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and NST Expert Group

Med Decis Making published online 2 July 2013

DOI: 10.1177/0272989X13493145

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Management of Undescended Testis: A Decision Analysis

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Background. Undescended testis (UDT) or cryptorchidism is the most common genital anomaly seen in boys and can be treated surgically by orchidopexy. The age at which orchidopexy should be performed is controversial for both congenital and acquired UDT. **Methods.** A decision analysis is performed in which all available knowledge is combined to assess the outcomes of orchidopexy at different ages. **Results.** Without surgery, unilateral congenital UDT and bilateral congenital UDT are associated with average losses in quality-adjusted life-years (QALYs) of 1.53 QALYs (3% discounting 0.66 QALYs) and 5.23 QALYs (1.91 QALYs), respectively. Surgery reduces this QALY loss to on average 0.84 QALYs (0.21 QALYs) for unilateral UDT and 1.66 QALYs (0.40 QALYs) for bilateral UDT. Surgery at detection will lead to the lowest QALY loss of 0.91 (0.34) and 1.73 (0.60) QALYs, respectively, for unilateral and bilateral acquired UDT compared with surgery during puberty and no

surgery. No sensitivity analysis is able to change the preferences for these strategies. **Conclusions.** Based on our decision analytic model using societal valuations of health outcomes, surgery for unilateral UDT (both congenital and acquired) yielded the lowest loss in QALYs. Given the modest differences in outcomes, there is room for patient (or parent) preference with respect to the performance and timing of surgery in case of unilateral UDT. For bilateral UDT (both congenital and acquired), orchidopexy at any age provides considerable benefit, in particular through improved fertility. As there is no strong effect of timing, the age at which orchidopexy is performed should be discussed with the parents and the patient. More clinical evidence on issues related to timing may in the future modify these results and hence this advice. **Key words:** decision analysis; cryptorchidism; orchidopexy. (**Med Decis Making XXXX;XX:XXX-XXX**)

Received 13 July 2012 from Department of Medical Decision Making, Leiden University Medical Center, Leiden, The Netherlands (MEVDAM, JK); Netherlands Organization for Applied Scientific Research, Leiden/Utrecht, The Netherlands (MK, HBMVG, FHP); and Youth Health Care South Holland West (GGD-ZHW), Zoetermeer, The Netherlands (MK). This study was funded by the Netherlands Organization for Health Research and Development (ZonMW), project number 150020040. The Netherlands Organization for Health Research and Development did not participate in the design and conduct of the study or in the preparation, review, or approval of the manuscript. NST Expert Group: J. Goede (resident in pediatrics, Medical Center Alkmaar/LUMC), F.W.J. Hazebroek (pediatric surgeon, Erasmus MC–Sophia Children’s Hospital), H.J.R. van der Horst (pediatric urologist, VU University Medical Center), S. de Muinck Keizer-Schrama (pediatric endocrinologist, Erasmus MC–Sophia Children’s Hospital), S.H.A.J. Tytgat (pediatric surgeon, UMC Utrecht–Wilhelmina Children’s Hospital), Tj. Wiersma (general practitioner, Dutch College of General Practitioners [NHG]), S.P. Verloove-Vanhorick (pediatrician, Netherlands Organization for Applied Scientific Research). Revision accepted for publication 30 March 2013.

DOI: 10.1177/0272989X13493145

Undescended testis (UDT) or cryptorchidism is the most common genital anomaly seen in boys, and it can be either congenital or acquired.¹ UDT is associated with higher risk of testicular tumors and, in particular if both testes are involved (bilateral UDT), of infertility.^{2–5}

UDT can be treated surgically by orchidopexy. However, controversy exists regarding the age at which orchidopexy should be performed both for congenital and for acquired UDT.^{6–10} Available

The online appendix for this article is available on the *Medical Decision Making* Web site at <http://mdm.sagepub.com/supplemental>.

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Table 1 Health Outcomes and Their Levels Included in the Model

Health Outcome	Level
Fertility	Paternity
Malignancy	No paternity
	No testicular cancer
Success of surgery	Testicular cancer without death
	Testicular cancer leading to death
	Successful surgery (normal scrotal position and no atrophy)
Complications of surgery	Nonsuccessful surgery because of atrophy, no reoperation possible
	Nonsuccessful surgery, reoperation possible
	No surgery
Cosmetic result	No complications of anesthesia and surgery
	Single complications ^a of anesthesia and surgery
	Death due to anesthesia and surgery
	No scar, normal scrotum
	No scar, abnormal scrotum ^b
	Scar, normal scrotum
	Scar, abnormal scrotum ^b

a. Single complications of anesthesia and surgery may include pain, distension, hematoma, hemorrhage, (wound) inflammation, nausea, sore throat after intubation, allergic reaction to medication, or numbness around scar.

b. Abnormal scrotum is defined as 1 scrotal testis (asymmetry) or no testes.

knowledge from literature can be interpreted differently and shows gaps.^{7,8,11,12}

Randomized controlled trials (RCTs) would be the ideal way to fill these knowledge gaps. However, the performance of RCTs is almost unfeasible, as relevant outcomes (malignancy, infertility) are rare and thus such studies require large numbers of participants and extremely long follow-up.

In this study, we performed a decision analysis in which presently available knowledge is combined to assess the outcomes of orchidopexy at different ages and no orchidopexy (base case analysis). The decision analysis, and in particular sensitivity analysis, is also used to assess which gaps in current knowledge should be filled in order to more reliably estimate the optimal age for surgical intervention.

