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Chapter 6

Cost and effects of risk factor guided screening strategies for retinopathy of prematurity

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Submitted

ABSTRACT

Purpose

To investigate the cost and effects of risk factor guided screening strategies for retinopathy of prematurity.

Methods

Clinical data from the Netherlands ROP study (NEDROP study), that included all infants screened for ROP and born in 2009 were used to assess the cost and effects of several screening strategies for ROP using different criteria: (1) Gestational age(GA), (2) Birth weight(BW), (3) combined GA-BW and (4) combined GA-BW and presence of risk factors.

Results

The most efficient screening strategy to include all infants treated for both treatment strategies is to screen all infants with a GA of 30 weeks or less and a BW of 1250 g or lower together with infants with a GA of 30-32 weeks and a BW of 1250-1500 g with at least one risk factor. The marginal cost ranged from €43,848 to € 226,914 per additional infant with improved vision.

Conclusion

The current Dutch guideline may be improved: the same effectiveness can be obtained for lower costs. Also releasing the precondition that no infants with severe ROP might be missed, will lead to lower costs, but this will also lead to a lower number of infants with improved visual acuity. However, the costs of detecting all infants with severe ROP seems acceptable for society when also including the QALY gain and savings from a societal perspective resulting from improved vision.

INTRODUCTION

Retinopathy of Prematurity (ROP) is still one of the most important causes of partial sight or blindness in premature born infants. Various studies showed that early detection and treatment of ROP improve visual outcome.[1]
As younger and sicker infants are surviving, the number at risk for (severe) ROP increases. We conducted a prospective population based study, the NEDROP study, to inventorize the incidence and risk factors for ROP in the Netherlands. Based on these data the former ROP-guideline was adjusted to focus screening on those infants with the highest risk of ROP and reduce the infants exposed to stressful screening examinations. The new screening guideline included all infants with gestational age (GA) < 30 weeks and/or birth weight (BW) < 1250 gram (g) as well as infants with GA 30-32 weeks and/or BW 1250-1500 g with one of the following risk factors: artificial ventilation (AV), necrotising enterocolitis (NEC), sepsis, postnatal glucocorticoids or treatment with cardiotonica in the period between birth and the first screening examination.[2] A precondition for adjustment of the inclusion criteria was that no infants with severe ROP would be missed. As costs become more and more important in health care, the aim of this study is to compare the effects and costs of the Dutch screening strategy with other risk factor guided screening strategies, including strategies in which not all infants with severe ROP are detected.[3]

MATERIAL AND METHODS

Data

Clinical data were retrieved from the Netherlands ROP study (NEDROP study), that included all infants screened for ROP and born in 2009. Eligible to enter this study were infants with GA < 32 wks and/or BW < 1500 gram. The incidence of blind and visually impaired children was obtained from retrospective data from the Dutch institutes of the visually impaired.[3]
ROP was classified according to the International Classification of ROP (ICROP), the highest stage in either eye being reported.[4] For risk factor analysis the NEDROP database, encompassing all ophthalmological data, was merged with the Netherlands Perinatal Registry (PRN) which is a medical, professional based registry where pediatricians and neonatologists report their data of neonates born in the Netherlands.

In the NEDROP database 2193 infants were reported, of which 164 died (4 screening completed). Of the remaining infants, 1888 infants had a registered GA < 32 wks and/or BW < 1500 gram, of which 1551 (82.2%) were screened for ROP. ROP developed in

323 (20.8 %) infants, mild ROP (stage 1 and 2) was found in 294 (19.0%) and severe ROP (stage ≥ 3) in 29 (1.9%) infants. Seventeen (1.1%) infants were treated.

Data analysis

Several screening strategies for ROP were studied using different criteria: (1) GA, (2) BW, (3) combined GA-BW and (4) combined GA-BW and presence of risk factors. An overview of the strategies studied is presented in table 1.

Merging of NEDROP- and PRN database was possible for 1380 infants of the 1551 that are included in the present study. Missing data on risk factors were substituted using multiple imputation by chained equations[5], with 10 iterations for the switching regression model. For each missing data item, an imputation regression model was used that included GA, BW, treatment, presence of risk factors and ROP classification.

