Economic evaluations

Title: Pharmacoeconomics of allergen immunotherapy compared with symptomatic drug treatment in patients with allergic rhinitis and asthma

Ariano 2006[222]

Journal

Allergy and Asthma Proceedings

Type of economic analysis

Cost–consequence analysis

Study population

Patients with seasonal *Parietaria* pollen-induced AR and asthma

Perspective

Societal, national health-care system and patient

Research question

Evaluation of the economic advantage of subcutaneous allergen immunotherapy plus standard antiallergic drugs compared with standard antiallergic drugs alone

Intervention (comparator)

Subcutaneous allergen immunotherapy + standard antiallergic drugs (standard antiallergic drugs only)

Country

Italy

Time horizon

6 years

Effectiveness data	Sample size	Discount rate	Cost year (currency)
SSs	30	Not reported	Not reported (US$)

Structure of model: N/A

Assumptions of model: N/A

Resource and cost data

Directs costs – GP or specialist visits, drugs, specialist examinations

Results

- Immunotherapy + drug treatment was associated with better SSs compared with drug treatment only over 6 years
- Immunotherapy + drug treatment was associated with better patient satisfaction scores compared with drug treatment only over 6 years
- Net savings associated with immunotherapy plus drug treatment were €623 (US$830) per year at year 6 (net savings start 3 years after treatment)

Sensitivity analysis: None

Assumption tested: N/A

Result: N/A

Author's conclusion

Subcutaneous immunotherapy is associated with significant economic advantages over antiallergic drug treatment in the long term

General comments

- Small patient numbers ($n = 30$) and loss to follow-up up to year 6 not stated
- SSs were evaluated at baseline and annually for 6 years. No utility-based outcome measure was used
- As is the case with CCA, no single measure of economic benefit was derived making it difficult to conclusively comment on whether the interventions were value for money
- No discounting is applied to costs and therefore cost estimates may not be appropriate
- As the price year is not reported, future reflation exercises based on results from this study will be hindered
- The authors also classified side effects as 0 = absent, 1 = local reactions such as itching and oedema around the site of the injection, 2 = slight systemic reaction, such as rhinitis or conjunctivitis, and 3 = moderate/severe systemic reactions, such as asthma, urticaria, angioedema and/or anaphylactic shock. However, there are no details on differences between groups and it is unclear if costs for side effects were included in the EE
- Data used were from a prospective randomised long-term study

N/A, not applicable.

Title: Cost-effectiveness of grass allergen tablet (GRAZAX) for the prevention of seasonal grass pollen induced rhinoconjunctivitis – a Northern European perspective

Bachert 2007[228]

Journal

Clinical and Experimental Allergy

Type of economic analysis	Study population	Perspective
Cost–utility analysis	Patients with grass pollen-induced rhinoconjunctivitis	Societal

Research question

Assessment of cost-effectiveness of Grazax (grass allergen tablet) compared with symptomatic treatment in seven northern European countries

Intervention (comparator)	Country	Time horizon
Sublingual Grazax (symptomatic treatment)	UK, Germany, Netherlands, Sweden, Denmark, Norway and Finland	Nine years (3 years with Grazax treatment and 6 years post Grazax discontinuation)

Effectiveness data	Sample size	Discount rate	Cost year (currency)
QALYs – based on EQ-5D	493	3–5% (depending on country)	2005 (euros)

Structure of model: N/A

Assumptions of model: N/A

Resource and cost data

Directs costs: visits to physician, acute ward visits, use of symptomatic rescue medication for AR and asthma and hospitalisation

Indirect costs: productivity losses (hours missed from work owing to AR)

Results

- Grazax associated with more QALY gains compared with symptomatic treatment (0.0287 additional QALYs per season and 0.222 QALYs gained over 9 years discounted at 4%)
- At an annual cost of <€2200 for the societal perspective, and based on a threshold of €29,000 (£20,000) per QALY, Grazax is cost-effective compared with standard (symptomatic) treatment in northern Europe

Sensitivity analysis

Univariate deterministic

Assumption tested	Result
• Including direct costs only	• Annual cost of Grazax should be below €2200 to be cost-effective at €29,000 threshold
• Using the upper threshold of €43,800 (£30,000) for cost-effectiveness (societal perspective)	• Annual cost of Grazax should be below €3400 to be cost-effective

Author's conclusion

For a tablet below €6, Grazax is a cost-effective intervention for the prevention of grass pollen-induced rhinoconjunctivitis

General comments

- Data used in the cost–utility analysis were collected prospectively alongside a randomised parallel group, DBPC trial conducted during the 2005 pollen season
- Although not many sensitivity analyses has been explicitly reported, it is important to note that wide ranges of values were used in the CUA, which increases the rigour of the results, for example discount rates (1.5–5%), annual costs for Grazax (€1200–4400), EQ-5D (country-specific versions of EQ-5D)
- No information has been given about private patient costs (other than indirect costs attributed to hours missed from work)
- Country-specific resource use and unit cost data were used
- Neither actual EQ-5D inputs (based on country specific valuations) nor QALY estimates for each arm are presented in the paper, which makes it impossible to apply effectiveness measures from this study in other studies
- The burden of AR was assumed to be uniform across all northern European countries
- This analysis was undertaken alongside a multinational clinical trial
- The study was funded by a manufacturer of SIT products

N/A, not applicable.

