ELECTRONIC SUPPLEMENTARY MATERIAL

**A conceptual framework for a long-term economic model of the treatment of attention-deficit/hyperactivity disorder**

**Expert Review of Pharmacoeconomics and Outcomes Research**

#

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# Appendix 1. The 3-iteration systematic review of methodologies

## 1.1. Overview of the design and key outcomes

|  |  |  |  |
| --- | --- | --- | --- |
|  | *Literature* *search I* | *Literature search II* | *Literature**search III* |
| **Models ofADHD populations** | **Long-term models of chronic mental disorders** | **Models with ADHD-related LTOs** |
| **PART 1 (search design)** |
| **Search criteria**a | **Population** | ADHD | Selected chronic mental disordersb | Any |
| **Time horizon** | Any | 2+ yr time horizon or covering adulthood | Any |
| **Disease outcomes** | Any | Any | LTO categories published earlier5,6,c |
| **Contains the information of interest** | Economic modelsspecific to ADHD | Economic modelstransferable to ADHD | General modelling methods of selected LTOs |
| **Databases searched** | Health & health economicsdNational HTA Agenciese | Health & health economicsd | Health & health economicsd National HTA AgencieseGeneral economicsf |

a. Shaded cells indicate the key aspect of the given systematic search.

b. Mental disorders requiring chronic therapy, suspected to be suitable for a similar modelling approach as ADHD: depression, bipolar disorder, schizophrenia, chronic insomnia, and the generic terms “mental disorder” or “mental disease”

c. High-level categories: Academic achievement, Antisocial behavior (incl. arrests/incarcerations), Driving (incl. accidents), Non-medical drug use/Addiction, Obesity, Occupation (incl. employment status, socioeconomic status), Public services use (incl. justice, emergency health care), Self-esteem (incl. suicide), Social function.

d. Sixteen English and German databases (MEDLINE, EMBASE, PsycINFO, INAHTA, NHS EED, DARE, Cochrane CRCT, Cochrane DSR, CCMED, gms & gms Meetings, MEDIKAT, HECLINET, German publishers’ databases, DAHTA Datenbank, PSYNDEX, SOMED) searched via the German Drug Information Agency [DIMDI]’s interface (http://www.dimdi.de/dynamic/de/db/recherche/)

e. UK (NICE, including the NIHR HTA Programme website), Germany (DAHTA), Canada (CADTH), Spain-Catalonia (CAHTA), Sweden (SBU and VG)

f. SciVerse Scopus (www.scopus.com) Economic Subarea; RePEc IDEAS database (ideas.repec.org)

|  |
| --- |
| **PART 2 (search results)** |
| **Search hits** | 205 | 226 | 995 |
| **Publications meeting the search criteria** | 18 | 20 | 9 |
| **Useful information identified** | One elaborated concept of ADHD lifetime impact(not quantified though);Various combinations of short-term outcomes;2-4 levels of symptomatic response (and relapse); Compliance and/or side-effects affect the response level.  | Additional outcomes (vs. ADHD models): suicide, caregiver time (societal perspective);Three-period modelling to handle the natural course of disease and the age-dependent outcomes. | Two-stage models on tobacco use: all tobacco-related LTOs are covered in a single model;Two-layer model on alcoholism with submodels for each LTOs;Model on bullied children may serve as a hint for ADHD children;Potential quick win: long-term birth cohorts with baseline assessments that can be mapped to ADHD characteristics. |
| **Gaps of information identified**  | No comprehensive model (psychometric outcomes only);No societal perspective;No childhood -to-adulthood model of benefits (adverse effect [SCD] only);Dependence of LTOs on patient attributes and prior events are not captured on a lifetime horizon;HTA agencies need/seek data in adult patients. | No comprehensive model (i.e., limited outcomes similar to ADHD models);No childhood-to-adulthood model (despite the need in depression, schizophrenia). | N/A |

## 1.2. Design and results of systematic search I (Models of ADHD populations)

### Databases included

*1. ENGLISH*

- MEDLINE

- EMBASE

- PsycINFO

- INAHTA Health Technology Assessment Database

- NHS EED (Economic Evaluation Database)