Using complete data the number of infants eligible for screening, severe ROP and treated were assessed for all screening strategies (table 1). This table was used to identify the strategies that screened the least number of infants for different numbers of

Table 1 Number of infants eligible for screening, diagnosed with severe ROP and treated for ROP for the different screening strategies

Nr	Criteria*	Eligible	Treated for ROP	Severe ROP
	GA, weeks			
1	<26	85	7	11
2	<27	179	13	21
3	<28	313	13	22
4	<29	477	13	22
5	<30	750	15	25
6	<31	1053	16	26
7	<32	1430	17	29
	BW, g			
8	< 700	72	5	6
9	< 1000	342	13	19
10	< 1100	465	15	22
11	< 1200	644	15	27
12	< 1250	726	15	27
13	< 1300	806	16	28
14	< 1400	956	16	28
15	< 1500	1134	17	29
	Combined, GA and BW			
16	< 29/<1200	382	13	22
17	< 29/<1250	407	13	22

Table 1 Number of infants eligible for screening, diagnosed with severe ROP and treated for ROP for the different screening strategies (continued)

Nr	Criteria*	Eligible	Treated for ROP	Severe ROP
18	< 29/<1500	456	13	25
19	< 30/<1200	485	14	24
20	< 30/<1250	529	14	24
21	< 30/<1500	672	15	25
22	< 31/<1200	572	15	25
23	< 31/<1250	628	15	25
24	< 31/<1500	871	16	26
25	< 32/<1200	610	15	27
26	< 32/<1250	678	15	27
27	< 32/<1500	1013	17	29
	Combined, GA and/or BW			
28	< 29/<1200	739	15	27
29	< 29/<1250	796	15	27
30	< 29/<1500	1155	17	29
31	< 30/<1200	909	16	28
32	< 30/<1250	947	16	28
33	< 30/<1500	1212	17	29
34	< 31/<1200	1125	16	28
35	< 31/<1250	1151	16	28
36	< 31/<1500	1316	17	29
37	< 32/<1200	1464	17	29
38	< 32/<1250	1478	17	29
39	< 32/<1500	1551	17	29
	Combined GA-BW-risk factor			
40	<30 wks and <1250 g and at least a risk factor	436	12	20
41	<32wks and <1500 g and at least a risk factor	687	15	25
	Combined GA-BW-risk factor			
42	<30 wks and/or <1250 g and at least a risk factor	666	14	24
43	<32 wks and/or <1500 g and at least a risk factor	899	15	25
44	< 30 wks and 1250 g OR 30-32 wks and/or 1250-1500 g and at least a risk factor	866	17	29
45	< 30 wks and/or 1250 g OR 30-32 wks and/or 1250-1500 g and at least a risk factor (current Dutch strategy)	1180	17	29

*Light grey: efficient strategies using the outcome of the NEDROP study (17 infants treated); Dark grey: efficient strategies using severe ROP as treatment strategy; Medium grey: efficient strategies for both the current treatment strategy and the severe ROP treatment strategy.

treated infants found (efficient strategies).[6] Two treatment strategies were evaluated: the infants actually treated in the NEDROP study (n=17) and the infants that would have been treated when early treatment guidelines would have been used (n=29).

Cost-effectiveness analysis

The efficient strategies were included in the cost-effectiveness analysis, in which the costs and effects of the different strategies were compared.

Cost of Screening

The costs resulting from the different strategies were estimated from a healthcare perspective. Costs are expressed in 2013 Euros. We used expert opinions to assess the personnel time and costs of equipment and disposables. Personnel time was valued using the salary costs increased with employers' costs.[7] Costs consisted of screening and treatment costs.

Costs of screening were assessed by multiplying the number of screening examinations per infant with the costs per screening. The mean number of screening examinations per infant was obtained from the NEDROP study[8] for infants diagnosed with no ROP (1.2), mild ROP (4.3) and severe ROP (8.0). Costs per screening consisted of nursing costs (40 minutes), costs of ophthalmologist (30 minutes), eyelid speculum and eye drops, resulting in €109 per screening.