Title : Influence of time horizon and treatment patterns on cost-effectiveness measures: the case of allergen-specific immunotherapy with Grazax

Beriot-Mathiot 2007[232]

Journal

Journal of Medical Economics

Type of economic analysis

Cost–utility analysis

Study population

Patients with grass pollen-induced rhinoconjunctivitis

Perspective

Societal

Research question

Estimation of cost-effectiveness of two treatment patterns for Grazax (seasonal and WHO-recommended pattern) relative to standard care, as well as the effect that time horizon has on this estimation. The seasonal scenario involves administering Grazax 16 weeks prior to, and during, the pollen season, whereas the WHO-recommended scenario involves daily intake of Grazax for 3 years

Intervention (comparator)

Seasonal or WHO-recommended sublingual Grazax (symptomatic treatment)

Country

UK, Netherlands, Denmark and Sweden

Time horizon

15 years (3 years with GRAZAX treatment and 12 years post GRAZAX discontinuation)

Effectiveness data

QALYs – based on EQ-5D

Sample size

493

Discount rate

3%

Cost year (currency)

2004/5 (euros)

Structure of model: N/A

Assumptions of model: N/A

Resource and cost data

Directs costs: visits to physician, acute ward visits, use of symptomatic rescue medication for AR and asthma and hospitalisation

Indirect costs: productivity losses (hours missed from work owing to AR)

Results

- In the seasonal scenario, Grazax is more cost-effective than standard care with an ICER of €21,829. This ICER is independent of the time horizon considered
- In the WHO-recommended SIT scenario, Grazax is more cost-effective than standard care (at a threshold of €29,200) if the sustained effect of treatment is 2 years. The ICER decreases from €47,844 at the 1-year time horizon to €7894 at the 9-year time horizon
- The WHO-recommended SIT scenario is the most cost-effective when the time horizon is 6.3 years or more

Sensitivity analysis

Univariate deterministic

Assumption tested

- Changing the time point when seasonal treatment commences from 16 weeks to 8 weeks before the pollen season

Result

- Grazax was still more cost-effective than standard care with an even lower ICER of €13,797

Author's conclusion

Grazax is cost-effective both for the WHO-recommended SIT and the seasonal treatment

General comments

- Data used in the cost–utility analysis were collected prospectively alongside a randomised parallel group, DBPC trial conducted during the 2005 pollen season
- The only sensitivity analysis carried out was changing the time point at which seasonal treatment commences
- No information has been given about private patient costs (other than indirect costs attributed to hours missed from work)
- Country-specific resource use and unit cost data were used
- Some actual EQ-5D inputs were provided, but not disaggregated for the SIT or standard treatment group. In the same vein, QALY estimates for each arm were also not presented in the paper which makes it impossible to apply effectiveness measures from this study in other studies
- This analysis was undertaken alongside a multinational clinical trial
- It is not clear what the treatment used in the no-SLIT control group is, but it seems to be standard treatment

N/A, not applicable; WHO, World Health Organization.

Title: Cost-effectiveness of sublingual immunotherapy in children with allergic rhinitis and asthma

Berto 2005[223]

Journal

European Annals of Allergy and Clinical Immunology

Type of economic analysis

Cost–consequence analysis

Study population

Children with either seasonal or perennial AR and asthma

Perspective

Societal

Research question

Assessment of the cost of treating children with AR using sublingual immunotherapy (SLIT)

Intervention (comparator)

SLIT (no SLIT control – for second analysis)

Country

Italy

Time horizon

Four years (1 year pre-SLIT and 3 years on SLIT)

Effectiveness data	Sample size	Discount rate	Cost year (currency)
No. of asthma and rhinitis exacerbations, visits, absence from nursery or school	135	Not reported	Not reported (euros)

Structure of model: N/A

Assumptions of model: N/A

Resource and cost data

Directs costs: concomitant pharmacological treatment for allergic disease, specialist visits, SLIT

Indirect costs: productivity losses (nursery/school days lost – proxy for working days lost by parents)

Results

- Compared with the pre-SLIT period and with no-SLIT control groups, SLIT was associated with substantial reductions in the no. of exacerbations, no. of school/nursery days lost and number of medical visits
- Mean direct and indirect costs per year during the SLIT period (again compared with pre-SLIT and no-SLIT groups) were also lower

Sensitivity analysis

None

Assumption tested: N/A

Result: N/A

Author's conclusion

High-dose SLIT may be effective in reducing the cost of AR and asthma

General comments

- Data were based on a sample from only one allergy centre in northern Milan but sample characteristics are not given making it difficult to know how generalisable the results are
- The interventions are not very well or clearly described
- As is the case with CCA, no single measure of economic benefit was derived, making it difficult to conclusively comment on whether the interventions were value for money
- No discounting is applied to costs and therefore cost estimates may not be appropriate
- It is not clear what the treatment is used in the no-SLIT control group, but it seems to be standard treatment

N/A, not applicable.