- DARE (Database of Abstracts of Reviews of Effects)

- Cochrane Central Register of Controlled Trials

- Cochrane Database of Systematic Reviews

*2. GERMAN/ENGLISH*

- CCMED (Current Contents – Medicine) – database of German medical journals

- gms & gms Meetings – German Medical Science database of medical research articles

- MEDIKAT – Catalogs of the German Central Medical Library

- HECLINET – German Health Care Literature Information Network

- German publishers' databases (Hogrefe, Karger, Krause & Pachernegg, Thieme)

- DAHTA Datenbank – HTA-reports database from the German Agency for HTA

- PSYNDEX – Database of psychological publications of German-speaking countries

- SOMED – Social Medicine database of the German Natl. Institute of Health & Labor Affairs

*3. Selected National HTA Agencies' websites*

UK (NICE), Germany (DAHTA), Canada (CADTH), Spain-Catalonia (CAHTA), Sweden (both central [SBU] and the VG region)

We placed no limitation on either the publication dates or the languages. Search terms were submitted via the German Drug Information Agency (DIMDI)'s expert search interface[[1]](#footnote-1) to “All Text Fields” in order to overcome differences in text field nomenclature across databases. Detailed search steps and results are shown in Table 7*.*

Table 7. Search steps, terms and hits for literature review I.



### Inclusion and exclusion criteria; appraisal of articles

Based on the review of titles and abstracts, we included all existing ADHD models if they considered both costs and outcomes. We appraised relevant publications for any potential links between ADHD outcomes and costs/QALYs/etc. (to identify economic drivers), and particularly searched for models of long-term disease progression/natural history of disease, with special attention paid to those covering both childhood and adulthood. Search hits were excluded if no economic model was described, and were transferred for appraisal in review II. if the economic model was not related to ADHD. Those including diagnoses *in addition to* ADHD were kept in this review.

### Results of literature search I.

1. Bernfort L et al. ADHD from a socio-economic perspective. Acta Paediatr 2008;97:239-245.

2. Denchev P et al. Modeled economic evaluation of alternative strategies to reduce sudden cardiac death among children treated for attention deficit/hyperactivity disorder. Circulation 2010;121:1329-1337.

3. Faber A et al. Long-acting methylphenidate-OROS in youths with attention-deficit hyperactivity disorder suboptimally controlled with immediate-release methylphenidate: a study of cost effectiveness in The Netherlands. CNS Drugs 2008;22:157-170.

4. King S et al. A systematic review and economic model of the effectiveness and cost-effectiveness of methylphenidate, dexamfetamine and atomoxetine for the treatment of attention deficit hyperactivity disorder in children and adolescents. Health Technol Assess 2006;10:iii-146.

5. Leslie LK et al. Costs and benefits of targeted screening for causes of sudden cardiac death in children and adolescents. Circulation 2012;125:2621-2629.

6. Benkert D et al. Drug treatment of ADHD (Attention-deficit/hyperactivity disorder) in adults in Germany. DIMDI HTA report 108e;2010.

7. Peiro S, Ridao Lopez M, Catala Lopez F. Informe tecnico sobre et costs-efectividad de las diferentes alternativas de tratamiento farmacologico del trastorno por deficit de atencion e hiperactividad. 2011.

8. Svedlund J, Holmberg H. Treatment of ADHD (Attention-deficit/hyperactivity disorder) in adults with central stimulants. HTA-protokoll; 2008. Report No.: 10.

9. Zupancic J, Miller A, Raina Pea. Part 3: economic evaluation of pharmaceutical and psychological/behavioural therapies for attention-deficit/hyperactivity disorder. Ottawa, Canada: Canadian Coordinating Office for Health Technology Assessment; 1998.

10. Cottrell S et al. A modeled economic evaluation comparing atomoxetine with stimulant therapy in the treatment of children with attention-deficit/hyperactivity disorder in the United Kingdom. Value Health 2008;11:376-388.

11. Hong J et al. A modelled economic evaluation comparing atomoxetine with methylphenidate in the treatment of children with attention-deficit/hyperactivity disorder in Spain. BMC Psychiatry 2009;9:15.

