**Appendix 1:** Electronic search strategy

1. exp Infant, Newborn/

2. (neonat\* or newborn or baby or babies or perinat\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]

3. 1 or 2

4. exp Neonatal Screening/

5. (screen\* or test\* or program\* or procedure).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]

6. 4 or 5

7. guthrie.ab,ti.

8. (blood spot\* or bloodspot\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]

9. (heel-prick\* or heelprick\*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]

10. 7 or 8 or 9

11. Economics/

12. exp "costs and cost analysis"/

13. Economics, Dental/

14. exp economics, hospital/

15. Economics, Medical/

16. Economics, Nursing/

17. Economics, Pharmaceutical/

18. (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab.

19. (expenditure$ not energy).ti,ab.

20. value for money.ti,ab.

21. budget$.ti,ab.

22. or/1-11

23. ((energy or oxygen) adj cost).ti,ab.

24. (metabolic adj cost).ti,ab.

25. ((energy or oxygen) adj expenditure).ti,ab.

26. 23 or 24 or 25

27. 22 not 26

28. letter.pt.

29. editorial.pt.

30. historical article.pt.

31. 28 or 29 or 30

32. 27 not 31

33. exp animals/ not humans/

34. 32 not 33

35. bmj.jn.

36. "cochrane database of systematic reviews".jn.

37. health technology assessment winchester england.jn.

38. journal of medical economics.jn.

39. 35 or 36 or 37 or 38

40. 34 not 39

41. 3 and 6 and 10 and 22 and 27 and 32 and 34 and 40

|  |  |  |
| --- | --- | --- |
| **Country** | **Region/ State/ Territory** | **Current Conditions Screened for** |
| Australia | New South Wales [42] | PKU, CH, CF, Galactosaemia and a range of Aminoacidopathies, Organic acidaemias, and Fatty acid oxidation defects |
|  | Western Australia [50] | PKU, CH, CF, Galactosaemia and a range of Aminoacidopathies, Organic acidaemias, and Fatty acid oxidation defects |
| Canada | Nova Scotia [46] | PKU, CH, CF, MCADD, MSUD, SCD, GA1, IVA, Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD), Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCADD), and 4 other conditions. |
|  | Ontario [39] | PKU, CH, CF, Galactosaemia, MCADD, Maple Syrup Urine Disease (MSUD), SCD, Glutaric Acidemia type 1 (GA1), Homocydtinuria, Isovaleric Acidemia (IVA), and 16 other conditions |
| Iran | Whole Country [45] | CH |
| Finland | Whole Country [38] | CH, PKU (generally for non-Finnish newborns) |
| France | Whole Country [52] | PKU, CH, CF, SCD, Congenital Adrenal Hyperplasia (CAH) and MCADD |
| Libya | Whole Country [57] | As of yet, no programme exists |
| The Netherlands | Whole Country [53, 60, 61, 63] | PKU, CH, CF, Galactomsaemia, SCD, CAH, GA1, MCADD, Homocystinuria, IVA, and 6 other conditions |
| The UK | Whole Country [17, 43, 58] | PKU, CH, CF, SCD, MCADD, MSUD, GA1, IVA, Homocystinuria |
| The USA | Alaska [51] | PKU, CH, CF, CAH, SCD, MSUD, MCADD, GAI, IVA, LCHAD, and 36 other conditions |
|  | California [40, 44] | PKU, CH, CF, CAH, SCD, MSUD, MCADD, GAI, IVA, Homocystinuria, and 47 other conditions |
|  | Indiana [48] | PKU, CH, CF, CAH, SCD, MSUD, MCADD, GA1, IVA, LCHAD, and 40 other conditions |
|  | Kentucky [62] | PKU, CH, CF, CAH, SCD, MSUD, MCADD, GA1, IVA, LCHAD, and 42 other conditions |
|  | Pennsylvania [47] | PKU, CH, CF, CAH, SCD, MSUD, MCADD, GA1, IVA, LCHAD, and 23 other conditions |
|  | Texas [59] | PKU, CH, CF, CAH, SCD, MSUD, MCADD, GA1, IVA, LCHAD, and 20 other conditions |
|  | Wisconsin [41] | PKU, CH, CF, CAH, SCD, MSUD, Homocysinuria, Galactosaemia, Severe Combined Immune Deficiency (SCID), Argininosuccinic Acidemia (ASA), and 34 other conditions. |

