

Standardization of Outcome Studies in Patients With Lower Urinary Tract Dysfunction: A Report on General Principles From the Standardisation Committee of the International Continence Society

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INTRODUCTION

Scientific evaluation of the outcome of therapeutic interventions in patients is not possible without assessment both before and after the intervention. The methods and measurements used must conform to set criteria in order that they may be applied to all interventions so that comparison between studies may be made. They must be valid, accurate, precise, reliable, and repeatable using a test-retest variation. Evaluations should be properly directed, such that the right variable is measured. Even though methods of intervention and evaluation may vary, certain domains of measurement should be represented and a multidimensional approach undertaken. The time scale for evaluations and interventions and the composition of the study group are important factors, so that some standardization exists, enabling understanding of the results by other investigators and comparison between studies.

Unfortunately, no consensus of opinion presently exists on the way in which studies should be performed, including interventions and evaluations, nor on how the results thus obtained should be represented. The scientific basis for many methods is also frequently unclear. A recent American survey of the literature on outcome in genuine stress incontinence classified almost all of the investigations as unsatisfactory and only a few as excellent. We thus have a dilemma between what we “know” as based on reliable scientific data, and what we “believe” based on clinical practice.

A.M. served as Coordinating Chairman. The other authors served as chairmen of the respective Outcome Subcommittees on Lower Urinary Tract Dysfunction: Children, Frail Elderly, Women, Men, and Neurogenic Dysfunction.

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This emphasizes the poor investigative technique and reporting presently in use and the need for the standardization of outcome measures.

STANDARDIZATION OF OUTCOME STUDIES

In 1993, the International Continence Society set up subcommittees within the frame of the Standardisation Committee in order to standardize outcome studies in patients with lower urinary tract dysfunction:

1. Children,
2. Frail Elderly,
3. Women,
4. Men, and
5. Neurogenic Dysfunction.

Each of these specific subcommittees was asked to make recommendations on how outcome studies should be performed in their respective fields. In this general report, common principles and outlines are discussed. These should be seen as recommendations rather than guidelines, representing a move towards a more rational and uniform presentation of outcome studies. In the separate reports from respective subcommittees, more specific recommendations are given.

DEFINITION OF OUTCOME MEASURES

No single measure can fully express the outcome of an intervention. It is necessary for outcome to incorporate improvement and deterioration in function, complications of the intervention, socioeconomic data, and the effect on quality of life. Both subjective and objective measurements should be included and bias eliminated where possible. It should be emphasized that frequently the perception of the patient, doctor, or therapist are at variance, and hence the choice and application of measurement tool is all the more important.

An intervention might have both primary and secondary outcome objectives. The primary objective might be an anatomical change (e.g., surgery), while the secondary objective might be functional (e.g., continence).

ENDPOINTS

In order for maximum information to be obtained, it is important that the correct endpoints are chosen and defined at the beginning of the study. This involves the stating of a null hypothesis, although other factors may be of importance and should be included where appropriate. Endpoints should be chosen so that they are relevant and may be incorporated into practice at the end of the study. The time frame of the intervention and its expected outcome should be considered when designing a study. Long-term outcome should be measured whenever possible. Statistical expertise is vital and should be applied from the beginning of the study.

OUTCOME MEASURES

Directed, accurate measures are necessary in order to reflect the degree of change or improvement with a high degree of correlation.

The groups of measures generally termed objective, subjective, compliance, quality of life, and socioeconomic can also be grouped into domains of interest. The use of domains describes another perspective, with the interests of the involved parts weighted according to their perceived importance. Certain measurements are not easy to make because of dearth of presently available instruments and a lack of agreement about which tool is most appropriate. At present, there is also a lack of correlation between the various measures mentioned.

Urinary incontinence as a symptom, a sign, and a condition is here redefined as far as the condition part is concerned. The condition “urinary incontinence” is comprised of the passage of urine through the urethra at an inappropriate point in time, and is thus not, as previously suggested, a part of the underlying pathophysiological process itself. Urinary incontinence is thus a consequence and not a cause, and this is valid for both the symptom, the sign, and the condition parts.

Outcome in studies of lower urinary tract function and dysfunction should be described using:

- Patient’s observations (symptoms)
- Quantification of symptoms (e.g., urine loss)
- Physician’s observations (anatomical and functional; compliance)
- Quality-of-life measures
- Socioeconomic evaluations.