12. Narayan S, Hay J. Cost effectiveness of methylphenidate versus AMP/DEX mixed salts for the first-line treatment of ADHD. Expert Rev Pharmacoecon Outcomes Res 2004;4:625-634.

13. Gilmore A, Milne R. Methylphenidate in children with hyperactivity: review and cost-utility analysis. Pharmacoepidemiol Drug Saf 2001;10:85-94.

14. Jensen PS et al. Cost-effectiveness of ADHD treatments: findings from the multimodal treatment study of children with ADHD. Am J Psychiatry 2005;162:1628-1636.

15. Foster EM et al. Treatment for ADHD: is more complex treatment cost-effective for more complex cases? Health Serv Res 2007;42:165-182.

16. Lord J, Paisley S. The clinical effectiveness and cost-effectiveness of methylphenidate for hyperactivity in childhood. National Institute for Clinical Excellence, London; 2000.

17. VanOverbeke N et al. A cost analysis of the management of attention-deficit/hyperactivity disorder (ADHD) in children in the UK. JME 2003;6:79-94.

18. Donnelly M et al. Cost-effectiveness of dexamphetamine and methylphenidate for the treatment of childhood attention deficit hyperactivity disorder. Aust N Z J Psychiatry 2004;38:592-601.

19. Marchetti A et al. Pharmacotherapies for attention-deficit/hyperactivity disorder: expected-cost analysis. Clin Ther 2001;23:1904-1921.

20. Dimond C, Hyde C. Parent education programmes for children's behaviour problems: medium to long term effectiveness. A West Midlands Development and Evaluation Service Report. Department of Public Health and Epidemiology, University of Birmingham; 2000.

21. Sikirica V et al. Cost effectiveness of guanfacine extended release as an adjunctive therapy to a stimulant compared with stimulant monotherapy for the treatment of attention-deficit hyperactivity disorder in children and adolescents. Pharmacoeconomics 2012;30:e1-15.

## 1.3. Design and results of systematic search II (Models of selected chronic mental disorders)

### Databases included

1. *1. ENGLISH*
2. - MEDLINE
3. - INAHTA Health Technology Assessment Database
4. - NHS EED (Economic Evaluation Database)
5. - DARE (Database of Abstracts of Reviews of Effects)
6. - Cochrane Database of Systematic Reviews
7. *2. GERMAN/ENGLISH*
8. - CCMED (Current Contents – Medicine) – database of German medical journals
9. - DAHTA Datenbank – HTA-reports database from the German Agency for HTA
10. - ETHMED – Publications database from the Information and Documentation Centre on Ethics in Medicine (IDEM) at the University of Göttingen, Germany
11. - MEDIKAT – Catalogs of the German Central Medical Library
12. - HECLINET – German Health Care Literature Information Network
13. - SOMED – Social Medicine database of the German Natl. Institute of Health & Labor Affairs

We placed no limitation on either the publication dates or the languages. Search terms were submitted via the German Drug Information Agency (DIMDI)'s expert search interface49 to “All Text Fields” in order to overcome differences in text field nomenclature across databases.

Detailed search steps and results are shown in *Table 8.*

*Table 8.* Search steps, terms and hits for literature review II.



### Inclusion and exclusion criteria; appraisal of articles

Based on the review of titles and abstracts, we included all existing economic models if they considered long-term outcomes (expanding for 2 years or more) of patients with the following diagnoses, which are similar to ADHD in a sense that they belong to mental diseases mostly necessitating chronic drug therapy:

1. schizophrenia,
2. depression and bipolar disorder,
3. chronic insomnia,
4. general term “mental disorder” or “mental disease”.

We appraised relevant publications for any potential links between ADHD-related mental disease outcomes and costs/QALYs/etc. (to identify economic drivers), and particularly searched for models of long-term disease progression/natural history of disease, with special attention paid to those covering both childhood and adulthood. Search hits were excluded if no economic model was described, or if the model did not apply to any of the potential economic drivers of ADHD (unless a methods paper on long-term modelling), or if the time horizon was shorter than 2 years.