**Appendix 2 –** Summary of current screening panels in countries where evaluations have been conducted

**Appendix 3:** Summary of identified economic evaluations of specific technologies used in NBSP

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Author (Year)**  **Country** | **Intervention & comparator** | **Study viewpoint and population** | **Evaluation vehicle (type) & time horizon (discount rate)** | **Resource Use & Price Year (currency)** | **Costs & harms related to information Provision** | **Valuation of Benefits** | **Key Results** |
| Autti-Rämö *et al.,*  [38]  (2005)  Finland | Intervention:  Tandem mass spectrometry for 5 conditions  Comparator:  No screening | Viewpoint:  Not stated (appears to be health service)  Study Population:  Cohort of newborns based on Finnish birth rate (n=56,000) | Model Based  (Type not stated)  Time Horizon:  Not stated (5%) | Resources: Information, blood samples, overheads, wages, equipment, analytes, diagnostic confirmation, quality control  Cost source:  Author assumptions, similar programmes  Price year: 2002 (€) | Costs: Yes €303,000 for information during pregnancy - €5.41 per child screened  €23,100 for information about screening results - €0.41 per child screened  Harms: No | QALYs | ICER:  Best Case - €5,500 per QALY  Worst Case - €25,500 per QALY |
| Cipriano *et al.,* [39]  (2007)  Canada  (Ontario) | Intervention:  Tandem mass spectrometry for 21 conditions.  Comparator:  Guthrie test for phenylketonuria (PKU) and hypothyroidism | Viewpoint: Canadian Health Service  Study Population: neonates born in Ontario in 1 year (n=130,000) | Model Based (Decision Tree)  Time Horizon:  Lifetime (3%) | Resources: Start-up costs, confirmatory testing, treatment, hospitalization, social services and education  Cost sources:  Primary data (trial)  Literature Review  Price year: 2004 (Canadian $) | Costs: No  Harms: Yes  Quality of life decrement of between 0.01 and 0.03 utility for parents during uncertain diagnosis period. The authors accounted for this decrement by decreasing each life year saved by the QoL loss. | Life Years gained | Incremental analysis: Yes  ICER: $5,492,114 per life year gained (screening for PKU only)  ICER: $68,346 per life year gained (PKU + 14 most cost-effective conditions)  Where parents experience 0.01 QoL loss, ICER: $73,500 per life year gained (PKU + 14 most cost-effective conditions)  Where parents experience 0.03 QoL loss, ICER: $104,000 per life year gained (PKU + 14 most cost-effective conditions) |
| Feuchtbaum *et al*.,  [40]  (2006)  USA  (California) | Intervention:  Tandem mass spectrometry for screening for PKU  Comparator:  No screening for PKU | Viewpoint: Californian Payers  Study Population:  neonates born in California in 1 year (n=540,000) | Model Based (Unspecified)  Time Horizon:  Lifetime (3%) | Resources:  Personnel and administration, equipment, supplies, laboratory contracts, follow-up centres  Cost Sources:  Primary data (pilot study)  Literature Review  Price year: 2004 (US $) | Costs: No  Harms: No | Life Years Saved  Cases Detected  Monetary Benefits (for life years saved)  QALYs | Incremental analysis: Yes  ICER: $708,000 per life year saved  ICER: $132,000 per case detected  ICER: Between $11,000 and $19,000 per QALY  Incremental Net Benefits: $47.1million (best case scenario)  Incremental Net Benefits: $14.1million (worst case scenario)  Benefit:Cost ratio: $9.32 (best case scenario)  Benefit:Cost ratio: $8.65 (worst case scenario) |
| Insinga *et al.,*  [41]  (2002)  USA  (Wisconsin) | Intervention:  Tandem mass spectrometry screening for 14 fatty acid disorders and organic acidemias  Comparator:  No screening | Viewpoint: Societal  Study Population: Infants in the Wisconsin Newborn Screening Programme (n=100,000) | Model Based (Decision Tree)  Time Horizon:  Lifetime (3%) | Resources:  MS/MS screening test, MS/MS test confirmation (positive for MCAD), MS/MS test confirmation (negative for MCAD), lifetime carnitine supplementation, lifetime follow-up testing, routine hospital admission, neurologic impairment  Cost sources:  Literature review  Price year: 2001 (US $) | Costs: No  Harms: No | Life expectancy  QALYs | Incremental analysis: Yes  ICER: $41,862 per QALY |