MATERIAL AND METHODS

Model Design

The decision model was designed and analyzed using TreeAge Pro 2009, Health care. We developed separate decision models for congenital and acquired inguinal UDT (see Appendix). For both congenital and acquired UDT, we distinguished further between unilateral and bilateral UDT, resulting in 4 decision models. For congenital UDT after full-term birth we compared the effects of 7 strategies: surgery at the age of 3 months, 6 months, 9 months, 12 months, 18

months, and 24 months, as well as no surgery. For acquired UDT, the Tanner stage of puberty¹³ was used to define different surgical moments. We compared the effects of surgery at detection, surgery in midpuberty (puberty stage G3), surgery in late puberty (puberty stage G5), and no surgery.

In the model, surgery is expected to affect different health outcomes, such as fertility, malignancy (testicular cancer), surgical success (defined as testis in normal scrotal position, without atrophy), complications of surgery, and cosmetic result. Table 1 shows the different levels of the included health outcomes used. Quantitative estimates for the probabilities of the occurrence of the different outcomes and for the valuation of these outcomes are needed to parameterize the decision model. Combining the probability values and valuation of the different health outcomes for the different ages of surgery, including no surgery, leads to an estimate of lost quality-adjusted life-years (QALYs) for the different ages of surgery. QALY losses are presented without and with discounting, the latter to account for a time preference: health effects obtained in the future count less than immediate health outcomes. A discount percentage of 3% is used.¹⁴ Future health outcomes are discounted to the age at which the clinical decision is made, that is, the first year after birth for congenital and the age of 9 years for acquired UDT (mean age of detection of acquired UDT).^{15,16}

Parameter values in the base case analysis were based on the results of extensive literature review,

analysis of primary data, and expert opinions (see Table 2).

Probability Values on Occurrence of Health Outcomes: Base Case Analysis

In Table 2, the probabilities used in the base case analysis are shown. We assumed conditional independence between the probabilities of paternity (as a parameter for fertility), malignancy, success of surgery, and complications of surgery. Cosmetic result (scar or no scar, normal scrotum or abnormal scrotum) is determined by whether surgery is performed and whether the surgery is successful.

For congenital UDT, the probability of spontaneous descent was based on prospective studies on the prevalence of congenital UDT.^{17–23} An exponential function describing the descent of congenital UDT was fitted on the results of the studies. The estimates are based on results of boys with a birth weight ≥ 2500 g as a proxy for full-term birth. This proxy is used because data on spontaneous descent by duration of pregnancy are hardly available. Using the exponential function, the descent after 12 months was extrapolated from data at earlier ages, as no empirical prevalence data are available for age over 12 months.

For acquired UDT, the percentage of UDT that descends by puberty stage was based on 2 cohort studies.^{15,24} For both congenital and acquired UDT, available data did not allow us to estimate specific percentages of descent for unilateral and bilateral UDT, so similar percentages are used.

Lee¹⁰ has studied paternity rates in a large epidemiologic study of men who underwent orchidopexy for either unilateral or bilateral UDT during childhood. Of the men who had had bilateral UDT, 65% (95% confidence interval [CI] 52.0%–78.6%) achieved paternity, as did 89.7% (95% CI 86.5%–92.8%) in the unilateral group and 93.2% in the control group. This latter percentage is used as paternity rate in case of spontaneous descent of UDT. In the model we assumed that men in whom spontaneous testicular descent would have occurred if no orchidopexy was performed would also have this higher paternity rate. As no paternity rates for bilateral UDT uncorrected by surgical intervention are available from the literature, the paternity rate is estimated at 5% (expert opinion). This low estimate is supported by the low semen quality found in untreated patients with bilateral UDT^{25,26}: 75% of the patients were azoospermic and the remaining 25% of the patients were oligospermic, which indicates that

the probability of paternity will be amply below 25%. For unilateral UDT we assumed a paternity rate of 89.7% without orchidopexy, based on results reported by Lee and Coughlin,²⁷ who found no suggestion that paternity is diminished among men with unilateral cryptorchidism compared with men whose unilateral cryptorchidism was corrected during childhood by orchidopexy.

In case of spontaneous descent of UDT, we assumed that the probability of developing testicular cancer was comparable to that of the general population. Combining age-specific incidence and mortality rates for testicular cancer in the Netherlands²⁸ with the survival table for Dutch men²⁹ resulted in an estimated lifetime risk of developing testicular cancer of 0.54% and of dying from testicular cancer of 0.03%. UDT that would have descended spontaneously if not operated also has these risks. Dieckman and Pichlmeier,³⁰ in a meta-analysis of 21 studies exploring the association of UDT with testicular cancer, found an overall relative risk of 4.8. In the primary analysis we assumed that UDT that will not descend spontaneously will have this higher risk whether orchidopexy is performed or not.

The probability of successful orchidopexy was assumed to be 96%, the average of success rates found in literature^{31–40} weighted by the number of orchidopexies on which they are based. We assumed that of all primary surgical interventions that were not successful, in half of them reoperation would be possible and in the remaining half reoperation would not be possible given the unacceptably high risk of testis atrophy. We assumed that reoperations would have the same success rates as the initial operations. All ultimately unsuccessful operations were assumed to lead to atrophy or an abnormal scrotum (uni- or bilateral absent testis).

The probability of single complications of anesthesia and surgery were assessed at 3.6%.^{34,41–43} In a prospective study among adults, Arbous and others⁴⁴ found that in 1.4 per 10,000 anesthetics, anesthesia has contributed to death. The incidence of death caused primarily by anesthesia may be 10–100 times lower. For children, this rate will be even lower. In this study, we assume a mortality rate of 1.4 per 1,000,000 surgical interventions.