### Results of literature search II.

(For comments, please refer to article text: Results: 1. Key aspects of model building)

1. Depression/bipolar disorder (11 publications)

1. Anton SF, Revicki DA. The use of decision analysis in the pharmacoeconomic evaluation of an antidepressant: a cost-effectiveness study of nefazodone. Psychopharmacology Bulletin 1995;31(2):249–258. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/7491376

2. Chisholm D et al. Reducing the global burden of depression: population-level analysis of intervention cost-effectiveness in 14 world regions. British Journal of Psychiatry 2004;184:393–403.

3. Kaltenhaler E, Shackley P, Stevens K. A Systematic Review and Economic Evaluation of Computerised Cognitive Behaviour Therapy for Depression and Anxiety. Health Technology Assessment 2002;6(22). Retrieved from http://www.nice.org.uk/nicemedia/pdf/ccbtassessmentreport.pdf

4. Revicki DA et al. Cost-effectiveness of newer antidepressants compared with tricyclic antidepressants in managed care settings. Journal of Clinical Psychiatry 1997;58(2):47–58. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9062373

5. Sclar DA et al. Antidepressant pharmacotherapy: economic evaluation of fluoxetine, paroxetine and sertraline in a health maintenance organization. Journal of International Medical Research, 1995; 23(6):395-412. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/0008746607>

6. Soares-Weiser K et al. A systematic review and economic model of the clinical effectiveness and cost-effectiveness of interventions for preventing relapse in people with bipolar disorder. Health Technology Assessment 2007;11(39). Retrieved from http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0014925/

7. Sobocki P et al. Model to assess the cost-effectiveness of new treatments for depression. International Journal of Technology Assessment in Health Care 2006;22(4), 469–477. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16984680

8. Sobocki P et al. The cost-utility of maintenance treatment with venlafaxine in patients with recurrent major depressive disorder. International Journal of Clinical Practice 2008;62(4):623–632.

9. Valenstein M et al. The cost-utility of screening for depression in primary care. Annals of Internal Medicine 2001;134(5):345–360. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/0011242495

10. Van den Berg M et al. Cost-effectiveness of opportunistic screening and minimal contact psychotherapy to prevent depression in primary care patients. PloS One 2011;6(8):22884.

11. Wang PS et al. The costs and benefits of enhanced depression care to employers. Archives of General Psychiatry 2006;63(12):1345–1353.

2. Schizophrenia (8 publications)

12. Almond S, O’Donnell O. Cost analysis of the treatment of schizophrenia in the UK. A simulation model comparing olanzapine, risperidone and haloperidol. PharmacoEconomics 2000;17(4):383–389. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10947493

13. Davies A et al. Cost-effectiveness of atypical antipsychotics for the management of schizophrenia in the UK. Current medical research and opinion 2008;24(11):3275–3285. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18947458

14. Davies LM, Drummond MF. Assessment of costs and benefits of drug therapy for treatment-resistant schizophrenia in the United Kingdom. British Journal of Psychiatry 1993;162:38–42. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8425137

15. Lindner LM et al. Economic evaluation of antipsychotic drugs for schizophrenia treatment within the Brazilian Healthcare System. Revista de Saude Publica 2009;43 Suppl 1:62–69.

16. Mehnert A et al. Cost effectiveness of paliperidone palmitate versus risperidone long-acting injectable and olanzapine pamoate for the treatment of patients with schizophrenia in Sweden. Journal of Medical Economics 2012;15(5):844–861. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/22458756

17. Palmer CS et al. A cost-effectiveness clinical decision analysis model for treatment of Schizophrenia. Archives of Medical Research 2002;33(6):572–580.

18. Sacristán JA, Gómez JC, Salvador-Carulla L. Análisis coste-efectividad de olanzapina frente a haloperidol en el tratamiento de la esquizofrenia en Espana. Actas Luso-Espanolas de Neurología, Psiquiatría y Ciencias Afines 1997;25(4):225–234.