Costs of treatment consist of ambulance transport costs, necessary for transfer to the treatment center, and costs of surgery. Ambulance transport cost amount to € 2282. Laser treatment was performed in 82.5% of the infants and the remaining part underwent vitrectomy. Cost of laser treatment amount to €2,755 (costs of operating theatre use, 2 surgery assistants, an anesthesiologist and an anesthetic nurse, an ophthalmologist (vitreoretinal surgeon), in 30% also a neonatologist during 105 minutes, and equipment costs of €31 per laser treatment) and cost of vitrectomy which amount to €5178 (costs of operating theatre, 2 surgery assistants, an anesthesiologist and an anesthetic nurse, ophthalmologist (vitreoretinal surgeon), in 30% also a neonatologist during 180 minutes, and equipment and disposable costs of €540).[9]

Effects

The effects of screening in terms of improved visual acuity depend on the improvement of visual acuity of early laser treatment compared to no treatment. However, only some smaller studies are available comparing the effects of early laser treatment with no treatment.[10-12] We therefore obtained the effect of laser treatment from the CRYO-ROP en ETROP study. The CRYO-ROP study[13] compared treatment with cryotherapy with no treatment and the ETROP compared the improved vision of early laser treatment with late treatment with cryotherapy.[14] Using the adjusted indirect comparison method[15;16],

we combined the improved vision of the CRYO-ROP study of 17.7% with an improved vision of 7.7% resulting from the ETROP study, giving an estimated improved vision of 25.4% of laser treatment versus no treatment.[13;14]

RESULTS

Table 1 presents the number of infants eligible for screening, diagnosed with severe ROP and treated for ROP for the different screening strategies.

Table 1 shows that the most efficient screening strategy to include all infants treated for both treatment strategies is to screen all infants with a GA of 30 weeks or less and a BW of 1250 g or lower together with infants with a GA of 30-32 weeks and a BW of 1250-1500 g with at least one risk factor. This requires screening of 866 children in the screening cohort.

The other shaded strategies are the most efficient strategies when detection of a lower number of children that need treatment would be accepted. In Table 2 the cost-effectiveness of the efficient screening strategies are shown. The strategies are presented by ascending order of persons with improved vision. In table 2a the efficient strategies are shown for the infants that were treated in the NEDROP study and in table 2b for treating all severe ROP. Also the cost and effects of the current and previous Dutch guidelines, respectively screening infants with GA <30 weeks *and* BW <1250 g and a selection of infants with GA 30-32 weeks and/or BW 1250-1500 g with at least one risk factor and screening infants with a BW <1500 g and/or a GA <32 weeks are presented for comparison.

The total costs per year of the different screening programmes (including treatment costs) range from €58,208 for the efficient strategy detecting 5 of the 17 infants that were treated in the NEDROP study (strategy nr 8) to €359,106 for the efficient strategy that detects all 17 infants (strategy nr 44). Detecting all 17 infants will on average lead to an improved vision in 4.3 infants. The average cost per person with improved vision (AC/PIV) ranges from €43,848 per person with improved vision when screening all infants with a GA of 26 weeks or less (strategy nr 1) to €82,953 for the efficient screening strategy that will detect all infants that were treated in the NEDROP study (strategy nr 44). Some efficient strategies were dominated by other strategies, i.e. there was an alternative strategy or combination of alternative strategies resulting in more infants with improved vision for lower costs.

The marginal cost per additional PIV is the most important outcome in the cost-effectiveness analysis. It indicates the additional cost of a unit of improved outcome of a dominant screening strategy compared to the next less intensive dominant screening strategy.