Valuation of Health Outcomes: Base Case Analysis

The valuation of health outcomes consists of multiplication of the utility and duration of the health outcome. To obtain a utility estimate of the different health outcomes related to UDT and its treatment,

Table 2 Probability Parameters Decision Analytic Model Primary Analysis (Univariate Sensitivity Analysis)

Parameter	Unilateral Congenital		Bilateral Congenital		Unilateral Acquired		Bilateral Acquired	
	Probability	Source	Probability	Source	Probability	Source	Probability	Source
Descent congenital UDT <3 months	65% (59%)	14-20	65% (59%)	14-20	—	—	—	—
Descent congenital UDT <6 months	65% (73%)	14-20	65% (73%)	14-20	—	—	—	—
Descent congenital UDT <9 months	65% (76%)	14-20	65% (76%)	14-20	—	—	—	—
Descent congenital UDT <12 months	65% (77%)	14-20	65% (77%)	14-20	—	—	—	—
Descent congenital UDT <18 months	65% (77%)	Extrapolation	65% (77%)	Extrapolation	—	—	—	—
Descent congenital UDT <24 months	65% (77%)	Extrapolation	65% (77%)	Extrapolation	—	—	—	—
Descent acquired UDT before midpuberty (G3)	—	—	—	—	43%	21-22	43%	21-22
Descent acquired UDT before late puberty (G5)	—	—	—	—	66%	21-22	66%	21-22
Descent acquired UDT total	—	—	—	—	66%	21-22	66%	21-22
Paternity after descent	93.2%	10	93.2%	10	93.2%	10	93.2%	10
Paternity without descent and without surgery	89.7% (85%)	10	5% (10%)	Experts	89.7% (93.2%)	10	5% (10%)	Experts
Paternity without descent and with surgery	89.7% (85%)	10	65% (55%)	10	89.7% (93.2%)	10	65% (75%)	10
Testicular cancer without dying in situation without descent and without surgery	2.49% (2.80%)	24-26, 42	2.49% (2.80%)	24-26, 42	2.49% (2.80%)	24-26, 42	2.49% (2.80%)	24-26, 42
Testicular cancer leading to death in situation without descent and without surgery	0.12% (0.14%)	24-26, 42	0.12% (0.14%)	24-26, 42	0.12% (0.14%)	24-26, 42	0.12% (0.14%)	24-26, 42
Testicular cancer without dying by surgically treated UDT in puberty that would not have descended without surgery	—	—	—	—	2.49% (2.80%)	24-26, 42	2.49% (2.80%)	24-26, 42

(continued)

Table 2 (continued)

Parameter	Unilateral Congenital		Bilateral Congenital		Unilateral Acquired		Bilateral Acquired	
	Probability	Source	Probability	Source	Probability	Source	Probability	Source
Testicular cancer leading to death by surgically treated UDT in puberty that would not have descended without surgery	—	—	—	—	0.12% (0.14%)	24–26, 42	0.12% (0.14%)	24–26, 42
Testicular cancer without dying by surgically treated UDT before puberty that would not have descended without surgery	2.49% (1.16%)	24–26, 42	2.49% (1.16%)	24–26, 42	2.49% (1.16%)	24–26, 42	2.49% (1.16%)	24–26, 42
Testicular cancer leading to death by surgically treated UDT before puberty that would not have descended without surgery	0.12% (0.06%)	24–26, 42	0.12% (0.06%)	24–26, 42	0.12% (0.06%)	24–26, 42	0.12% (0.06%)	24–26, 42
Testicular cancer without dying by spontaneous descent UDT in situation without surgery and situation in which surgery takes place before spontaneous descent	0.52%	42	0.52%	42	0.52%	42	0.52%	42
Testicular cancer leading to death by spontaneous descent UDT in situation without surgery and situation in which surgery takes place before spontaneous descent	0.03%	42	0.03%	42	0.03%	42	0.03%	42
Successful orchidopexy	96%	27–36 Experts	96%	27–36 Experts	96%	27–36 Experts	96%	27–36 Experts
Unsuccessful orchidopexy, atrophy	2% (1%, 3%)	Experts	2% (1%, 3%)	Experts	2% (1%, 3%)	Experts	2% (1%, 3%)	Experts
Unsuccessful orchidopexy, reoperation	2% (1%, 3%)	Experts	2% (1%, 3%)	Experts	2% (1%, 3%)	Experts	2% (1%, 3%)	Experts
Single complications of anesthesia and surgery	3.6%	30, 37–39	3.6%	30, 37–39	3.6%	30, 37–39	3.6%	30, 37–39
Death due to anesthesia/surgery	0.00014% (0.000007%)	50, Expert	0.00014% (0.000007%)	50, Expert	0.00014% (0.000007%)	50, Expert	0.00014% (0.000007%)	50, Expert

Table 3 Mean VAS Scores Associated with the Different Health Outcomes Associated with UDT as Valued by the General Population, Mean Utilities (Sensitivity Analysis), Duration of the Health Outcomes, and Resulting Loss in QALYs without Discounting.

Health Outcome	VAS Score	Utility ^a	Duration	QALY loss
No paternity	53.24	0.660 (0.830)	44.1 years ^b	9.2 ^c
Testicular cancer				3.0
Surgery and surveillance	46.05	0.598 (0.799)	7.4 years ^d	31.9
Death due to testicular cancer		0.000	31.9 years ^e	
Abnormal aspect scrotum congenital UDT				
Unilateral	78.24	0.895 (0.947)	20.0 years ^f	2.1
Bilateral	62.71	0.757 (0.879)	20.0 years ^f	4.9
Abnormal aspect scrotum acquired UDT				
Unilateral	78.24	0.895 (0.947)	15.7 years ^g	1.7
Bilateral	62.71	0.757 (0.879)	15.7 years ^g	1.7
Successful surgery				
No complications	89.93	0.963 (0.982)	2 weeks	0.0
Single complications	72.23	0.852 (0.923)	2 weeks	0.0
Unsuccessful surgery due to testis atrophy				
No complications	64.80	0.780 (0.890)	2 weeks	0.0
Single complications	54.15	0.680 (0.840)	2 weeks	0.0
Unsuccessful surgery, reoperation needed				
No complications	67.68	0.810 (0.905)	2 weeks	0.0
Single complications	57.92	0.718 (0.859)	2 weeks	0.0
Scar	83.46	0.919 (0.960)	1 year	0.1
Death due to anesthesia/surgery		0.000	78.3 years— age at surgery	Dependent on age at surgery

