxazosin, prazosin and terazosin, when used in the treatment of BPH, relax bladder neck and prostate smooth muscle.

Anticholinergic agent

Agent that acts by blocking the transmission of nerve impulses to effector organs by the neurotransmitter acetylcholine.

Androgens

Substances conducive to masculinisation such as the hormone testosterone.

Autonomic neuropathy

A disease affecting nerves of the autonomic nervous system (part of the nervous system that regulates body functions not under conscious control).

Benign

A condition that may be bothersome but does not progress to anything more serious.
<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign prostatic hyperplasia</td>
<td>A non-cancerous histological change that occurs when there is an increase in the number of cells (hyperplasia) in the glandular and stromal elements of the prostate causing enlargement of the gland. [NB This term has frequently, but erroneously, been used to refer to the clinical condition of LUTS.]</td>
</tr>
<tr>
<td>Bladder neck contracture</td>
<td>Narrowing or scarring of the bladder neck that sometimes occurs as a late complication of prostate surgery.</td>
</tr>
<tr>
<td>Bladder outlet obstruction</td>
<td>An obstruction in the outflow of the bladder caused by anatomical or neurogenic causes.</td>
</tr>
<tr>
<td>Case-series</td>
<td>Report of the outcome(s) of a series of selected patients seen in a specified clinical setting.</td>
</tr>
<tr>
<td>Cholinergic innervation</td>
<td>Nerves that release acetylcholine, which is a neurotransmitter for effector organ (in this case bladder smooth muscle) stimulation.</td>
</tr>
<tr>
<td>Cholinergic receptors</td>
<td>Receptors for the neurotransmitter, acetylcholine, which cause effector organ stimulation when activated.</td>
</tr>
<tr>
<td>Creatinine</td>
<td>A normal metabolic waste product excreted in the urine; it is generally produced at a constant rate. The clearance rate and the serum level are widely used as indices of renal function.</td>
</tr>
<tr>
<td>Cystourethroscopy</td>
<td>Direct endoscopic viewing of the urethra and bladder using an instrument called a cystoscope.</td>
</tr>
<tr>
<td>Cystometrography (filling cystometry)</td>
<td>Measures changes in bladder pressure during filling of the bladder.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>----------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Detrusor</td>
<td>The smooth muscle in the wall of the urinary bladder that contracts the bladder and expels the urine.</td>
</tr>
<tr>
<td>Detrusor instability</td>
<td>Also known as detrusor hyperactivity, it describes the occurrence of detrusor muscle contractions while the patient is trying to inhibit urination. It is diagnosed by cystometry.</td>
</tr>
<tr>
<td>Diagnostic-related</td>
<td>A classification system for acute hospital in-patients based on diagnoses and procedures; AN-DRGs (Australian National Diagnosis-Related Groups) is a variant of the DRG system designed specifically for use in Australia.</td>
</tr>
<tr>
<td>Digital rectal</td>
<td>Examination in which tissues around the rectum, including the prostate, are palpated using the practitioner’s finger inserted into the rectum.</td>
</tr>
<tr>
<td>Dilatation</td>
<td>Widening — as a normal process or may imply stretching beyond normal dimensions, either as part of a disease process or as a deliberate surgical act.</td>
</tr>
<tr>
<td>Diuresis</td>
<td>Abnormally large output of urine.</td>
</tr>
<tr>
<td>Diverticulum</td>
<td>An out-pouching from, or sac formation of variable size on, a hollow organ or structure.</td>
</tr>
<tr>
<td>Dysuria</td>
<td>Painful or difficult urination.</td>
</tr>
<tr>
<td>Endoscope</td>
<td>An internal viewing instrument.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Flow rate (urine)</td>
<td>The volume per time unit of urinary fluid expelled via the urethra, expressed in millilitres per second.</td>
</tr>
<tr>
<td>Haematuria</td>