Patient- and physician-observed measures should be regarded as compulsory in all outcomes of lower urinary tract dysfunction; compliance measurements from patients and healthy volunteers should be given, and quality-of-life and socioeconomic data included when available. These data should be increasingly incorporated into study designs, so that the picture becomes complete.

EVALUATION AND GRADING OF OUTCOME

Although the ideal result of treatment should be cure and normalization, outcome may sometimes be better described as a degree of improvement in addition to measuring cure. Even if the elimination of symptoms often is the goal for a treatment and thus comprises the expected outcome, some other aspects have to be considered. “Cure” usually refers to a single dimension. That a patient becomes symptom-free does not mean that the underlying pathophysiological process is completely reversed. The patient might experience normalization, but structural as well as functional changes might remain. Examples of such remaining changes could be displacement of the bladder neck, a subnormal intraurethral pressure, a hyperactive bladder, or a hyperplastic prostate. When a given treatment is directed against symptoms and not against the pathophysiological process itself, we can of course never expect to cure. An alternative measure could therefore use the terms “responders” and “nonresponders,” which describe less extreme degrees of improvement than those implied by cure and normalization. However, it may be necessary to divide this into degrees of response, so that differentiation may be made between maximum responders and minimal responders who gain only small benefit from the intervention. The size of such a response should exceed the value of the test-retest variation as performed and reported by the investigators.

REPORTING OF OUTCOME STUDIES

The editors of journals considering outcome studies on patients with lower urinary tract dysfunction for publication are recommended to include a passage referring to this document in their instructions for authors.

FUTURE DIRECTIONS

Considerable effort is needed to describe the way in which various measures correlate with each other. It may be a considerable time before final decisions can be made on what outcome means for different patient groups. This requires a multidimensional and multidisciplinary approach, including the continuous and active participation of all the members of our International Continence Society.

CONCLUSIONS AND RECOMMENDATIONS

Data from five groups of measures should be represented in every scientific investigation of outcome in patients with lower urinary tract dysfunction:

- Patient's observations (symptoms)
 - Quantification of symptoms (e.g., urine loss)
 - Physician's observations (anatomical and functional; compliance)
 - Quality of life
 - Socioeconomic data.
- Measurements should be directed and accurate.
 - A null hypothesis should be formulated.
 - Endpoints should be defined.
 - A grading of response should be measured, using the terms "responders" and "nonresponders."
 - A multidimensional, multidisciplinary approach should be used.

ADDENDUM

Was the study in any part supported by commercial interest?

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APPENDIX

Practical Points for Outcome Studies in Patients With Lower Urinary Tract Dysfunction*

Purpose of the study

What are the reasons for this particular study?

What do the investigators want to show?

Patient groups

Definition of patient groups

Inclusion/exclusion criteria*Disease/disorder*

Causal or symptomatic treatment?

Arrest of a process?

Reversible changes?

Intervention

Description of the intervention

Intervention related complications, morbidity, and mortality

Study design and controls

Intervention studies should have a control group and should be randomized

Define endpoints

Define response criteria

Nature of trial, e.g., double-blind, placebo controlled, crossover

Adverse events, dropouts

Methods of measurement

Characterization of methods, test-retest data in the hands of the investigators

Change in circumstances or procedures prior to and after intervention

Interindividual variation (+ differences between centers in multicenter trials)

Normal values

Statistics

Power of the study

Reason for choice of statistical method

Compliance

Statistician involved?

Time scale

Why was outcome evaluated at a particular time in relation to the intervention?

Long-term outcome?

Expected outcome

Degree of improvement

Risk-benefit analysis

Patient expectations

Quality-of-life effects

Socioeconomic factors

Interpretation of data

Comparison with outcome in other studies

Unexpected/adverse findings

Limitations

Clinical significance

Theoretical importance

Possible ways of improving the study

Conclusions for future investigations

*Whenever an outcome study on lower urinary tract dysfunction is planned, a series of questions should ideally be considered and appropriately addressed in the manuscript at the time of submission for publication. The following list serves only as a reminder. More specific information concerning the different topics is represented in the reports from the subcommittees. ICS terminology should be used wherever practicable.