Title: Economic evaluation of sublingual immunotherapy vs symptomatic treatment in adults with pollen-induced respiratory allergy: the Sublingual Immunotherapy Pollen Allergy Italy (SPAI) study

Berto 2006[226]

Journal

Annals of Allergy, Asthma and Immunology

Type of economic analysis

Cost-effectiveness analysis

Study population

Young adults with seasonal pollen-induced AR with or without asthma

Perspective

National health-care system (NHS) and societal

Research question

Assessment of cost and consequences of SLIT added to pharmacotherapy in comparison to pharmacotherapy alone

Intervention (comparator)

SLIT + pharmacotherapy (pharmacotherapy only)

Country

Italy

Time horizon

6 years

Effectiveness data

No. of patients improved; number of asthma cases avoided

Sample size

2230

Discount rate

3%

Cost year (currency)

2002 (euros and US $)

Structure of model

Decision-tree model

Assumptions of model

Same rate of hospitalisation attributed to both the SLIT and no-SLIT groups

Resource and cost data

NHS perspective: direct medical costs (visits, diagnostic procedures, drugs, SLIT and hospitalisations)

Societal perspective: direct (as above), indirect (working days lost) and patient out-of-pocket costs

Results

From both the NHS and societal perspectives and for both outcomes (cost per additional improved patient and cost per additional asthma case avoided), SLIT dominates no-SLIT (i.e. it is cheaper and more effective)

Sensitivity analysis

Univariate deterministic

Assumption tested	Result
• Changing perspective from NHS to societal	• SLIT still dominates no-SLIT
• Varying distribution of disease and severity level	• SLIT still dominates no-SLIT
• Varying the cost of hospitalisations (from €1491.11 to €864.00)	• SLIT still dominates no-SLIT

Author's conclusion

SLIT is less expensive and more effective that pharmacotherapy alone from both perspectives and for both effectiveness outcomes

General comments

- It is not clear whether the two arms are comparable in terms of baseline characteristics
- The lack of details on the study sample characteristics makes it difficult to ascertain how generalisable the results of the study are to a wider population
- Effectiveness estimates were based on a retrospective cohort study in which clinicians enrolled in the study reported the outcomes for 100 of their patients. It is not clear whether this introduced any selection bias and, if it did, what effect it had on the results
- The data used to populate the model was not clearly presented making it problematic to replicate the decision tree model-based analysis
- The study was funded by a manufacturer of SIT products

Title: Cost-effectiveness of specific subcutaneous immunotherapy in patients with allergic rhinitis and allergic asthma

Brüggenjürgen 2008[229]

Journal

Annals of Allergy, Asthma and Immunology

Type of economic analysis

Cost–utility analysis

Study population

Patients with either seasonal or perennial AR and allergic asthma

Perspective

Societal and third-party payer

Research question

Assessment of cost-effectiveness of SCIT in addition to ST compared with ST alone

Intervention (comparator)

SCIT + ST (ST alone)

Country

Germany

Time horizon

15 years

Effectiveness data

Utilities

Sample size

2000

Discount rate

3%

Cost year (currency)

Not reported (euros)

Structure of model

Markov model

Assumptions of model

Markov cycle length = 1 year

Six disease/health states: mild AR; moderate to severe AR; moderate to severe AR and mild allergic asthma; moderate to severe AR and severe allergic asthma; no symptoms; and dead

Resource and cost data

Annual costs from Schramm *et al.*[271]

Direct costs associated with disability, early retirement and loss of work

Other data

Transition probabilities from published literature sources

Results

- From a societal point of view at 15 years, SCIT + ST dominates ST only (ICER of €–19,787 per QALY) (break-even point is reached after 10 years)
- From a third-party payer's perspective, SCIT + ST is associated with an ICER of €8308 per QALY

Sensitivity analysis: Univariate deterministic

Assumption tested	Result
• Shortening SCIT treatment length from 3 to 2 years	• SCIT + ST still dominates but is associated with even greater cost savings
• Varying price of SCIT	• Reducing cost of SCIT resulted in even greater savings – SCIT + ST still dominates
• Varying the discount rate between 0% and 10%	• SCIT + ST still dominates ST alone
• Using third-party payers' perspective	• SCIT + ST was associated with an ICER of €8308 per QALY
• Extending SCIT to all patients	• SCIT + ST was associated with an ICER of €3713 per QALY

Author's conclusion

Subcutaneous immunotherapy + ST was associated with cost savings and improved medical outcomes