Table 2a Costs, effects and cost-effectiveness of efficient screening strategies for ROP (based on treatment practice determined in NEDROP study) compared to the current and previous Dutch strategy

Cost derivation	Screening strategy									
	BW <700	GA<26	GA<30 and BW <1250 and risk factor	GA<27	GA <30 and BW <1200	BW <1100	BW <1300	(GA < 30 and BW < 1250) OR GA 30-32 and/ or BW 1250-1500 and risk factor	Current NL strategy (GA < 30 and/or BW < 1250) OR GA 30-32 and/or BW 1250-1500 and risk factor	Previous NL strategy (GA<32 and/or BW<1500)
Infants to be treated for ROP detected	5	7	12	13	14	15	16	17	17	17
Number of screenings	267	341	1355	677	1497	1426	2214	2375	2997	3707
Total cost	58,208	77,692	220,067	149,563	244,843	242,918	334,824	358,190	426,080	503,563
No of PIV	1.3	1.8	3.1	3.3	3.6	3.8	4.1	4.3	4.3	4.3
AC/PIV	45,833	43,848	69,871	45,295	68,854	63,758	82,388	82,953	98,675	116,620
MC/APIV	Dominated	43,848*	Dominated	46,982	Dominated	183,769	Dominated	226,914	Dominated	Dominated

*compared to a situation without screening

(A)PIV: (additional) persons with improved vision; AC: average cost; MC: marginal costs

Table 2b Costs, effects and cost-effectiveness of efficient screening strategies for ROP (using severe ROP as criterion for treatment) compared to the current and previous Dutch strategy

Cost derivation	Screening strategy													
	BW <700	GA<26	BW <1000	GA <30 and BW<1250 and risk factor	GA <27	GA < 28	GA <30 and/or BW<1250 and risk factor	GA < 31 and BW<1200	GA < 31 and BW<1500	GA <32 and BW<1200	BW <1300	(GA < 30 and BW < 1250) OR GA 30-32 and/ or BW 1250-1500 and risk factor	Current NL strategy (GA < 30 and/ or BW < 1250) OR GA 30-32 and/ or BW 1250-1500 and risk factor	Previous NL strategy (GA<32 and/or BW <1500)
Infants to be treated for ROP detected	**6**	11	19	20	21	22	24	25	26	27	28	29	29	29
Number of screenings	267	341	1131	1355	677	1045	2214	1685	2347	1785	2214	2375	2997	3707
Total cost	64,023	101,224	233,971	266,591	196,087	242,017	350,222	329,319	407,403	351,955	404,611	427,976	495,866	573,349
No of PIV	1.5	2.8	4.8	5.2	5.3	5.6	6.2	6.4	6.6	6.9	7.1	7.4	7.4	7.4
AC/PIV	42,010	36,229	48,481	51,450	36,762	43,310	56,509	51,861	61,690	51,320	56,891	58,102	67,318	77,837
MC/APIV	Domi-nated	36,229*	Domi-nated	Domi-nated	37,348	Domi-nated	Domi-nated	Domi-nated	Domi-nated	102,276	Domi-nated	149,647	Dominated	Domi-nated

*compared to a situation without screening

(A)PIV: (additional) persons with improved vision; AC: average cost; MC: marginal costs

Detecting 7 or 13 children that need treatment, lead to marginal costs less than €100,000 per infant with improved vision (respectively €43,848 in strategy nr 8 and €46,982 in strategy nr 2). However, detecting also (some of) the other children that need treatment leads to higher marginal costs ranging from €183,769 (strategy nr 10) to € 226,914 (strategy nr 44) per additional infant with improved vision.
Total costs treating all infants with severe ROP are higher (table 2b), but as also the number of persons with improved vision will be higher, average and marginal cost per (additional) person with improved vision are lower, ranging respectively from €36,229 (strategy nr 1) to €61,690 (strategy nr 24) and from €36,229 (strategy nr 1) to €149,647 (strategy nr 42).