Note: QALYs = quality-adjusted life-years; UDT = undescended testis; VAS = visual analogue scale.

a. Utilities are calculated by transforming the values indicated on the VAS scale using the power transformation $1 - (1 - \text{VAS}/100)^{1.61}$. Death states were not valued by respondents; the utility of death states was set at 0.000.

b. 78.3 years (life expectancy men²⁹) – 34.2 years (mean age of men at birth first child²⁹).

c. During 10 years utility loss as indicated by respondents; for the remaining period of 34.1 years this utility loss is halved.

d. Duration treatment and surveillance 10 years after chemotherapy and/or lymph node dissection, otherwise 5 years; 48.3% of men with testicular cancer underwent chemotherapy and/or lymph node dissection.⁶³

e. 78.3 years (life expectancy men²⁹) – 46.4 years (mean age of dying due to testicular cancer²⁸).

f. From age of 5 years (awareness of having abnormal aspect scrotum) to 25 years (having stable relationship).

g. From age of 9.3 years (mean age diagnosis acquired UDT^{15,16}) to 25 years (having stable relationship). In case of successful surgery during puberty, the duration of the period of abnormal aspect scrotum is from the age of 9.3 years to the age at surgery.

a questionnaire was developed in which respondents are asked to value the different health outcomes on a visual analogue scale (VAS) ranging from 0 (worst imaginable health state: death) to 100 (best imaginable health state: perfect health) assuming that there were no other (health) problems. By means of a market research agency, written questionnaires were sent to the Dutch general population in August 2010, resulting in 41 soundly completed questionnaires. The valuations indicated on the VAS scale are transformed to approximate time tradeoff (TTO) scores using the power transformation $1 - (1 - \text{VAS}/100)^{1.61}$ (Stiggelbout and others⁴⁵). The duration of the health outcomes was assessed by literature and expert opinions. In Table 3, the estimates for the duration and utility of the different health outcomes are shown.

In the analysis, the loss in QALYs is calculated by multiplying the loss in utility ($1 - \text{utility}$) for the different health outcomes by the duration of these outcomes (see Table 3). The QALY losses of the separate outcomes are summed to calculate the loss of QALYs for a combination of health outcomes, as, for example, successful surgery with single complications and testicular cancer leading to death.

Sensitivity Analysis

In univariate sensitivity analyses, we assessed the influence of alternative model assumptions concerning descent of congenital UDT, fertility, and risk of developing testicular cancer. We dropped the restriction on birth weight to estimate the percentage of congenital UDT descended by age, resulting in higher

and age-dependent percentages of descending UDT. Concerning fertility, it is suggested that acquired UDT might have other causes than congenital UDT and will have possibly fewer consequences for fertility.⁶ In the sensitivity analysis, we therefore assumed that acquired UDT contributes to successful paternity of 93.2% and 75% for unilateral and bilateral UDT, respectively, while the corresponding percentages for congenital UDT are assumed to be 85% and 55%.

Petterson and colleagues⁴⁶ observed a higher incidence of testicular cancer among men who were surgically treated when they were 13 years or older than among those who underwent the surgery before the age of 13 years. The relative risk of developing testicular cancer, as compared with the general population, was 2.23 among those who underwent orchidopexy before reaching 13 years of age and 5.40 for those treated at 13 years of age or older. In the univariate sensitivity analysis it was assumed that children who underwent surgery before the age of 13 years, that is, before puberty, have a cumulative risk of 1.21% of developing testicular cancer, while this risk is 2.93% for those treated after the age of 13 years or not at all.

Additional univariate sensitivity analyses were performed for parameters that were based on expert opinions (see Table 2 for values in base case and sensitivity analysis) and for utility values. Because it is known that VAS usually results in low scores compared with standard gamble and TTO scores,⁴⁵ we halved the utility losses for the different outcome utilities (see Table 3) except for death.

RESULTS

Base Case Analysis

For congenital UDT, in the base case analysis, orchidopexy results in better outcome (lower loss in QALYs) than no surgery for both unilateral and bilateral UDT. The QALY loss is 0.84 QALYs (3% discounting 0.21 QALYs) for all ages of surgery for unilateral UDT and 1.66 QALYs (0.40 QALYs) for bilateral UDT, compared with, respectively, 1.53 QALYs (0.66 QALYs) and 5.23 QALYs (1.91 QALYs) in case of no surgery (Table 4a). The larger loss in QALYs in case of no surgery is caused by the higher probability and associated utility loss of maintaining an asymmetric scrotum during life (Table 5a). This is not compensated by the absence of utility loss due to surgery and possible complications if no surgery is

performed. For bilateral UDT, the higher probability of infertility contributes to the even higher loss in QALYs if no surgery is performed (Table 5b). No differences in QALY loss are observed between the different ages of surgery included in the model.

For acquired UDT, surgery at the time of diagnosis leads to the lowest loss in QALYs as valued by the general population of 0.91 (0.34) and 1.73 (0.60) QALYs for respectively unilateral and bilateral UDT. The QALY loss is higher if surgery is postponed and highest if no surgery is performed (Table 4b). This is caused by the fact that if no surgery is performed at diagnosis, there is 100% chance of scrotum asymmetry during some period (Table 5c). If the age at surgery is higher, this period will be longer and the QALY loss larger. In case of no surgery this period is longest leading to the highest QALY loss, and for bilateral UDT this is fortified by the higher probability of infertility (37% compared with 16% in case of surgery, see Table 5d). QALY loss due to surgery and possible complications is highest for surgery at diagnosis, as at later ages part of the UDT will be descended. However, this QALY loss is outweighed by the QALY loss due to abnormal scrotum in case of no surgery.