General comments

- No probabilistic sensitivity analysis carried out
- It is not clear what instrument was used to derive the 'utilities' – reference cited is a report on acupuncture
- Assumptions that could not be validated by any literature sources were based on the consensus of a board of experts in paediatrics, dermatology, allergy, pneumonia and otolaryngology
- The interventions were not presented clearly in the article
- The resource use and cost data details were not reported in sufficient details to allow for replication
- Further, future reflation exercises will be hindered as the price year was not reported
- Because of the foregoing (i.e. lack of detail), it is hard to assess the rigour of the results obtained
- Study was funded by a manufacturer of SIT products

Title: Cost-effectiveness of GRAZAX for the prevention of grass pollen induced rhinoconjunctivitis in Southern Europe

Canonica 2007[230]

Journal

Respiratory Medicine

Type of economic analysis

Cost–utility analyses

Study population

Patients with seasonal grass pollen-induced rhinoconjunctivitis

Perspective

Societal

Research question

Assessment of cost-effectiveness of Grazax (grass allergen tablet) compared with symptomatic treatment in four southern European countries

Intervention (comparator)

Sublingual Grazax (symptomatic treatment)

Countries

Spain, France, Italy and Austria

Time horizon

Nine years (3 years with GRAZAX treatment and 6 years post GRAZAX discontinuation)

Effectiveness data

QALYs – based on EQ-5D

Sample size

634

Discount rate

3–6% (depending on country)

Cost year (currency)

2004/5 (Euros)

Structure of model: N/A

Assumptions of model: N/A

Resource and cost data

Directs costs: visits to physician and acute wards, symptomatic medication, asthma medication, eventual hospitalisation

Indirect costs: productivity losses (hours missed from work due to AR)

Other data

Risk of developing asthma

Results

- Grazax associated with more QALY gains compared with symptomatic treatment (0.0167 additional QALYs per season and 0.134 discounted QALYs gained over 9 years)
- At an annual cost of between €1500 and €1900, and based on a threshold of €29,000 (£20,000) per QALY, Grazax is cost-effective compared with standard (symptomatic) treatment

Sensitivity analysis

Univariate deterministic

Assumption tested	Result
• Impact of allergic asthma (including future costs related to asthma)	• ICERs associated with Grazax become even more favourable
• Excluding patients from Spain from the analysis (due to low pollen counts in Spain in 2005 which had impact on QoL)	• Mean QALY in Grazax group increased from 0.9492 to 0.9686
• Using the upper threshold of €43,800 (£30,000) for cost-effectiveness (societal perspective)	• Annual cost of Grazax should be <€2550 to be cost-effective

Author's conclusion

Grazax is cost-effective compared with standard (symptomatic) treatment in southern Europe

General comments

- Data used in the cost–utility analysis were collected prospectively alongside a randomised parallel group, DBPC trial conducted during the 2005 pollen season
- Even although not many sensitivity analyses has been explicitly reported, it is important to note that ranges of values were used in the CUA, for example discount rates (3–6%), annual costs for Grazax (€900–2900), EQ-5D (country-specific versions of EQ-5D)
- No information has been given about private patient costs (other than indirect costs attributed to hours missed from work)
- Neither actual EQ-5D inputs (based on country-specific valuations) nor QALY estimates for each arm are presented in the paper, which makes it impossible to apply effectiveness measures from this study in other studies
- This analysis was undertaken alongside a multinational clinical trial

N/A, not applicable.

Title: Health economic model of allergen–specific immunotherapy in seasonal allergic rhinitis from a health care payer's perspective

Claes 2009[224]

Journal

Allergo Journal

Type of economic analysis

Cost analysis

Study population

Paediatric and adult patients with SAR

Perspective

Health insurers

Research question

Comparative assessment of costs of five forms of immunotherapy:

- Long-term subcutaneous immunotherapy (LT SCIT)
- sublingual immunotherapy (SLIT)
- short-term subcutaneous immunotherapy with maintenance injections (ST SCIT + injections)
- short-term subcutaneous immunotherapy without maintenance injections (ST SCIT)
- short-term subcutaneous immunotherapy with an adjuvant-supported allergoid (allergoid + MPL) (ST SCIT MPL)

Intervention (comparator)

LT SCIT (SLIT; ST SCIT; ST SCIT + injections; ST SCIT MPL)

Country

Germany

Time horizon

Three years

Other scenarios look at 15-year time period

Effectiveness data

For base case assume 100% effectiveness for all different treatment strategies

Sample size

Not stated. Hypothetical paediatric and adult cohorts

Discount rate

5%

Cost year (currency)

Not reported (euros)

Structure of model

Markov model

Assumptions of model

Markov cycle length = 1 week

Base case: 100% effectiveness for all treatments being compared, no discontinuations and 100% compliance

Resource and cost data

Costs of diagnosis, clinician time, services, supplies (e.g. injections), SAR medication, hospital visits, costs of treating asthma

Other data

Transition probabilities (children) given for development over time of SAR (from non-SAR population), lower airway symptoms or asthma. Data mainly from PAT study[272]