| Norman *et al.,*  [42]  (2009)  Australia | Intervention:  Tandem mass spectrometry for 5 categories of disorders: aminoacidurias, urea cycle disorders, organic acidurias, medium-chain acyl-CoA dehydrogenase deficiency (MCADD) and other fatty acid oxidation defects  Comparator:  Individual screening for 5 categories of conditions | Viewpoint: Health Service  Study Population:  Neonates | Retrospective-cohort based (before and after cohort study)  Time Horizon: 4 years (6%) | Resources:  screening (including follow-up testing for true-positive and false-positive cases), treatment of conditions, general health care  Cost Sources:  Primary data (trial)  Literature Review  Price year:2002 (AUS $) | Costs: No  Harms: No | Life Years Saved  Death Years Averted | Incremental analysis: Yes  ICER: AUS $472,913 per death averted  ICER: AUS $10,779 per life-year saved |
| Pandor *et al.,*  [43]  (2004)  UK | Intervention:  Tandem mass spectrometry screening for PKU and MCADD  Comparator: vs Traditional screening for PKU only. | Viewpoint: Health and other public sector providers  Study Population:  neonates (n=100,000) | Model Based (not specified)  Time Horizon:  Lifetime (6%) | Resources:  Screening, treatment of condition, treatment of symptomatic presentation, social care and education  Cost Sources:  Literature Review  Price year: 2001 (£) | Costs: yes (£0.30 per specimen collected)  Harms: No | Life years gained | Incremental Analysis: Yes  ICER: £-395 per life year saved (intervention dominates) |
| Pollitt *et al*.,  [17]  (1997)  UK | Intervention:  Tandem mass spectrometry screening for a large range of conditions  Comparator:  Standard screening for PKU | Viewpoint: Health Service  Study Population:  neonates (n=100,000) | Model Based (Decision Tree)  Time Horizon:  Lifetime (6%) | Resources:  Specimen collection costs, laboratory analysis, follow-up, treatment, misclassification  Cost Sources:  Primary data (Surveys)  Literature Review  Price year: Not reported | Costs: No  Harms: No | Life Years saved | Incremental Analysis: Yes  ICER: £31 per  life-year saved |
| Schoen *et al.,*  [44]  (2003)  USA  (California) | Intervention:  Tandem mass spectrometry screening for PKU, galactosemia, congenital hypothyroidism and haemoglobinopathies  Comparator:  Usual screening for the above conditions | Viewpoint: Payer (HMO)  Study Population: neonates (n=100,000) | Model Based (not reported)  Time Horizon:  Lifetime (3%) | Resources:  diagnosis, false-positive results, lifetime treatment  Cost Sources:  Literature Review  Price year: Not reported (US $) | Costs: No  Harms: No | QALYs | Incremental analysis: Yes  ICER: $5,827 per QALY |
| Shamshiri *et al.,*  [45]  (2012)  Iran | Interventions:  Various screening thresholds for congenital hypothyroidism  Comparator:  The current cut off point for Guthrie testing for congenital hypothyroidism | Viewpoint: Iranian health service  Study Population: neonates (n=10,000) | Model Based (Decision Tree)  Time Horizon:  Lifetime - to 82 years (3%) | Resources:  Guthie test, confirmatory tests, diagnosis, laboratory tests, visits by physicians, drugs, education, care  Cost Sources:  Literature Review  Price year: not reported (US $) | Costs: No  Harms: No | DALYs | Incremental Analysis: Yes  ICER: $-4.58k per DALY (intervention dominates) for best case scenario with cut-off point of 5mU/l |
| Tran *et al.,*  [46]  (2006)  Canada  (Nova Scotia) | Intervention:  Tandem mass spectrometry screening for MCADD  Comparator:  Clinical diagnosis of MCADD | Viewpoint: Canadian Health Care System  Study Population: Not reported explicitly | Model Based (Decision Tree)  Time Horizon: Lifetime (not reported) | Resources:  Screening, acute episode, management, severe neurological impairment  Cost sources:  Primary Data (Nova Scotia Screening programme)  Systematic Review  Price year: Not reported (CAN $) | Costs: No  Harms: No | QALYs | Incremental Analysis: Yes  ICER: $2,676 per QALY |
| Venditti *et al.,*  [47]  (2003)  USA  (Pennsylvania) | Intervention:  Tandem mass spectrometry screening for MCADD  Comparator:  No screening | Viewpoint: Societal  Study Population: Infants up to 19 years old | Model Based (Decision Tree & Markov Model)  Time Horizon: 20 and 70 years (3%) | Resources:  Screening and follow-up, confirmatory evaluation for positive screen, carnitine for screened MCADD, care for severely affected.  Cost Sources:  Primary Data (Patient- family interviews)  Literature Review  Expert Opinion  Price year: 2001 (US $) | Costs: No  Harms: Yes (False-positive: disutility between 0.01 to 0.03 for 3 months) | Life Years gained  QALYs | Incremental analysis: Yes  ICER: $11,000 per Life Year (20 years)  ICER: $300 per Life Year (70 years)    ICER: $5600 per QALY (20 years)  ICER: $100 per QALY (70 years) |