19. Tilden D et al. An economic assessment of quetiapine and haloperidol in patients with schizophrenia only partially responsive to conventional antipsychotics. Clinical Therapeutics 2002;24(10):1648–1667. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12462294

3. Chronic insomnia (no relevant publication identified)

4. “Mental disorder”/“Mental disease” in general (1 publication)

20. Soeteman DI et al. Cost-effectiveness of psychotherapy for cluster C personality disorders: a decision-analytic model in the Netherlands. Journal of Clinical Psychiatry 2011;72(1):51–59.

## 1.4. Design and results of systematic search III (Models of ADHD-related LTOs)

The search strategy consisted of three complementary elements:

* + 1. a systematic search of the essential English- and German-language medical and health economic literature for value-driver candidates;
		2. a targeted search of the economic literature (SciVerse Scopus – economic subarea, and RePEc IDEAS) for value-driver candidates;
		3. a focussed search of selected National HTA Agencies' websites: UK (NICE), Germany (DAHTA), Canada (CADTH), Spain/Catalonia (CAHTA), Sweden (both central [SBU] and the VG region).

The selection of databases and search terms in parts III/2. and 3. reflected rather a sporadic than systematic strategy due to the lack of pre-defined information about the required data. We searched for any information potentially relevant to the conceptual framework we aim to build, rather than trying to identify all relevant economic models.

### III/1. Systematic search of medical and health-economic literature

#### Databases included

*1. ENGLISH*

- MEDLINE

- INAHTA Health Technology Assessment Database

- NHS EED (Economic Evaluation Database)

- DARE (Database of Abstracts of Reviews of Effects)

- Cochrane Database of Systematic Reviews

*2. GERMAN/ENGLISH*

- CCMED (Current Contents – Medicine) – database of German medical journals

- DAHTA Datenbank – HTA-reports database from the German Agency for HTA

- ETHMED – Publications database from the Information and Documentation Centre on Ethics in Medicine (IDEM) at the University of Göttingen, Germany

- MEDIKAT – Catalogs of the German Central Medical Library

- HECLINET – German Health Care Literature Information Network

- SOMED – Social Medicine database of the German Natl. Institute of Health & Labor Affair

We placed no limitation on either the publication dates or the languages. Search terms were submitted via the German Drug Information Agency (DIMDI)'s expert search interface49 to “All Text Fields” in order to overcome differences in text field nomenclature across databases.

Included also were the terms (and their German translations) describing each long-term outcomes as listed in Table 1 of a recent review paper by Hodgkins et al.2

Detailed search steps and results are shown in *Table 9.*

*Table 9.* Search steps, terms and hits for literature review III/1 (For *s*teps 1 through 13 please refer to *Table 8* above.)



*Table 9***.** Search steps, terms and hits for literature review III/1 (cont'd.)



### III/2. Targeted search of the economic literature

#### Databases included

* *SciVerse Scopus* covers publications in the scientific, technical, medical, and social sciences (including arts and humanities), and incorporates searches of scientific web pages through Scirus. Therefore the search was restricted to the economic subarea only.
* *RePEc IDEAS* (ideas.repec.org) is claimed to be “the largest bibliographic database dedicated to economics”.

##### Search strategies:

*Scopus search terms:* (("economic evaluation") OR ("economic model?")) AND ("indirect cost?" OR "societal cost?" OR "economic effect?" OR "cost implication?" OR burden) AND (salary OR taxation OR employment OR education OR qaly OR daly OR "socioeconomic status" OR "antisocial behaviour" OR suicide OR criminal OR driving OR accident? OR disabilit? OR alcohol OR drug? OR "substance abuse" OR self-esteem OR "marital status" OR divorce OR "family income" OR STD?) AND ( LIMIT-TO(SUBAREA,"ECON" ) ).

Search terms combined expressions related to economic modelling, the societal or indirect cost of interventions, and relevance to the economic drivers selected.

*RePEc search terms:* ("economic evaluation" | "economic model") + ("indirect cost" | "societal cost" | "economic effect" | "cost implication" | burden)

Since RePEc is a general economic database, this part of the search was not restricted to the selected economic drivers in order to identify publications about the methods of including non-direct costs in economic modelling.