Results

- Three-year average direct costs for the five forms of immunotherapy were: €2584 (LT SCIT), €4269 (SLIT), €1533 (ST SCIT), €2523 (ST SCIT + injections) and €2080 (ST SCIT MPL)
- Direct costs of the ST SCIT MPL arm, compared with those of other forms SCIT and SLIT, are higher at the beginning of therapy
- Other scenarios show that, compared with other forms of immunotherapy, ST SCIT and ST SCIT MPL have favourable sustainability and adherence-related outcomes

Sensitivity analysis

Univariate deterministic

Assumption tested

- Variation in discontinuation rates, discount rates, time horizon (5, 12 and 15 years), some costs and effectiveness (source for effectiveness data not clear)

Result

- Sensitivity analyses have an influence on costs, but overall no effect on the relative cost differences between different treatment strategies

Author's conclusion

Short-term SCIT and allergoid + MPL seem to be associated with fewer costs compared with other forms of immunotherapy. After 3 years giving no SIT is still the cheapest option, whereas after 15 years it becomes the most expensive option

General comments

- The authors assume 100% effectiveness, 0% discontinuation rates and 100% compliance for all therapies (base case), which seems infeasible
- Some of these assumptions are varied in sensitivity analyses but at least for effectiveness do not seem to be based on any clinical data
- Only total direct costs considered, no utilities estimated (not a CBA)

Title: A cost-effectiveness analysis of immunotherapy with SQ allergen extract for patients with seasonal allergic rhinoconjunctivitis in selected European countries

Keiding and Jørgensen 2007[233]

Journal

Current Medical Research and Opinion

Type of economic analysis

Cost-effectiveness analysis and cost–utility analyses

Study population

Patients with seasonal (grass-induced) allergic rhinoconjunctivitis

Perspective

Not stated

Research question

Assessment of cost-effectiveness of Alutard SQ (ASQ) compared with emergency/standard treatment in six European countries

Intervention (comparator)

Subcutaneous ASQ (emergency/standard treatment)

Countries

Austria, Denmark, Finland, Germany, Netherlands and Sweden

Time horizon

Nine years (updosing and maintenance in year 1, follow-up in years 2 and 3, and emergency treatment for rest of time)

Effectiveness data

Symptom free and well-days (based on RQLQ), MSs, VAS, QALYs – based on mapping from RQLQ to EQ-5D

Sample size

Not reported

Discount rate

3%

Cost year (currency)

2005 (euros)

Structure of model: N/A

Assumptions of model: N/A

Resource and cost data

Directs costs: updosing visits, maintenance visits, cost of ASQ, cost of specific immunotherapy, rescue medication, other direct costs

Indirect costs: productivity gain (through reduced number of working days lost)

Results

- ICERs associated with ASQ are between €9716 and €25,863 per QALY without accounting for indirect costs. When indirect costs are included, ASQ dominates emergency treatment in all countries except two, in which it is associated with low ICERs (€6458 per QALY for The Netherlands and €5024 per QALY for Sweden)
- ASQ was more favourable when outcomes were expressed as cost per symptom-free day and cost per well-day

Sensitivity analysis

None reported

Assumption tested: N/A

Result: N/A

Author's conclusion

ASQ is cost-effective compared with emergency treatment regardless of whether indirect costs are included or not

General comments

- Indirect costs relating to loss of working days were not considered, as data were not available in all of the six countries; instead those relating to productivity gain through reduced number of working days lost were used
- Difficult to assess the robustness of the results as sensitivity analyses were not conducted or reported
- The sample size should have also been given to give an idea of the how robust the analyses were
- The 'other direct costs' could have been enumerated to enable testing of the costing procedure. In addition, the cost perspective should have also been specified
- Data for the study came from the UK Immunotherapy Study Group (UKIS) trial
- A 10-cm VAS was used to measure allergic symptoms with '0' representing 'no symptoms' and '10' representing 'severe symptoms'

N/A, not applicable.

Title: Cost-effectiveness of specific immunotherapy with Grazax in allergic rhinitis co-existing with asthma

Nasser 2008[231]

Journal
Allergy

Type of economic analysis	Study population	Perspective
Cost–utility analysis	Patients with grass pollen-induced rhinoconjunctivitis including those with co-existing asthma	Societal

Research question

Assessment of cost-effectiveness of Grazax (tablet-base allergen-SIT) plus ST compared with ST only

Intervention (comparator)	Countries	Time horizon
Sublingual Grazax + ST (ST only)	United Kingdom, Germany, Netherlands, Denmark, Sweden, Spain, Austria and Italy	Nine years (3 years of GRAZAX treatment and 6 years of sustained effect)

Effectiveness data	Sample size	Discount rate	Cost year (currency)
QALYs – based on EQ-5D	151	3.5%	2005 (UK £)

Structure of model: N/A

Assumptions of model: N/A

Resource and cost data

Directs costs: emergency physician visits, acute ward visits, acute ward visits, hospitalisations