DISCUSSION

We found that even if we do not want to miss infants with severe ROP, there is a more efficient screening guideline than the current Dutch guideline, namely screening infants with GA <30 weeks *and* BW <1250 g and a selection of infants with GA 30-32 weeks and/or BW 1250-1500 g, with at least one risk factor. This screening strategy reduces the number of infants to be screened with 27% ((1180-866)/1180). In determining the current Dutch guideline a safety approach was chosen. Based on the results of 2009 stricter inclusion criteria for screening could be chosen to reduce the number of infants screened while still detecting all infants with severe ROP, as illustrated by the results of our economic evaluation. The current guideline has led to a reduction in yearly costs of €77,500 compared to the previous Dutch guideline dating from 1997 advising screening infants with a BW <1500 g and/or a GA <32 weeks[17], however further savings of €67,900 each year might be obtained by the more stringent screening strategy resulting from this study.
However, the probability that in another year infants with severe ROP will be missed will be higher if a more stringent screening strategy is used. Therefore, it is interesting to investigate the stability of the current results in follow-up studies of the NEDROP, using data from other calendar years or in large cohorts from other countries.
If we release the precondition that no infants with severe ROP should be missed, there are other strategies having lower costs per infant with improved vision (see table 2). To decide whether we accept missing children with severe ROP, we have to determine which costs per additional infant with improved vision are acceptable for society. For the current treatment strategy these marginal costs range from €43,848 to €226,914. These costs should be compared to the benefits of improved vision. These benefits include both gains in quality of life and societal cost savings, for example due to lower educational costs as these infants don't need special education. Assuming a mean visual acuity

of 0.20 in non-treated eyes and 0.48 in treated eyes[18], a yearly gain in utility of 0.10 can be obtained according to the formula of Sharma et al.[19] For an average life expectancy around 80 years[20] and applying a discount rate of 3% over this period, this amounts to 3.3 quality adjusted life-years (QALYs) for an infant with improved vision during lifetime. Relating this to the marginal costs of €226,914 results in a cost-utility ratio of €70,000 QALY, which is high compared to the acceptable range of €20,000-€40,000 per QALY in the Netherlands. To reach this acceptable range, improved vision should also lead to cost savings of more than €100,000 during lifetime. This may be attained by savings in special education which amount to about €6,000 per year (personal communication). With an average of 15-20 years of education in the Netherlands, these cost savings will be attained. Next to savings in special education, also other savings may be attained for example in home modifications and devices and costs for carers.

Infants with improved vision will also have a higher chance of getting a paid job. Goertz et al evaluated unemployment among 500 clients of Royal Visio, a large institute for the visually disabled, and found that 36.8% had a job.[21] However, when using the friction cost method to assess productivity costs, which is the preferred method in economic evaluations in the Netherlands [22;23], this will not lead to additional cost savings. Finally, infants born prematurely are at greater risk to have concomitant disabilities in later life.[3;24;25] To preserve as much vision as possible in infants with ROP is important for lifelong independency.

In the NEDROP study not all infants with severe ROP were treated, we therefore not only calculated the costs and effects of the treatment practice determined in the NEDROP-study (table 2a), but also the costs and effects if all infants with severe ROP were treated (table 2b), as it is expected that further implementation of the treatment guidelines according to ETROP will lead to the treatment of all infants detected with severe ROP. As shown in our analyses the efficient strategies of both treatment strategies largely overlap indicating that further implementation of treatment guidelines will not change which screening strategies are efficient in the Netherlands, but will lead to lower average and marginal cost per (additional) person with improved vision.

Several cost-effectiveness studies in retinopathy of prematurity are performed previously.[6;18;26-31] Part of them compared different treatment methods[26;31] or screening methods[27;28], a single screening strategy with no treatment[18] or different screening frequencies.[30] Lee et al 2001[6] and Yanovitch et al[29] compared different screening strategies, comparable with our analysis. Lee et al[6] found a screening strategy of screening only infants having a BW of 1200 g and less to be the most cost-effective strategy for routine ROP screening. In our cohort, we would have missed 2 infants treated for ROP using this strategy. Yanovitch et al [29] found a screening strategy with a BW <1500 g and a selection of infants with BW 1501 to 2000 g and greater than or equal to two significant risk factors to have the most favourable cost-benefit per infant screened. For our cohort,

this strategy would have detected all infants treated for ROP but at the expense of 1292 children to be screened, which is 49% more than in the most efficient strategy to detect all infants treated for ROP.