### Inclusion and exclusion criteria for literature searches III/1 and III/2

Include if any information relevant to our conceptual framework (target LTO categories) is available in the study (does not have to be relevant to either ADHD or any mental or somatic disease). Exclude if the study did not use any economic drivers (not if methods paper); exclude if study did not report any calculations (not if methods paper).

### Aggregated results of literature searches III/1 and III/2



#### Results of literature search III/1

Health and health-economic literature (via http://www.dimdi.de/dynamic/de/db/recherche/):

* 1. Adi Y et al. Oral naltrexone as a treatment for relapse prevention in formerly opioid-dependent drug users: a systematic review and economic evaluation. Health Technology Assessment 2007;11(6):1–85. Retrieved from http://www.hta.ac.uk/project/1491.asp
	2. Alemi F et al. Costs and benefits of combining probation and substance abuse treatment. The Journal of Mental Health Policy and Economics 2006;*9*(2):57–70.
	3. Andrés AR, Halicioglu F. Determinants of suicides in Denmark: evidence from time series data. Health Policy *2010;98*(2-3):263–269.
	4. Annemans L et al. Economic evaluation of Campral (Acamprosate) compared to placebo in maintaining abstinence in alcohol-dependent patients. European Addiction Research 2000;6(2):71–78. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10899732
	5. Annemans et al. Cost effectiveness of varenicline in Belgium, compared with bupropion, nicotine replacement therapy, brief counselling and unaided smoking cessation: a BENESCO Markov cost-effectiveness analysis. *Clinical Drug Investigation 2009*;*29*(10):655–65. doi:10.2165/11317730-000000000-00000
	6. Barnett PG. The cost-effectiveness of methadone maintenance as a health care intervention. Addiction 1999;94(4):479–488. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10605844
	7. Blomquist G. A utility maximization model of driver traffic safety behavior. Accident; Analysis and Prevention;1986;18(5):371–375.
	8. Bolin K et al. (2009). Cost-effectiveness of varenicline compared with nicotine patches for smoking cessation--results from four European countries. European Journal of Public Health;*19*(6):650–4. doi:10.1093/eurpub/ckp075
	9. Boyd KA, Briggs AH. Cost-effectiveness of pharmacy and group behavioural support smoking cessation services in Glasgow. Addiction 2009;104(2):317–25. doi:10.1111/j.1360-0443.2008.02449.x
	10. Carliner G, Robinson C, Tomes N. Lifetime models of female labor supply, wage rates, and fertility. Research in Population Economics 1984;5:1–27. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12266408
	11. Chaplin EH. Forensic aspects in people with intellectual disabilities. Current Opinion in Psychiatry 2006;19(5):486–491.
	12. Cornuz J et al. Cost-effectiveness of pharmacotherapies for nicotine dependence in primary care settings: a multinational comparison. Tobacco Control 2006;15(3):152–159. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2564651/
	13. Cornuz J et al. Cost-effectiveness analysis of the first-line therapies for nicotine dependence. European Journal of Clinical Pharmacology 2003;59(3):201–206.
	14. Downs SM, Klein JD. Clinical preventive services efficacy and adolescents’ risky behaviors. Archives of Pediatrics and Adolescent Medicine 1995;149(4):374-9. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/7704164
	15. Ensor T, Godfrey C Modelling the interactions between alcohol, crime and the criminal justice system. Addiction 1993;88(4):477–487. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8485425
	16. Folland S. An economic model of social capital and health. Health Economics, Policy, and Law 2008;3(Pt 4):333–348. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18793476
	17. Franz W. An economic analysis of female work participation, education, and fertility: theory and empirical evidence for the Federal Republic of Germany. Journal of Labor Economics 1985;3(1 Part 2):218–234. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12146348
	18. Frezza EE, Wachtel MS, Ewing BT. The impact of morbid obesity on the state economy: an initial evaluation. Surgery for Obesity and Related Diseases 2006;2(5):504–508. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/17015201
	19. Hakim S et al. A critical review of macro models for road accidents. Accident; Analysis and Prevention 1991;23(5):379–400. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1741894