**Appendix 4:** Summary of identified economic evaluations of NBSP

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Author (Year)**  **Country** | **Intervention & comparator** | **Study viewpoint and population** | **Evaluation vehicle (type) & time horizon (discount rate)** | **Resource Use & Price Year (currency)** | **Costs & harms related to information Provision** | **Valuation of Benefits** | **Key Results** |
| Carrol & Downs  [48]  (2006)  USA  (Indiana) | Intervention:  The cost-effectiveness of each component part of a tandem mass spectrometry screening panel  Comparator:  No screening | Viewpoint: Societal  Study Population: Not reported | Model Based (Decision Tree)  Time Horizon:  Lifetime (3%) | Resources:  screening tests, caring for disease, sequelae from disease  Cost Sources:  Literature Review  Expert Opinion  Price year: 2004 (US $) | Costs: No  Harms: No | QALYs | Incremental Analysis: Yes  ICER: $4838.71 per QALY |
| Chan *et al.,*  [49]  (2011)  USA  (Not limited to one state) | Intervention:  Newborn Screening for Severe Combined Immunodeficiency (SCID)  Comparator:  Clinical diagnosis of SCID | Viewpoint:  Societal  Study Population:  Full cohort of US newborns of 4,112,052 (based on 2003 figures) | Model Based  (Decision Tree leading to Markov Model)  Time Horizon:  70 years (3%) | Resources:  Screening and confirmatory testing, late haematopoietic cell transplantation (HCT), early HCT, hospital inpatient and outpatient visist, intravenous immunoglobin therapy (IVIG)  Cost sources:  Primary Data (hospital records, patient surveys)  Price year: 2005 (US $) | Costs: No  Harms: No | QALYs | Incremental Analysis: Yes  ICER: $27,907 per QALY |
| Geelhoed *et al*.,  [50]  (2005)  Australia | Intervention: Phenylketonuria (PKU) & congenital hypothyroidism (CH) screening  Comparator: Symptomatic diagnosis (late detection) | Viewpoint: public sector  Study Population: newborns (n=25,000) | Retrospective-cohort based  Time Horizon:  Lifetime (5%) | Resources:  Programme (specimen collection, equipment, staff, reagents, paper & printing), treatment, intellectual disability, maternal PKU, productivity losses  Cost Sources:  Primary Data (Western Australia screening programme)  Literature Review  Price year: 2001 (AUS $) | Costs: Yes (= $6.54 per child screened)  Harms: No | Monetary benefit of a healthy child developing (avoided costs from gain in life years) | Incremental Analysis: Yes  ICER: Cost per case of PKU or CH detected: Aus $59,340  Aus $4,375,442 total averted cost of PKU  Aus $12,236,160 total averted cost of CH  Aus $2,879,776 net annual cost savings |
| Gessner *et al*.,  [51]  (1996)  USA  (Alaska) | Intervention:  Universal screening for sickle cell disease  Comparator: Targeted screening of African Americans for sickle cell disease | Viewpoint: Payers  Study Population: Not reported | Model Based (Decision Tree)  Time Horizon: 1.75 years (no discounting) | Resources:  screening, physician visits, programme, medical and home care  Cost Sources:  Primary Data (Oregon Public Health Laboratory)  Literature Review  Price year: 1993 (US $) | Costs: No  Harms: No | Death years averted  Cases of mental retardation averted | Incremental Analysis: Yes  ICER: $2,040,000 per death averted  ICER: £53,000,000 per case of mental retardation averted |