This study has some limitations. First, the analyses are based on the outcomes of ROP screening of a single year (2009), repeating the analysis for another year may lead to different results. Secondly, the results are assessed for the Dutch situation and may not be directly applicable to other countries. This is illustrated by the fact that Lee et al [6] and Yanovitch et al[29] found different screening strategies to be efficient for their study population. In future studies the stability of the current results over time and place have to be assessed.

Furthermore, we used the same percentage of improved vision due to early laser treatment for all children with severe ROP, independent of the ROP stage (3, 4 or 5). Also the use of the adjusted indirect comparison method to assess the improved vision, may be less reliable than a direct estimate.

In conclusion, based on our economic evaluation, the current Dutch guideline may be improved: the same effectiveness can be obtained for lower costs. Also releasing the precondition that no infants with severe ROP might be missed, will lead to lower costs, but this will also lead to a lower number of infants with improved visual acuity. However, the marginal costs of detecting all infants with severe ROP seems acceptable for society when also including the QALY gain and savings from a societal perspective resulting from improved vision.

REFERENCES

1. Dobson V, Quinn GE, Summers CG, Hardy RJ, Tung B, Good WV. Grating visual acuity results in the early treatment for retinopathy of prematurity study. Arch.Ophthalmol. 2011;129:840-6.
2. van Sorge AJ, Schalij-Delfos NE, Kerkhoff FT, van Rijn LJ, van Hillegersberg JL, van Liempt IL et al. Reduction in screening for retinopathy of prematurity through risk factor adjusted inclusion criteria. Br.J.Ophthalmol. 2013;97:1143-7.
3. van Sorge AJ, Termote JU, de Vries MJ, Boonstra FN, Stellingwerf C, Schalij-Delfos NE. The incidence of visual impairment due to retinopathy of prematurity (ROP) and concomitant disabilities in the Netherlands: a 30 year overview. Br.J.Ophthalmol. 2011;95:937-41.
4. The International Classification of Retinopathy of Prematurity revisited. Arch.Ophthalmol. 2005; 123:991-9.
5. van Buuren S, Boshuizen HC, Knook DL. Multiple imputation of missing blood pressure covariates in survival analysis. Stat.Med. 1999;18:681-94.
6. Lee SK, Normand C, McMillan D, Ohlsson A, Vincer M, Lyons C. Evidence for changing guidelines for routine screening for retinopathy of prematurity. Arch.Pediatr.Adolesc.Med. 2001;155:387-95.
7. Tan SS, Bouwmans CA, Rutten FF, Hakkaart-van RL. Update of the Dutch Manual for Costing in Economic Evaluations. Int.J.Technol.Assess.Health Care 2012;28:152-8.
8. van Sorge AJ, Termote JU, Simonsz HJ, Kerkhoff FT, van Rijn LJ, Lemmens WA et al. Outcome and quality of screening in a nationwide survey on retinopathy of prematurity in The Netherlands. Br.J.Ophthalmol. 2014.
9. van den Akker ME, Arts MP, van den Hout WB, Brand R, Koes BW, Peul WC. Tubular diskectomy vs conventional microdiskectomy for the treatment of lumbar disk-related sciatica: cost utility analysis alongside a double-blind randomized controlled trial. Neurosurgery 2011;69:829-35.
10. McLoone EM, O'Keefe M, McLoone SF, Lanigan BM. Long-term refractive and biometric outcomes following diode laser therapy for retinopathy of prematurity. J.AAPOS. 2006;10:454-9.
11. Gunn DJ, Cartwright DW, Yuen SA, Gole GA. Treatment of retinopathy of prematurity in extremely premature infants over an 18-year period. Clin.Experiment.Ophthalmol. 2013;41:159-66.
12. Yang CS, Wang AG, Sung CS, Hsu WM, Lee FL, Lee SM. Long-term visual outcomes of laser-treated threshold retinopathy of prematurity: a study of refractive status at 7 years. Eye (Lond) 2010;24: 14-20.
13. Multicenter Trial of Cryotherapy for Retinopathy of Prematurity: ophthalmological outcomes at 10 years. Arch.Ophthalmol. 2001;119:1110-8.
14. Good WV, Hardy RJ, Dobson V, Palmer EA, Phelps DL, Tung B et al. Final visual acuity results in the early treatment for retinopathy of prematurity study. Arch.Ophthalmol. 2010;128(6):663-71.
15. Glenny AM, Altman DG, Song F, Sakarovitch C, Deeks JJ, D'Amico R et al. Indirect comparisons of competing interventions. Health Technol.Assess. 2005;9:1-iv.
16. Vandermeer BW, Buscemi N, Liang Y, Witmans M. Comparison of meta-analytic results of indirect, direct, and combined comparisons of drugs for chronic insomnia in adults: a case study. Med.Care 2007;45:S166-S172.
17. Schalij-Delfos NE, Zijlmans BL, Wittebol-Post D, Tan KE, Cats BP. Screening for retinopathy of prematurity: do former guidelines still apply? J.Pediatr.Ophthalmol.Strabismus 1996;33:35-8.
18. Dunbar JA, Hsu V, Christensen M, Black B, Williams P, Beauchamp G. Cost-utility analysis of screening and laser treatment of retinopathy of prematurity. J.AAPOS. 2009;13:186-90.
19. Sharma S, Brown GC, Brown MM, Shah GK, Snow K, Brown H et al. Converting visual acuity to utilities. Can.J.Ophthalmol. 2000;35:267-72.