Sensitivity Analysis

The alternative model assumptions concerning descent of congenital UDT, paternity, and risk of developing testicular cancer do not alter the preference for strategies resulting from the base case analysis. Only the QALY loss of surgery till 9 months of age in case of congenital UDT is slightly higher than at advanced ages, due to spontaneous descent of the testis in children with low birth weight in the first year.

Likewise, sensitivity analysis performed on parameters obtained by experts does not change preferences for strategies; neither does the sensitivity analysis in which the utility losses for all health outcomes are halved.

The Tornado plots in Figure 1 show the influence on the difference in QALY loss between surgery and no surgery for the parameters included in the sensitivity analysis, and for acquired UDT the plots also show the impact of these parameters on the decision at which age orchidopexy should be performed. The difference in QALY loss is highly sensitive to the utilities. However, the differences do not reach zero, indicating that surgery, and for acquired UDT surgery at diagnosis, will result in lower QALY losses for all values assumed in the univariate sensitivity analyses.

Table 4 Loss in QALYs for UDT Dependent on Age at Surgery, Base Case, and Sensitivity Analysis (with 3% Discounting in Parentheses)
a. Congenital UDT

	Age at Surgery						No Surgery
	3 Months	6 Months	9 Months	12 Months	18 Months	24 Months	
Unilateral congenital UDT (base case)	0.84 (0.21)	0.84 (0.21)	0.84 (0.21)	0.84 (0.21)	0.84 (0.21)	0.84 (0.21)	1.53 (0.66)
Sensitivity analysis							
Descent age dependent	0.80 (0.21)	0.78 (0.20)	0.78 (0.19)	0.78 (0.19)	0.78 (0.19)	0.78 (0.19)	1.23 (0.49)
Paternity low	0.99 (0.25)	0.99 (0.25)	0.99 (0.25)	0.99 (0.25)	0.99 (0.25)	0.99 (0.25)	1.69 (0.66)
Testicular cancer dependent on surgery	0.82 (0.21)	0.82 (0.21)	0.82 (0.21)	0.82 (0.21)	0.82 (0.21)	0.82 (0.21)	1.54 (0.66)
Probability unsuccessful orchidopexy, atrophy low	0.83 (0.21)	0.83 (0.21)	0.83 (0.21)	0.83 (0.21)	0.83 (0.21)	0.83 (0.21)	1.53 (0.66)
Probability unsuccessful orchidopexy, atrophy high	0.85 (0.22)	0.85 (0.22)	0.85 (0.22)	0.85 (0.22)	0.85 (0.22)	0.85 (0.22)	1.53 (0.66)
Probability death due to anesthesia/surgery low	0.84 (0.21)	0.84 (0.21)	0.84 (0.21)	0.84 (0.21)	0.84 (0.21)	0.84 (0.21)	1.53 (0.66)
Utility values high	0.43 (0.11)	0.43 (0.11)	0.43 (0.11)	0.43 (0.11)	0.43 (0.11)	0.43 (0.11)	0.78 (0.33)
Bilateral congenital UDT (base case)	1.66 (0.40)	1.66 (0.40)	1.66 (0.40)	1.66 (0.40)	1.66 (0.40)	1.66 (0.40)	5.23 (1.91)
Sensitivity analysis							
Descent age dependent	1.34 (0.34)	1.32 (0.32)	1.31 (0.32)	1.31 (0.32)	1.31 (0.32)	1.31 (0.32)	3.66 (1.30)
Paternity low	1.98 (0.48)	1.98 (0.48)	1.98 (0.48)	1.98 (0.48)	1.98 (0.48)	1.98 (0.48)	5.07 (1.87)
Testicular cancer dependent on surgery	1.63 (0.30)	1.63 (0.30)	1.63 (0.30)	1.63 (0.30)	1.63 (0.30)	1.63 (0.30)	5.23 (1.91)
Probability unsuccessful orchidopexy, atrophy low	1.64 (0.39)	1.64 (0.39)	1.64 (0.39)	1.64 (0.39)	1.64 (0.39)	1.64 (0.39)	5.23 (1.91)
Probability unsuccessful orchidopexy, atrophy high	1.67 (0.42)	1.67 (0.42)	1.67 (0.42)	1.67 (0.42)	1.67 (0.42)	1.67 (0.42)	5.23 (1.91)
Probability death due to anesthesia/surgery low	1.66 (0.40)	1.66 (0.40)	1.66 (0.40)	1.66 (0.40)	1.66 (0.40)	1.66 (0.40)	5.23 (1.91)
Utility values high	0.84 (0.20)	0.84 (0.20)	0.84 (0.20)	0.84 (0.20)	0.84 (0.20)	0.84 (0.20)	2.62 (0.95)

b. Acquired UDT

	Age at Surgery			No Surgery
	Diagnosis	Midpuberty	Late Puberty	
Unilateral acquired UDT (base case)				
Sensitivity analysis	0.91 (0.34)	1.16 (0.60)	1.31 (0.77)	1.59 (0.94)
Paternity high	0.80 (0.31)	1.05 (0.57)	1.20 (0.74)	1.48 (0.90)
Testicular cancer dependent on age at surgery	0.89 (0.33)	1.16 (0.60)	1.31 (0.77)	1.60 (0.94)
Probability unsuccessful orchidopexy, atrophy low	0.89 (0.32)	1.15 (0.60)	1.30 (0.77)	1.59 (0.94)
Probability unsuccessful orchidopexy, atrophy high	0.93 (0.35)	1.17 (0.61)	1.31 (0.77)	1.59 (0.94)
Probability death due to anesthesia/surgery low	0.91 (0.34)	1.16 (0.60)	1.31 (0.77)	1.59 (0.94)
Utility values high	0.46 (0.17)	0.59 (0.30)	0.66 (0.39)	0.81 (0.47)
Bilateral acquired UDT (base case)				
Sensitivity analysis	1.73 (0.60)	2.35 (1.30)	2.72 (1.71)	5.20 (2.65)
Paternity high	1.41 (0.50)	2.04 (1.21)	2.40 (1.62)	5.13 (2.60)
Testicular cancer dependent on age at surgery	1.71 (0.59)	2.36 (1.30)	2.72 (1.71)	5.29 (2.65)
Probability unsuccessful orchidopexy, atrophy low	1.69 (0.56)	2.34 (1.29)	2.71 (1.71)	5.29 (2.65)
Probability unsuccessful orchidopexy, atrophy high	1.76 (0.63)	2.37 (1.31)	2.72 (1.71)	5.29 (2.65)
Probability death due to anesthesia/surgery low	1.73 (0.60)	2.35 (1.30)	2.72 (1.71)	5.29 (2.65)
Utility values high	0.87 (0.30)	1.18 (0.65)	1.36 (0.85)	2.65 (1.32)