| Hamers & Rumeau-Pichon  [52]  (2012)  France | Intervention:  Screening for five conditions + MCADD and switching PKU screening to tandem mass spectometry  Comparator:  Screening for current five conditions only | Viewpoint: Societal  Study Population: birth cohort (n=821,000) | Model Based (Decision Tree)  Time Horizon: Lifetime (4%) | Resources:  screening test, confirmatory test, treatment of MCADD sequelae  Cost Sources:  Literature Review  Price year: not reported | Costs: No  Harms: No | QALYs  Life Years Gained | Incremental Analysis: Yes  ICER: €19,478 per Life Year Gained (MCADD)  ICER: €18,033 per QALY (MCADD)  ICER: €8189 per Life Year Gained (MCADD with PKU)  ICER: €7,851 per QALY (MCADD with PKU) |
| Lanting *et al*.,  [53]  (2004)  The Netherlands | Intervention:  Cost-effectiveness of various laboratory methods for identification of children with congenital hypothyroidism | Viewpoint: health service  Study Population: newborns (n=1,181,079) | Retrospective-cohort study based (cohort Study)  Time Horizon: 5 years (not reported) | Resources:  Laboratory, initial diagnostic tests  Cost sources:  Primary Data (Dutch Neonatal Screening Programme)  Literature Review  Price year: Not reported | Costs: No  Harms: no | Number of cases of congenital hypothyroidism detected | Incremental Analysis: No  Average cost per case detected by strategy:  (T4)+TSH = $6353  T4 + TSH = $6209  T4+THS+TBG = $6851 |
| McGhee *et al.,*  [54]  (2005)  USA  (Not limited to one state) | Intervention:  Threshold willingness to pay at which universal newborn screening for SCID would be cost-effective  Comparator:  Clinical diagnosis of SCID and screening based on family history | Viewpoint: health service  Study Population:  National cohort of newborns (n=4,000,000) | Model Based  (Decision Tree)  Time Horizon: Lifetime (3%) | Resources:  Test cost, treatment cost, infection treatment cost, follow-up cost, IVIG cost  Cost sources: Author assumptions based on current costs, adjusted hospital charges  Price year: 2000 (US $) | Costs: No  Harms: No | QALYs | ICER: $53,560 per QALY |
| Panepinto *et al*.,  [55]  (2000)  USA  (Not limited to one State) | Intervention:  Universal screening and targeted screening of African Americans for Sickle Cell Disease  Comparator: No screening | Viewpoint: Health Service  Study Population: newborns (n=1,000,000) | Model Based (Markov Model)  Time Horizon:  Birth to three years of age (3%) | Resources:  Screening test, confirmatory tests, follow-up, treatment of condition, treatment of serious sequelae  Cost Sources:  Literature Review  Price year: 1994 (US $) | Costs: No  Harms: No | Life Years Saved | Incremental Analysis: Yes  ICER: $6709 per additional year of life saved (targeted versus no screening)  ICER: $30,760 per additional year of life saved (universal versus targeted) |
| Prosser *et al.,*  [56]  (2010)  USA  (Not limited to one State) | Intervention:  Tandem mass spectrometry screening for MCADD  Comparator: Clinical diagnosis of MCADD | Viewpoint: Payers  Study Population: newborns (n=100,000) | Model Based (Patient Level Simulation)  Time Horizon:  Lifetime (3%) | Resources:  Treatment, hospitalisation, caring for a child with developmental delay, screening test, clinical workup, treating a presumed diagnosis  Cost Sources:  Primary Data (New England Newborn Screening Programme)  Literature Review  Price year: 2006 (US $) | Costs: No  Harms: Yes (TTO values: loss due to false-positive results = 0.0005) | QALYs | Incremental Analysis: Yes  ICER: $21,273 per QALY |