Indirect costs: hours missed from work, reduced productivity

Results

- Grazax was associated with more QALY gains than symptomatic treatment (0.0250 additional QALYs per season and 0.197 QALYs gained over 9 years discounted at 3.5%)
- Grazax was associated with a cost per QALY gained of £4319

Sensitivity analysis

Univariate deterministic

Assumptions tested	Results
Excluding influence of reduced productivity at work	Grazax was associated with an ICER of £8816 per QALY gained
Varying time horizon to 7 years but including influence of reduced productivity at work	Grazax was associated with an ICER of £7272 per QALY gained
Varying time horizon to 7 years but excluding influence of reduced productivity at work)	Grazax was associated with an ICER of £11,769 per QALY gained
Varying annual costs of Grazax from £1000 to £3000	Grazax remains cost-effective up to an annual cost of £1850 (£5.07 per tablet). Base-case price was £2.25 per tablet

Author's conclusion

SIT with Grazax is cost-effective compared with standard (symptomatic) treatment

General comments

- Data used in the cost–utility analysis were collected prospectively alongside a randomised parallel group, DBPC trial conducted during the 2005 pollen season
- No information has been given about private patient costs (other than indirect costs attributed to hours missed from work)
- Actual EQ-5D inputs (based on country-specific valuations) are not presented in the paper
- No EQ-5D values or QALY estimates for each arm are presented in the paper, which makes it impossible to apply effectiveness measures from this study in other studies
- This analysis was undertaken alongside a multinational clinical trial

N/A, not applicable.

Title: Pharmacoeconomic assessment of specific immunotherapy vs current symptomatic treatment for allergic rhinitis and asthma in France

Author

Omnes 2007[227]

Journal

European Annals of Allergy and Clinical Immunology

Type of economic analysis

Cost-effectiveness analysis

Study population

Adults and children suffering from either seasonal or perennial AR (with or without asthma)

Perspective

Health insurers

Research question

Assessment of comparative cost-effectiveness of three strategies: (i) symptomatic treatment (CST) alone; (ii) injectable specific immunotherapy (SCIT) plus CST (SCIT + CST); and (iii) sublingual immunotherapy (SLIT) plus CST (SLIT + CST)

Intervention (comparator)

SCIT + CST (SLIT + CST; CST only)

Country

France

Time horizon

Six years (adult population) and 7 years (juvenile population)

Effectiveness data

Proportions of individuals with rhinitis or allergic asthma in the four models (juvenile, adult, dust mite allergy and pollen allergy), distribution of severity levels, and treatment efficacy (the numbers of improved patients and asthma cases)

Sample size

1000

Discount rate

3%

Cost year (currency)

2003 (euros)

Structure of model

Decision-tree model

Resource and cost data

Direct costs: costs associated with drugs, visits and diagnostic tests. Expert opinion (Delphi panel) and recommendations from both French and international guidelines used to determine resource quantities

Indirect costs: no. of work-days lost

Results

Adults (6 years)

When compared with CST only:

- The incremental costs per asthma case avoided with SCIT + CST were €393 and €1327 for dust mite and pollen allergy, respectively
- The incremental costs per asthma case avoided with SLIT + CST were €3158 and €1708 for dust mite and pollen allergy, respectively

Children (over 7 years)

When compared with CST only:

- The incremental costs per asthma case avoided with SCIT + CST were €583 and €597 for dust mite and pollen allergy, respectively
- The incremental costs per asthma case avoided with SLIT + CST were €3938 and €824 for dust mite and pollen allergy, respectively

Sensitivity analysis: Univariate deterministic

Assumptions tested	Results
• Use of the official GP's tariff for SCIT from the nomenclature générale des actes professionnels (NGAP) nomenclature instead of the GP's tariff in adult model	• SCIT became the dominant strategy compared with CST in dust mite and pollen allergy • Results were unchanged
• Alternative distributions of severity levels were derived from two published studies in adult model	• Results were unchanged
• Ranges of values defined by the Delphi panel were also used for other clinical data in child model	

Author's conclusion

Injectable specific immunotherapy (SCIT) is a more cost-effective treatment in children with pollen allergy and in adults with dust mite allergy in comparison with both CST and sublingual SIT. Sublingual SIT was more cost-effective than CST in pollen-induced rhinitis, especially in children

General comments

- Most (all) of the epidemiological data for the adult (child) model were based on expert opinion, i.e. a Delphi panel of 11 members (10 allergologists and one epidemiologist); although this was justified (due to heterogeneity in published estimates), this was one weakness of the study
- Another limitation of the analysis was the lack of more rigorous assessment of uncertainty, for example using probabilistic sensitivity analysis
- Other aspects of the study were adequately addressed
- Although no head-to-head comparisons were made between SCIT + CST and SLIT + CST, SCIT + CST was associated with better outcome, i.e. lower ICERs, when both were compared with CST only

Title: Health-economic analyses of subcutaneous specific immunotherapy for grass pollen and mite allergy

Petersen 2005[234]