<td>Blood in the urine.</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>Distension with urine of the pelvis and calices of the kidney usually as a result of obstruction of the ureters.</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>Abnormal multiplication or increase in the number of normal cells in normal arrangement in a tissue.</td>
</tr>
<tr>
<td>Hypospadias</td>
<td>A congenital abnormality of the penis in which the urethra opens on the underside of the organ.</td>
</tr>
<tr>
<td>Infravesical obstruction</td>
<td>Blockage to the outflow of urine from the bladder by an obstruction distal to the bladder.</td>
</tr>
<tr>
<td>Intravenous urography</td>
<td>Radiological imaging of the urinary tract using an intravenous contrast agent which is excreted by the kidneys.</td>
</tr>
<tr>
<td>Lower urinary tract symptoms</td>
<td>Term used to describe a complex of clinical symptoms of the lower urinary tract; also known as the acronym LUTS.</td>
</tr>
<tr>
<td>Macroscopic BPH</td>
<td>Enlargement of the prostate that is palpable during digital rectal examination and does not have the clinical characteristics of cancer (see also Microscopic BPH).</td>
</tr>
<tr>
<td>Meatal abnormalities</td>
<td>Abnormality to any passage or opening to the body.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Meta-analysis</td>
<td>A systematic review that employs statistical methods to combine and summarise the results of several studies.</td>
</tr>
<tr>
<td>Microscopic BPH</td>
<td>Hyperplasia of the prostate gland that can only be identified by microscopic examination (see also Macroscopic BPH).</td>
</tr>
<tr>
<td>Micturition</td>
<td>The act of passing urine.</td>
</tr>
<tr>
<td>Morbidity</td>
<td>The state of being diseased or suffering.</td>
</tr>
<tr>
<td>Muscarinic receptors</td>
<td>Visceral receptors for the neurotransmitter, acetylcholine (on smooth muscle, cardiac muscle and exocrine glands).</td>
</tr>
<tr>
<td>Neuropathic bladder</td>
<td>Dysfunction of the urinary bladder caused by a lesion of the central or peripheral nervous system.</td>
</tr>
<tr>
<td>Nocturia</td>
<td>Needing to pass urine during the night.</td>
</tr>
<tr>
<td>Obstructive uropathy</td>
<td>Any pathologic change in the urinary tract due to obstruction.</td>
</tr>
<tr>
<td>Peak flow urine rate</td>
<td>The maximum flow rate achieved during voiding; also known as Qmax.</td>
</tr>
<tr>
<td>Phimosis</td>
<td>Tightness of the foreskin that can prevent retraction (can be either congenital or the result of inflammation).</td>
</tr>
<tr>
<td>Phytotherapy</td>
<td>Treatment using plant extracts.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>------</td>
<td>------------</td>
</tr>
<tr>
<td>Placebo</td>
<td>A pharmacologically inactive substance made up in an apparently identical way to the active drug under trial. The subjects are unaware of whether they have received the active agent or placebo.</td>
</tr>
<tr>
<td>Polyuria</td>
<td>Formation of unusually large quantities of urine.</td>
</tr>
<tr>
<td>Post-void residual urine volume</td>
<td>The volume of urine remaining in the bladder on completion of voiding.</td>
</tr>
<tr>
<td>Prostate</td>
<td>A gland situated at the base of the bladder which produces secretions for the maintenance of sperm in the ejaculate.</td>
</tr>
<tr>
<td>Prostatectomy</td>
<td>Surgical removal of part or all (total) of the prostate gland.</td>
</tr>
<tr>
<td>Prostate specific antigen</td>
<td>A glycoprotein produced by the glandular component of the prostate.</td>
</tr>
<tr>
<td>Prostatism</td>
<td>Symptom complex consisting of irritative symptoms (such as urgency, frequency, nocturia, and urge incontinence) and obstructive symptoms (such as hesitancy, weak stream, straining, prolonged micturition, urinary retention and outflow incontinence).</td>
</tr>
<tr>
<td>Qmax</td>
<td><em>see</em> Peak flow urine rate</td>
</tr>
<tr>
<td>Randomised controlled trials</td>
<td>An experimental study in which subjects are randomly assigned to treatment and control groups.</td>
</tr>
<tr>
<td>Serum creatinine test</td>
<td><em>see</em> Creatinine</td>
</tr>
</tbody>
</table>
Stent A device placed inside the lumen (canal) of a duct (such as the prostatic urethra) to maintain an opening and allow the contents to drain.