| Sladkevicius *et al.,*  [57]  (2010)  Libya | Intervention:  Establishing a newborn screening programme for PKU  Comparator:  No screening for PKU | Viewpoint:  Societal  Study Population:  Hypothetical cohort of newborns screened over a 15 year time horizon (n=2.6 million) | Model Based  (Decision Tree)  Time Horizon:  The programme runs for 15 years and costs and outcomes accrue for the lifetime of these cohorts (3%) | Resources:  Diagnostic tests, hospital admissions, nutrition as treatment, medications, outpatient visits, mental institution accommodation  Cost sources:  Structured interviews with paediatric specialists, directors of mental institutions, buyers and suppliers of medical equipment and two families of patients with PKU  Price year: 2007 (US $) | Costs: No  Harms: No | Life years gained | ICER: $12,183 per life year gained |
| Simpson *et al.,*  [58]  (2005)  UK | Intervention:  Cost-effectivenes of adding cystic fibrosis to a newborn bloodspot screening programme  Comparator:  Newborn bloodspot screening for PKU and CH only | Viewpoint:  Hypothetical UK health authority with existing screening programme  Study Population:  Hypothetical cohort of 500,000 newborns | Model Based  (Decision tree leading to Markov model)  Time Horizon:  Lifetime (Costs inflated to current price year at 5% inflation. Future costs discounted at 6%. QALYs discounted at 2%) | Resources:  Counselling time to receive consent, immunoreactive trypsin test, DNA analysis, sweat chloride test, pre-diagnosis costs, disease state specific costs  Cost Sources:  Audit of notes of 25 children with CF, medical records  Price year: 1998 (UK £) | Costs: Yes (Incremental costs of £0.40 per screened child for CF information. This is 2.1 minutes of midwife. A range of 0-7.6 minutes was used in the sensitivity analysis)  Harms: No | QALYs | Incremental Analysis: Yes  ICER: £6,864 per QALY |
| Tiwana *et al*.,  [59]  (2012)  USA  (Texas) | Intervention:  Expanded screening programme (27 disorders)  Comparator: current screening programme (7 disorders) | Viewpoint: Payers  Study Population:  Texas birth cohort | Model Based (Markov Model)  Time Horizon:  Lifetime (3%) | Resources:  screening, confirmatory testing, false-positive result, disease management, disease sequelae.  Cost Sources:  Literature Review  Price year: 2007 (US $) | Costs: No  Harms: Yes (Venditti et al. published disutility for false-positive result = 0.03) | QALYs | Incremental Analysis: Yes  ICER: $11,560 per QALY |
| Van der Akker-Van Marle *et al.,*  [60]  (2006)  The Netherlands | Intervention:  Different laboratory tests to identify children with cystic fibrosis:  IRT-IRT (Immunoreactive trypsin);  IRT-DNA; IRT-DNA-IRT; IRT-DNA-DGGE (Denaturing gradient gel electrophoresis)  Comparators:  Comparison depends on strategy but comparators include;  No screening, IRT-DNA-DGCE, IRT-IRT | Viewpoint: health service  Study Population: neonates (n=200,000) | Model Based (not reported)  Time Horizon: Lifetime (3%) | Resources:  Organisation, screening and diagnosis, genetic counselling for carriers, clinical diagnosis for CF carriers, diagnosis of non-CF patients, treatment of patients identified by screening, treatment for clinically diagnosed patients  Cost sources:  Literature Review  Expert Opinions  Price year: not reported (€) | Costs: No  Harms: No | Life years gained | Incremental Analysis: Yes  ICER: €24,800 per life-year gained (IRT-IRT) vs no screening  ICER: €2,154,300 per life year gained (IRT-DNA) vs IRT-DNA-DGCE  ICER: €133,700 per life year gained (IRT-DNA-DGGE) vs IRT-IRT |