Note: QALYs = quality-adjusted life-years; UDT = undescended testis.

Table 5 Percentage of Patients Experiencing Health Outcome Dependent on Age at Surgery
a. Congenital Unilateral UDT

Health Outcome	Age at Surgery						No Surgery
	3 Months	6 Months	9 Months	12 Months	18 Months	24 Months	
No paternity	8.0%	8.0%	8.0%	8.0%	8.0%	8.0%	8.0%
Testicular cancer without death	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%
Testicular cancer leading to death	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Abnormal scrotum	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	35.0%
Single complications of anesthesia and surgery	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	0.0%
Reoperation	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.0%
Death due to anesthesia and surgery	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

b. Congenital Bilateral UDT

Health Outcome	Age at Surgery						No Surgery
	3 Months	6 Months	9 Months	12 Months	18 Months	24 Months	
No paternity	16.7%	16.7%	16.7%	16.7%	16.7%	16.7%	37.7%
Testicular cancer without death	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%
Testicular cancer leading to death	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Abnormal scrotum	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	35.0%
Single complications of anesthesia and surgery	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	0.0%
Reoperation	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.0%
Death due to anesthesia and surgery	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%

c. Acquired Unilateral UDT

Health Outcome	Age at Surgery			No Surgery
	Diagnosis	Midpuberty	Late Puberty	
No paternity	8.0%	8.0%	8.0%	8.0%
Testicular cancer without death	1.2%	1.2%	1.2%	1.2%
Testicular cancer leading to death	0.07%	0.07%	0.06%	0.06%
Abnormal scrotum	2.0%	100%	100%	100%
Single complications of anesthesia and surgery	3.7%	2.1%	1.3%	0.0%
Reoperation	2.0%	1.1%	0.7%	0.0%
Death due to anesthesia and surgery	0.0%	0.0%	0.0%	0.0%

d. Acquired Bilateral UDT

Health Outcome	Age at Surgery			No Surgery
	Diagnosis	Midpuberty	Late Puberty	
No paternity	16.4%	16.4%	16.4%	36.8%
Testicular cancer without death	1.2%	1.2%	1.2%	1.2%
Testicular cancer leading to death	0.06%	0.06%	0.06%	0.06%
Abnormal scrotum	2.0%	100%	100%	100%
Single complications of anesthesia and surgery	3.7%	2.1%	1.3%	0.0%
Reoperation	2.0%	1.1%	0.7%	0.0%
Death due to anesthesia and surgery	0.0%	0.0%	0.0%	0.0%

Note: UDT = undescended testis.