20. statline.cbs.nl. Statistic Netherlands. Consumer price index. 11-3-2014.
21. Goertz, Y. H. H. Houkes I. Nijhuis F. J. N. Labor participation of visually impaired persons in the Netherlands. submitted(Journal of Visual Impairment & Blindness.). 2014.
22. Brouwer WB, Koopmanschap MA. The friction-cost method: replacement for nothing and leisure for free? Pharmacoeconomics. 2005;23:105-11.
23. van den Hout WB. The value of productivity: human-capital versus friction-cost method. Ann. Rheum.Dis. 2010;69 Suppl 1:i89-i91.
24. Serenius F, Kallen K, Blennow M, Ewald U, Fellman V, Holmstrom G et al. Neurodevelopmental outcome in extremely preterm infants at 2.5 years after active perinatal care in Sweden. JAMA 2013;309:1810-20.
25. Moore T, Hennessy EM, Myles J, Johnson SJ, Draper ES, Costeloe KL et al. Neurological and developmental outcome in extremely preterm children born in England in 1995 and 2006: the EPICure studies. BMJ 2012;345:e7961.
26. Kamholz KL, Cole CH, Gray JE, Zupancic JA. Cost-effectiveness of early treatment for retinopathy of prematurity. Pediatrics 2009;123:262-9.
27. Jackson KM, Scott KE, Graff ZJ, Bateman DA, Flynn JT, Keenan JD et al. Cost-utility analysis of telemedicine and ophthalmoscopy for retinopathy of prematurity management. Arch.Ophthalmol. 2008;126:493-9.
28. Castillo-Riquelme MC, Lord J, Moseley MJ, Fielder AR, Haines L. Cost-effectiveness of digital photographic screening for retinopathy of prematurity in the United Kingdom. Int.J.Technol.Assess. Health Care 2004;20:201-13.
29. Yanovitch TL, Siatkowski RM, McCaffree M, Corff KE. Retinopathy of prematurity in infants with birth weight>or=1250 grams-incidence, severity, and screening guideline cost-analysis. J.AAPOS. 2006;10:128-34.
30. Javitt J, Dei CR, Chiang YP. Cost-effectiveness of screening and cryotherapy for threshold retinopathy of prematurity. Pediatrics 1993;91:859-66.
31. Brown GC, Brown MM, Sharma S, Tasman W, Brown HC. Cost-effectiveness of treatment for threshold retinopathy of prematurity. Pediatrics 1999;104:e47.