| Van der Hilst *et al.,*  [61]  (2007)  The Netherlands | Intervention:  Tandem mass spectrometry screening for MCADD  Comparator:  No screening for MCADD | Viewpoint: Societal  Study Population: newborns (n=66,216) | Model Based (Decision Tree)  Time Horizon: Lifetime (4%) | Resources:  Inpatient and outpatient visits, travel expenses, ambulance services, laboratory tests, consultations, diagnostic imaging, medication and food supplements, special education, institutionalisation, parents productivity losses  Cost sources:  Primary Data (5 Dutch Screening Centres)  Literature Review  Price year: 2004 (US $) | Costs: No  Harms: No | Life Years Gained | Incremental Analysis: Yes  ICER: $1653 per Life Year gained |
| Wells *et al.,*  [62]  (2012)  USA  (Kentucky) | Cost and consequences comparison of two strategies of laboratory testing for cystic fibrosis  IRT/DNA  IRT/IRT | Viewpoint: Societal  Study Population:  newborns (n=100,000) | Model Based (Decision Tree)  Time Horizon:  From birth to confirmed diagnosis (not reported) | Resources:  Screening, laboratory equipment and personnel, insurance for parents and parents productivity (missed work, travel etc)  Cost Sources:  Literature Review  Price year: 2010 (US $) | Costs: No  Harms: No | Number of newborns diagnosed with cystic fibrosis | Incremental Analysis: No  $45,400 per diagnosis (IRT/IRT)  $39,700 per diagnosis (IRT/DNA) |
| Wildhagen *et al.,*  [63]  (1998)  Netherlands | 4 strategies: prenatal screening (single entry two step couple screening (SETS) & double entry two step couple screening (DETS)); preconceptional screening (SETS & DETS); school screening; neonatal carrier screening  Comparator: No CF gene carrier screening | Viewpoint: societal  Study Population: depends on the intervention – couples; school children in last year of compulsory education; neonates | Model Based (simulation model)  Time Horizon:  two-years (5%) | Resources:  Information provision before screening, testing, further diagnosis and treatment  Cost Sources:  Primary Data (Dutch Screening Programme)  Literature Review  Price year: 1996 (UK £) | Costs: Yes (£5.36 per child)  Harms: No | Number of detected carrier couples  Number of avoided patients | Incremental Analysis: No  £58,000 per detected carrier couple (prenatal SETS)  £70,000 per detected carrier couple (prenatal DETS)  £69,000 per detected carrier couple (preconception SETS)  £80,000 per detected carrier couple (preconception DETS)  £85,000 per detected carrier couple (school)  £21,000 per detected carrier couple (neonatal)  £177,000 per avoided patient (prenatal SETS)  £213,000 per avoided patient (prenatal DETS)  £223,000 per avoided patient (preconception SETS)  £258,000 per avoided patient (preconception DETS)  £367,000 per avoided patient (school)  £178,000 per avoided patient (neonatal) |