Symptom scores Rating system used to assess the severity of the individual urinary symptoms (eg AUA-SS or IPSS, etc).

Trabeculation Formation of muscular bands of tissue (trabeculae) usually recognised by cystoscopic examination of the bladder.

Transrectal ultrasound (TRUS) Ultrasound imaging performed using a rectal probe.

Transurethral balloon laser thermotherapy (TUBAL-T) Treatment for LUTS involving a urethral cooling system, a balloon catheter and an irradiating laser via the urethra moving through 360 degrees causing deep necrosis and coagulation of prostatic tissue while preserving the urethral mucosa.

Transurethral evaporation of the prostate tissue (TUEP) Transurethral vapourisation of prostatic tissue using a contact laser fibre tip.

Transurethral incision of the prostate or bladder neck incision (TUIP) Transurethral incision of the bladder neck and posterior prostatic tissue, usually by a resectoscope point electrode with an electrical cutting and coagulation current or, less often, by a laser probe.

\^Tansurethral = via the urethra
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transurethral resection of the prostate (TURP)</td>
<td>Transurethral surgical removal of prostatic tissue by a resectoscope using an electrical cutting and coagulation current.</td>
</tr>
<tr>
<td>Transurethral microwave thermotherapy (TUMT)</td>
<td>Transurethral coagulation of prostatic tissue by a special catheter transmitting microwaves.</td>
</tr>
<tr>
<td>Transurethral needle ablation (TUNA)</td>
<td>Transurethral coagulation of prostatic tissue by needle probes inserted into the prostatic lobes and transmitting low frequency radiowaves.</td>
</tr>
<tr>
<td>Transurethral ultrasound guided laser prostatectomy (TULIP)</td>
<td>Nonvisual coagulation of prostatic tissue using a transurethral ultrasound-guided laser.</td>
</tr>
<tr>
<td>Transurethral vaporisation of the prostate (TUVP)</td>
<td>Transurethral evaporation of prostatic tissue by a modified resectoscope loop using an electrical cutting and coagulation current at high power settings.</td>
</tr>
<tr>
<td>Ultrasonography</td>
<td>A noninvasive technique that uses high frequency sound waves (ultrasound) aimed at a structure inside the body to produce an image (sonogram) of the internal structure or feature under scrutiny.</td>
</tr>
<tr>
<td>Uninhibited detrusor contraction</td>
<td>Involuntary contraction of the detrusor muscle of the bladder.</td>
</tr>
<tr>
<td>Urethra</td>
<td>The tube that carries urine from the bladder to the exterior.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Urodynamic tests</td>
<td>Tests designed to determine the functional status of the urinary bladder and urethra; they include cystometry, electromyography, urethral pressure profilometry, uroflowmetry and videourodynamics.</td>
</tr>
<tr>
<td>Uroflowmetry</td>
<td>Electronic measurement of urinary flow rate throughout the course of urination.</td>
</tr>
<tr>
<td>Urolithiasis</td>
<td>Stones in the urinary tract.</td>
</tr>
<tr>
<td>Visual laser assisted</td>
<td>Transurethral coagulation of prostatic tissue by a visually-positioned laser probe.</td>
</tr>
<tr>
<td>prostatectomy (VLAP)</td>
<td></td>
</tr>
<tr>
<td>Watchful waiting</td>
<td>Term frequently used in the literature to describe initial reassurance with regular surveillance.</td>
</tr>
</tbody>
</table>
References


NHMRC (National Health and Medical Research Council) (1994). Treatment Options for Benign Prostatic Hyperplasia (BPH). Canberra: AGPS.


The National Health and Medical Research Council

The National Health and Medical Research Council (NHMRC) is a statutory authority within the portfolio of the Commonwealth Minister for Health and Aged Care, established by the National Health and Medical Research Council Act 1992. The NHMRC advises the Australian community and Commonwealth, State and Territory Governments on standards of individual and public health, and supports research to improve those standards.

The NHMRC advised the Commonwealth Government on the funding of medical and public health research and training in Australia and supports many of the medical advances made by Australians.

The NHMRC also develops guidelines and standards for the ethical conduct of health and medical research.

The Council comprises nominees of Commonwealth, State and Territory health authorities, professional and scientific colleges and associations, unions, universities, business, consumer groups, welfare organisations, conservation groups and the Aboriginal and Torres Strait Islander Commission.

The Council considers and makes decisions on reports prepared by committees and working parties following wide consultation on the issue under consideration.

A regular publishing program ensures that Council’s recommendations are widely available to governments, the community, scientific, industrial and education groups.

The Council publishes extensively in the following areas:

- Aged care
- Child health
- Clinical practice
- Communicable diseases
- Dentistry
- Drugs and poisons
- Drug and substance abuse
- Environmental health
- Ethics
- Infection control
- Mental health
- Men’s health
- Nutrition
- Public health
- Research
- Technology assessment
- Women’s health

A list of current publications is available from:

The Publications Officer
Office of NHMRC
MDP 50
GPO Box 9848
Canberra ACT 2601

Telephone: (02) 6289 1430 (24-hour voicemail service)
Toll free: 1800 020 103
Facsimile: (02) 6289 1351
Email: nhmrc.publications@health.gov.au
Internet: http://www.nhmrc.health.gov.au