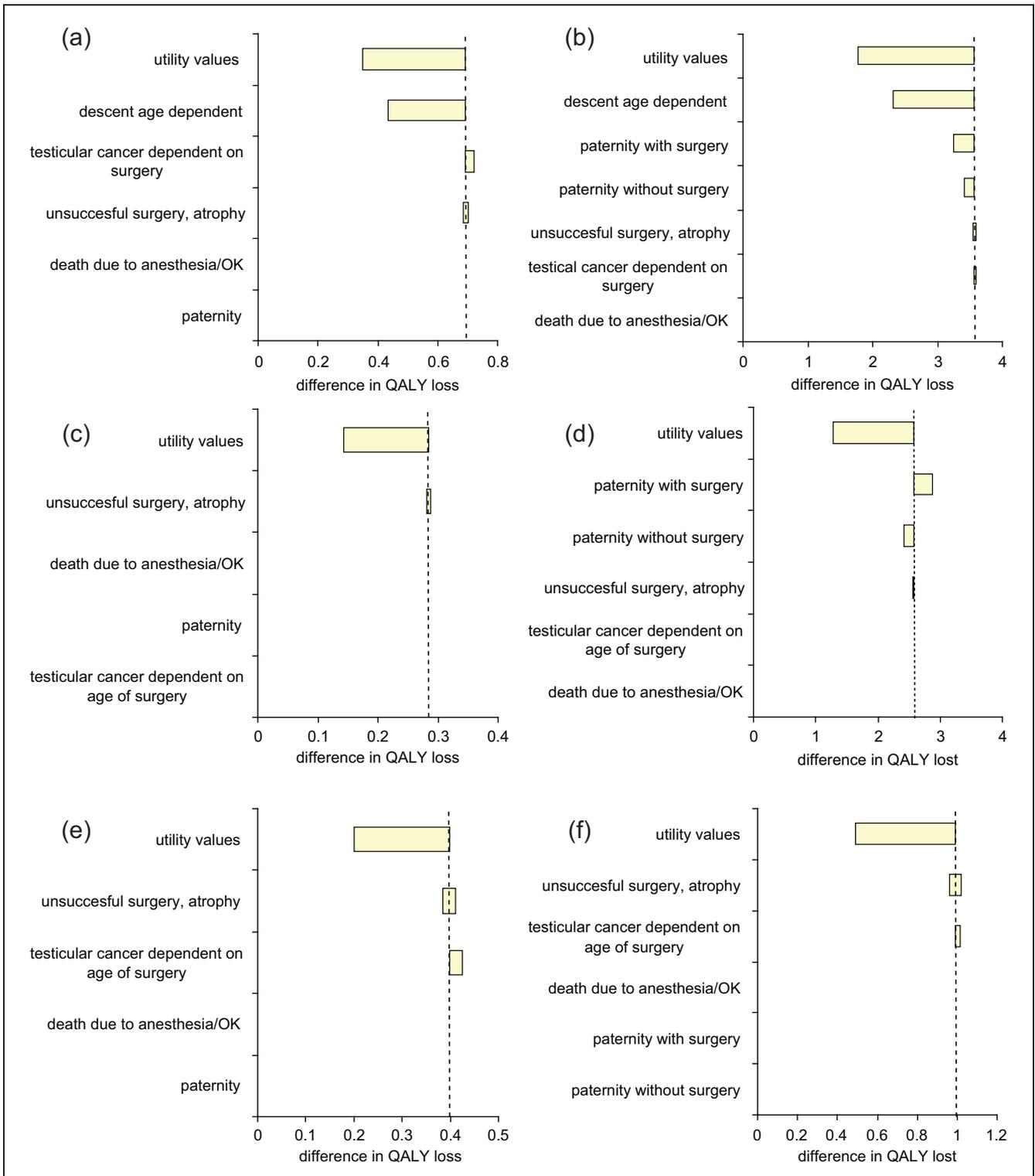


Figure 1 Tornado plots on the difference in quality-adjusted life-year (QALY) loss between surgery and no surgery for (a) congenital unilateral UDT, (b) congenital bilateral UDT, (c) acquired unilateral UDT, and (d) acquired bilateral UDT, and on the difference in QALY loss between surgery at diagnosis and surgery in late puberty for (e) acquired unilateral UDT and (f) acquired bilateral UDT. Dotted line represents differences in QALY loss in base case analysis.

DISCUSSION

Decision analysis can be used in situations in which no agreement exists on the basis of available knowledge. In sensitivity analysis, the influence of model uncertainty and parameter uncertainty on the outcome can be assessed and analyzed. We used a decision analytic model to assess the optimal age at surgery for UDT and studied the impact of model uncertainty and parameter uncertainty.

We found that for congenital UDT (both unilateral and bilateral), surgery will result in the lowest QALY loss. For congenital unilateral UDT, the higher QALY loss for the no-surgery option is the consequence of lifelong scrotal asymmetry. For congenital bilateral UDT, lower fertility in case of no surgery adds to this QALY loss.

In acquired UDT, surgery at the time of detection leads to the lowest QALY loss. For acquired unilateral UDT, this is caused by scrotal asymmetry. For untreated acquired bilateral UDT, reduced paternity further adds to this loss. The different losses in QALYs at the different moments of surgery (Table 4b) are the consequences of effects on cosmesis and of adverse outcomes of anesthesia and surgery. The later the surgery is performed, the longer the period of scrotal asymmetry and thus the higher the QALY loss. However, if surgery is postponed till puberty, the QALY loss caused by adverse effects of surgery will be less because, given spontaneous descent, fewer orchidopexies will be needed.

Based on the societal valuation of the health outcomes used in this study, surgery for unilateral UDT (both congenital and acquired) yields the lowest QALY loss, caused by the cosmetic effect of scrotal asymmetry. In clinical practice these utilities may differ from patient to patient. This means that in clinical practice, (the parents of) the patient have to conduct their own valuations to decide whether orchidopexy is performed in case of unilateral UDT and, if so, at what age.

For bilateral UDT (both congenital and acquired), orchidopexy is the preferred option in order to improve fertility; however, the age at which orchidopexy is performed should be discussed with the parents and the patient. The choice for the optimal age to treat congenital UDT should take into account both the cosmetic effect of having an asymmetric scrotum and the vulnerability of young children for congenital UDT. For acquired UDT, the optimal age is determined by weighing the cosmetic aspect and complications of anesthesia and surgery for acquired UDT.

No univariate sensitivity analysis leads to significant changes in the results over the range tested. Only in case of congenital UDT we found that it is advantageous to wait till at least 6 months of age before orchidopexy is performed, because spontaneous descent of UDT might still occur.

We have performed our analyses for UDT that can be palpated in the inguinal region; however, in a minority, undescended testes are located in the abdomen. Model assumptions do not differ much for these abdominal UDT, mainly because no distinction is made in literature on descent, paternity, and malignancy between inguinal and abdominal UDT, but the success rate of orchidopexy is lower for abdominal UDT.⁴⁷ Lowering the success percentage of orchidopexy to 87%,⁴³ however, did not lead to different results for abdominal UDT compared with inguinal UDT.

Taking costs into account will likewise not affect strategic preferences. Costs of orchidopexy amount to €821⁴⁴ in case of orchidopexy without complications and €1728^{48,49} if hospital admission is needed for complications of anesthesia or surgery. These costs relate favorably to the QALY gain due to orchidopexy, which ranges from at least 0.28 QALYs (0.17 QALYs with 3% discounting) in case of orchidopexy for acquired unilateral UDT at late puberty compared with no surgery to 3.57 QALYs (1.51 QALYs) in case of orchidopexy for congenital bilateral UDT compared with no surgery when assuming a societal willingness to pay for a QALY between €20,000 and €40,000.⁵⁰ Because surgery for bilateral UDT will reduce need for later fertility treatment, these additional savings will further strengthen the preference for surgery.

The analysis of congenital UDT was restricted to full-term birth. However, as indicated by the results of the sensitivity analysis in which also testicular descent in boys with a birth weight less than 2500 g is included, which may represent preterm birth, correcting the age for prematurity will make the results also applicable to preterm birth.