Journal

Allergol et Immunopathol

Type of economic analysis	Study population	Perspective
CBA and CEA	Patients with grass pollen or mite allergy (seasonal or perennial allergy)	Societal

Research question

Assessment of the health and monetary consequences of treating allergy with SIT compared with standard (symptomatic) treatment

Intervention (comparator)	Country	Time horizon
SCIT (standard/symptomatic treatment)	Denmark	Eight years (3 years treatment with SIT and 5 years' extrapolation)

Effectiveness data	Sample size	Discount rate	Cost year (currency)
Monetary benefits and measure of psychological well-being	204	5%	2002 (Danish krone, DKK)

Structure of model: N/A – retrospective observational study

Assumptions of model: N/A

Resource and cost data

Direct costs: medicine use; visits to medical doctors; visits to emergency rooms; visits to doctors on emergency duty; hospital stays pre-, per- and post-SIT

Patient costs: transportation; time costs

Indirect costs: work-related sick days; leisure activity sick days

Results

Subcutaneous immunotherapy is associated with an ICER of DKK 2.784 per patient/year of improved well-being. From a CBA perspective, SCIT was shown to be net beneficial

Sensitivity analysis: Univariate deterministic

Assumption tested	Result
Varying the time horizon considered after the start of SIT from 4 to 9 years	Cost per patient year of improved well-being lies in the range DKK 16,408 to DKK 2784

Author's conclusion

SIT is associated with increases in societal welfare

General comments

- The methodology for determining outcomes in the CBA is also not very clear (it seems only indirect costs associated with sick days were included in estimation)
- The results of the CEA (based on cost per year improvement in psychological well-being) are difficult to generalise
- It is also not clear what technique was used to value the monetary benefits used in the CBA

N/A, not applicable.

Title: Economic evaluation of sublingual vs subcutaneous allergen immunotherapy

Pokladnikova 2007[225]

Journal

Annals of Allergy, Asthma and Immunology

Type of economic analysis

CCA

Study population

Patients with seasonal allergic rhinoconjunctivitis

Perspective

Third-party payer, patient and societal

Research question

Evaluation of the cost and cost-effectiveness of SLIT compared with SCIT and standard ST

Intervention (comparator)

SLIT (SCIT; ST)

Country

Czech Republic

Time horizon

15 years

Effectiveness data

RQLQ score; VAS score; symptomatic medication reduction; health-care utilisation

Sample size

64 (19 = SLIT, 23 = SCIT and 22 = ST)

Discount rate

0%

Cost year (currency)

2002 (euros)

Structure of model: N/A – within-trial-based analysis

Assumptions of model: N/A

Resource and cost data

- Direct medical costs: costs of treatment and health-care services. Health-care services include specialist visits (consultations, laboratory tests, diagnostic tests, nurse services)
- Costs associated with adverse effects of treatment (medication, emergency department visits and hospitalisations)
- Patient costs: medication co-payment, over-the-counter drugs, travel costs, loss of income due to allergy symptoms, treatment and productivity costs (using human capital approach)

Results

- Clinical benefits for SLIT were comparable to those for SCIT but SCIT patients showed a slightly better improvement especially in VAS and symptomatic MSs
- Compared with SCIT, SLIT was associated with lower costs (from all perspectives)

Sensitivity analysis

Univariate deterministic

Assumption tested

- Varying costs of interventions by ± 50% for the third-party payer perspective

Result

- SLIT associated with lower costs compared with SCIT

Author's conclusion

Compared with SCIT, SLIT is a less expensive alternative from all perspectives except for patients who do not experience loss of income and travel costs associated with treatment (from the patients' perspective)

General comments

- SA conducted for only third-party payer perspective, making it difficult to ascertain the rigour of all the results
- The sample also seems to be fairly small, implying that one needs to interpret the results obtained with caution
- As is the case with CCA, no single measure of economic benefit was derived, making it difficult to conclusively comment on whether the interventions were value for money
- Data used in this study was derived from an open-label randomised clinical trial

N/A, not applicable.

Title: Economic evaluation of specific immunotherapy (SIT) vs symptomatic treatment of allergic rhinitis in Germany

Schädlich and Brecht 2000[235]

Journal

Pharmacoeconomics

Type of economic analysis

CEA, CCA

Study population

Patients with either pollen or mite allergy (seasonal or perennial allergy)

Perspective

Societal, national health-care system and SHI provider

Research question

Evaluation of the economic consequences of SIT lasting 3 years in comparison to those of continuous symptomatic treatment

Intervention (comparator)

Specific subcutaneous immunotherapy (continuous symptomatic treatment)

Country

Germany

Time horizon

10 years

Effectiveness data

No. of additional patients free from asthma symptoms; break-even points of costs/expenses per patient and difference in costs/expenses per patient after 10 years

Sample size

Cohort of 2000 patients

Discount rate

5%

Cost year (currency)

1997 (Deutschmarks, DM)

Structure of model

Decision-tree model

Assumptions of model

Base-case results based on average values of clinical effectiveness parameters and average case-related treatment costs and statutory health insurer (SHI) expenses