	20. Hojgaard B et al. The potential of smoking cessation programmes and a smoking ban in public places: comparing gain in life expectancy and cost effectiveness. Scandinavian Journal of Public Health 2011;39(8):785–796. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21976052
	21. Kedikoglou S, et al. A maternity hospital-based infant car-restraint loan scheme: public health and economic evaluation of an intervention for the reduction of road traffic injuries. Scandinavian Journal of Public Health 2005 2005;33(1):42-9.
	22. Kennelly B, O’Shea E, Garvey E. Social capital, life expectancy and mortality: a cross-national examination. Social Science & Medicine 2003;56(12), 2367–2377. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12742601
	23. Kim HS, Kim HJ, Son B. Factors associated with automobile accidents and survival. Accident; Analysis and Prevention 2006;38(5):981–987. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16696930
	24. Lehrer E, Nerlove M. The labor supply and fertility behavior of married women: a three-period model. Research in Population Economics 1981;3:123–145. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12265057
	25. Lehrer E, Nerlove M. An econometric analysis of the fertility and labor supply of unmarried women. Research in Population Economics 1982;4:217–235. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12264902
	26. Leigh JP, Waldon HM. Unemployment and highway fatalities. Journal of Health Politics, Policy and Law 1991;16(1):135–156. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/2066533
	27. Lollivier S. Revenu offert, pretentions salariales et activite des femmes mariees: un modele d’analyse. Economie & Statistique 1984;(167):3–15.
	28. Masson CL et al. Cost and cost-effectiveness of standard methadone maintenance treatment compared to enriched 180-day methadone detoxification. Addiction 2004;99(6):718–726.
	29. Moffitt R. Profiles of fertility, labour supply and wages of married women: a complete life-cycle model. The Review of Economic Studies 1984;51:263–278. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12266589
	30. Müller-Riemenschneider F et al. Wirksamkeit und Wirtschaftlichkeit von verhaltensbezogenen Massnahmen zur Prävention des Zigarettenrauchens. Schriftenreihe Health Technology Assessment no date, 74. Retrieved from http://portal.dimdi.de/de/hta/hta\_berichte/hta232\_bericht\_de.pdf
	31. Olsen KR et al. Cost-effectiveness of the Danish smoking cessation interventions: subgroup analysis based on the Danish Smoking Cessation Database. European Journal of Health Economics 2006;7(4):255-64. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16816946
	32. Palmer AJ et al The long-term cost-effectiveness of improving alcohol abstinence with adjuvant acamprosate. Alcohol and Alcoholism 2000;35(5):478–492.
	33. Pollack HA. A cost-effectiveness analysis of AOTAL, a drug used to prevent relapse in weaned alcoholics. Medical Decision Making 2001. John Wiley & Sons, Ltd, Chichester, UK.
	34. Reynolds AJ et al. Age 26 cost-benefit analysis of the child-parent center early education program. Child Development 2011;82(1):379–404.
	35. Rychlik R et al. (2003). Cost-effectiveness of adjuvant treatment with acamprosate in maintaining abstinence in alcohol dependent patients. European Addiction Research 2003;9(2):59–64. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12644731
	36. Schackman BR et al. Cost-effectiveness of long-term outpatient buprenorphine-naloxone treatment for opioid dependence in primary care. Journal of General Internal Medicine 2012;27(6):669–676. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/22215271
	37. Schadlich PK, Brecht JG. The cost effectiveness of acamprosate in the treatment of alcoholism in Germany: economic evaluation of the Prevention of Relapse with Acamprosate in the Management of Alcoholism (PRAMA) study. Pharmacoeconomics 1998;13(6):719–730. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10179707
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# Appendix 2. Further considerations regarding the definition of life-stages

The age bands used for the example follow a simplified pattern and have to be set more carefully for a real-life model implementation. For instance, in the example we assume that a higher-level degree can be completed at the age of 23, which is not always the case: a patient’s 23rd year can only be regarded as the first possible year of obtaining a higher-level degree, and not the only age when such degrees are completed. These details have to be elaborated during the real-life model implementation.

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