Standard gamble (SG), TTO, and VAS are the methods used most often to assess values for health outcomes. In this study we used the VAS, as this method is relatively easy and can be self-administered.^{51,52} It is known that the 3 methods will result in different outcomes, usually with the VAS yielding the lowest results, the standard gamble yielding the highest, and the TTO in an intermediate position. We therefore used the power transformation of VAS scores to TTO scores as proposed by Stiggelbout and others.⁴⁵ They supposed that this

relationship existed independently of disease state and health status. Torrance and others,⁵³ however, show that no consistent power function has been found between VAS and SG, and this might also apply to TTO. Furthermore, measurement bias may have occurred given that respondents have been found reluctant to use the portion of the scale near the ends of the VAS (end-aversion bias). This may have underestimated the utility values. Also compared with VAS estimates from other studies for infertility and cancer,^{54,55} our estimates were quite low: 0.49 v. 0.46 and 0.59–0.70 v. 0.53, respectively. However, sensitivity analyses show that these differences will not change the preferences for strategies.

In this study the values for the health outcomes were used additively in case patients had more than 1 less optimal health outcome, for example, reoperation, testicular cancer, and nonpaternity. This might have overestimated the disutility for these patients.

To our knowledge, this is the first decision analysis comparing the health outcomes of surgical treatment for different ages. Two earlier analyses in the management of UDT focused on costs. Lorenzo and others⁵⁶ performed a cost analysis of laparoscopic versus open orchidopexy in the management of unilateral nonpalpable testicles and concluded that laparoscopic evaluation has a costs saving advantage over initial inguinal-scrotal exploration. Hsieh and others⁵⁷ performed an economic analysis of infant versus postpubertal orchidopexy specifically with respect to testicular cancer development and management. Their results showed that infant orchidopexy is less costly than later surgery, because of slightly higher costs of postpubertal orchidopexy and assuming higher probability of developing cancer if orchidopexy is performed after 13 years of age.⁴⁶

The main limitation of the study is the availability and quality of data necessary for the decision analytic model. Most data that were available did not discern between different forms of UDT, namely congenital and acquired, inguinal and abdominal, and unilateral and bilateral. For unilateral and bilateral UDT, no distinction could be made in percentage descent, so similar descent percentages are assumed, whereas it might well be that the probability of spontaneous descent of both testes in case of bilateral UDT is lower compared with unilateral UDT. As a result, the QALY loss without surgery for bilateral UDT may have been underestimated, indicating an even more profound difference in QALY loss between orchidopexy and no surgical treatment, in favor of orchidopexy. In

other cases of missing data, we used expert opinions, including a range of uncertainty, representing the best available knowledge.

Furthermore, some parameters were based on rather old data because more recent data were not available. Rates of paternity after orchidopexy, for example, are based on men who underwent orchidopexy between 1955 and 1974.

Finally, obtaining valuation of health states and combining them with durations to obtain QALY losses is a delicate procedure. For example, we asked respondents to indicate the value of health states on the VAS assuming that there were no other (health) problems, and we therefore subtracted the indicated value from 1 (best imaginable health state). However, some respondents may have kept their own health status as reference point, which will have led to an overestimation of the QALY loss in our analysis. Furthermore, a constant utility loss of testicular cancer has been applied over the entire surveillance period. As this utility loss is a combination of anxiety that the cancer will reoccur and symptoms of testicular cancer, of which the latter are likely to lessen after treatment, this might have overestimated the QALY loss due to testicular cancer. However, given the low probability of testicular cancer, the resulting overestimation of the difference between surgery and no surgery will be small.

The results of this decision analysis were intended as input for a multidisciplinary guideline on when to observe or refer UDT in the Netherlands. Despite the collaborative development of the decision analytic model between modelers and medical professionals, additional clinical considerations were only identified after the results of the decision analysis were known, at the time they were to be translated into guidelines. In particular the conclusion, that the decision to treat unilateral UDT (both congenital and acquired) is amenable to patient preference (such as cosmesis), was found to be clinically counterintuitive. An additional (post hoc) argument against such a policy was thought to be the facilitation of (self-) detection of a possible testis tumor by orchidopexy, leading to a more favorable prognosis. However, the literature does not support this argument, as cancer survival rates are comparable for tumors detected in a scrotal and nonscrotal testis.^{58–60} Other post hoc arguments for orchidopexy in case of unilateral UDT were that the nondescended testis can give complaints/pain in the inguinal region (e.g., torsion of the undescended testis) and that orchidopexy means there is a second scrotal testis, as it were, “in reserve” in case something might

happen to the originally descended testis. Although case reports are available on torsion of the undescended testis^{61,62} indicating that this is a relatively rare phenomenon but requires immediate treatment, no incidence can be estimated from the available literature to include in the decision model. More evidence is needed on these subjects to obtain evidence-based recommendations.

Currently, a consensus-based guideline was developed in which surgery was recommended for both unilateral and bilateral UDT (congenital and acquired). The age at surgery for congenital UDT is advised to be between 6 and 12 months; for acquired UDT the age at surgery is to be discussed with parents and patient.

CONCLUSION

Based on our decision analytic model using societal valuations of health outcomes, we conclude that surgery for unilateral UDT (both congenital and acquired) provides the best outcome, that is, yields the lowest QALY loss, mainly through scrotal cosmesis. In clinical practice, these utilities may differ from patient to patient. This suggests that in clinical practice, (the parents of) the patient, after being optimally informed on all aspects of UDT, may assess their own valuations to decide whether orchidopexy is performed in case of unilateral UDT and, if so, at what age.

For bilateral UDT (both congenital and acquired) orchidopexy is the preferred strategy contributing to improved fertility, and the age at which orchidopexy is performed should be discussed with the parents and the patient. Such evidence may in addition contribute to the adoption of our conclusions into clinical practice guidelines and to their implementation and acceptance in actual care.

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