Resource and cost data

Directs costs: drugs (injections), medical services, diagnoses, adverse effects, SHI costs, rehabilitation

Indirect cost: loss of productivity caused by absence from work, premature retirement and premature death

Results

- Break-even point reached between 6 and 8 years after commencement of therapy
- Net savings associated with therapy were between DM650 and DM1190 per patient after 10 years
- SIT associated with ICERs of between DM3640 and DM7410 per additional patient free from asthmatic symptoms

Sensitivity analysis

Univariate deterministic

Assumption tested

- Use of best-/worst-case scenarios for SIT
- Impact of exogenous parameters on target variables

Results

- Best-case scenario – SIT was superior; worst-case scenario – symptomatic treatment superior
- Direct medical cost for symptomatic treatment has greatest impact on the target variable followed by average increase of asthma prevalence with symptomatic treatment

Author's conclusion

SIT results in net savings after 10 years from societal, health-care and SHI perspectives

General comments

- Target variables used in CCA not very clearly described, i.e. break-even points of costs/expenses per patient and difference in costs/expenses
- Difficult to ascertain the internal validity of the estimate of benefit as there is limited reporting of the literature review from where these estimates are sourced
- The results provided have, however, been subjected to some rigorous sensitivity analysis

SHI, statutory health insurance.

Title: Economic studies of immunotherapy: a review

Berto 2008[247]

Journal

Current Opinion in Allergy and Clinical Immunology

Type of economic analysis

Review of cost analyses (cost and cost–cost analyses) and EEs

Study population

Patients with seasonal and PAR and asthma

Perspective

Societal, national health-care system and patient

Research question

Assessment of evidence on the economic advantages offered by immunotherapy

Intervention (comparator)

Immunotherapy (standard pharmaceutical treatment – for cost–cost analyses and EEs)

Countries

USA, UK, Spain, Italy, Germany, France, northern EU, southern EU, Austria, Denmark, Finland, Netherlands and Sweden

Time horizon

10 years

Effectiveness data

QALYs and other (unreported) physical/natural outcomes

Sample size

14 papers

Discount rate: N/A

Cost year (currency)

Not reported (euros)

Structure of model: N/A

Assumptions of model: N/A

Resource and cost data

Directs costs: outpatient and inpatient visits, specialist visits, immunotherapy, symptomatic medication, asthma medication, eventual hospitalisation

Indirect costs: productivity losses (working days lost by patients and nursery/school days lost – proxy for working days lost by parents)

Results

- Cost analyses: costs per patient/year varied from €96 to €348.50
- Cost–cost analyses: average costs/patient for immunotherapy ranged from €288 to €1182, whereas those for pre-immunotherapy/controls ranged from €116 to €2672
- EEs: immunotherapy is more cost-effective than standard treatment

Sensitivity analysis: None

Assumption tested: N/A

Result: N/A

Author's conclusion

Immunotherapy can be cheaper and also more cost-effective than standard therapy alone

General comments

- The results of the review are not reported in enough detail, for example the outcomes used in the cost-effectiveness analyses were not presented
- The results of head-to-head comparisons between SCIT and SLIT are not reported in sufficient detail

N/A, not applicable.

Title: The Health Economics of Allergen Immunotherapy

Hankin 2011[237]

Journal

Immunology and Allergy Clinics of North America

Type of economic analysis

Review of cost analyses (cost and cost-to-cost analyses) and EEs

Study population

Patients with seasonal or PAR and/or asthma

Perspective

Health-care system, societal and patient

Research question

Evaluation of the economic benefit of allergen-specific immunotherapy (SIT) compared

Intervention (comparator)

SIT [standard drug treatment (SDT) in certain instances]

Countries

USA, Germany, France, Italy, Denmark and northern Europe

Time horizon

From 1995 to 2011

Effectiveness data

QALYs, net benefits and other physical/natural outcomes

Sample size

15 studies

Discount rate

N/A

Cost year (currency)

2010 (US$)

Structure of model: N/A – systematic review

Assumptions of model: N/A

Resource and cost data

- Direct costs: encounters (visits), tests, allergic reactions, procedures, drugs, hospital services, SIT
- Indirect costs: productivity losses (days lost from work, disability and premature death)

Results

SIT provides cost benefits ranging from $96 to $5465. Average annual costs for SIT per patient ranged from US$247 to US$10,200; average annual costs for STD per patient ranged from US$1,335 to US$24,243; mean cost of allergy medications per patient year varied from US$23 to $37 and costs per QALY gained ranged from US$14,536 to US$38,695

Sensitivity analysis: N/A

Assumption tested: N/A

Result: N/A

Author's conclusion

SIT has cost benefits over SDT and therefore introduction of new SDTs must be carefully assessed in terms of clinical effectiveness and cost-effectiveness

General comments

- The details of the studies included in the review are presented with adequate details making a distinction between cost analyses and EEs

N/A, not applicable.