

7

HEALTH ECONOMIC ANALYSIS OF ALLERGEN IMMUNOTHERAPY (AIT) FOR THE MANAGEMENT OF ALLERGIC RHINITIS, ASTHMA, FOOD ALLERGY AND VENOM ALLERGY

A SYSTEMATIC OVERVIEW

🌀 Supplementary materials 🌀

Miqdad Asaria¹, Sangeeta Dhama², Ronald van Ree³, Roy Gerth van Wijk⁴, Antonella Muraro⁵, Graham Roberts⁶, Aziz Sheikh⁷

AFFILIATIONS

¹ Centre for Health Economics, University of York, UK

² Evidence-Based Health Care Ltd, Edinburgh, UK

³ Departments of Experimental Immunology and of Otorhinolaryngology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

⁴ Section of Allergology, Department of Internal Medicine, Erasmus MC Rotterdam, The Netherlands

⁵ Food Allergy Referral Centre Veneto Region Department of Women and Child Health Padua General University Hospital, Italy

⁶ The David Hide Asthma and Allergy Research Centre, St Mary's Hospital, Newport Isle of Wight, Southampton NIHR Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust, Southampton, UK, and Faculty of Medicine, University of Southampton, Southampton, UK

⁷ Asthma UK Centre for Applied Research, Usher Institute of Population Health Sciences and Informatics, The University of Edinburgh, Edinburgh, UK

APPENDIX 1: DATA EXTRACTION FORMS

Rhinitis and asthma

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

Author / Year: Nasser / 2008 (14)

Journal: Allergy

| Type of economic analysis | Perspective | Countries |
|--|---|-----------------------|
| CUA | Health system | UK |
| Study population | | |
| Patients suffering from grass pollen induced rhinoconjunctivitis co-existing with asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT (Grazax) / Standard Care | 9 years | RCT 1 year follow up |
| Sample size | Outcome measure | Outcome discount rate |
| 151 | EQ5D - QALYs | 3.5% |
| Cost data | Cost year / currency | Cost discount rate |
| RCT patient diary linked to unit costs | 2005 / GBP | 3.5% |
| Results | Sensitivity analysis | |
| ICER £8816 per QALY | One way sensitivity analysis to explore impact of changing time horizon | |
| General comments | | |
| <ul style="list-style-type: none"> • results based on patients in UK, Germany, the Netherlands, Denmark, Sweden, Spain, Austria and Italy • treatment effect assumed to persist through 3 years of treatment and 6 years following treatment discontinuation | | |

Title: Economic evaluation of sublingual immunotherapy vs symptomatic treatment in allergic asthma

Author / Year: Ariano / 2009 (13)

Journal: Annals of Allergy, Asthma & Immunology

| Type of economic analysis | Perspective | Countries |
|--|----------------------|-----------------------|
| CEA | Health system | Italy |
| Study population | | |
| Patients with dust mite induced allergic asthma and rhinitis | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT / Standard Care | 5 years | RCT 5 year follow up |
| Sample size | Outcome measure | Outcome discount rate |
| 70 | VAS symptom score | 0% |
| Cost data | Cost year / currency | Cost discount rate |
| RCT patient diary and unit costs | ? / Euros | 0% |
| Results | Sensitivity analysis | |
| Overall costs lower in SLIT patients and lower symptom score | NA | |
| <ul style="list-style-type: none"> • very little detail provided of the analysis performed • no real economic analysis or interpretation of the results provided | | |

Data extraction of Rhinitis with or without Asthma studies

Title: Economic evaluation of specific immunotherapy versus symptomatic treatment of allergic rhinitis in Germany

Author / Year: Schadlich / 2000 (29)

Journal: Pharmacoeconomics

| Type of economic analysis | Perspective | Countries |
|---|------------------------------------|-----------------------------|
| CEA | Health System | Germany |
| Study population | | |
| Patients with seasonal (pollen) and perennial (mite) allergy with or without asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SIT / Standard Care | 10 years | Unclear |
| Sample size | Outcome measure | Outcome discount rate |
| - | Patients who do not develop asthma | 0% |
| Cost data | Cost year / currency | Cost discount rate |
| Resource use surveys | 1990 / DM | 0% |
| Results | | Sensitivity analysis |
| SIT was found to be cost saving as compared to standard care and reduced the chances of patients developing asthma | | NA |
| <ul style="list-style-type: none"> It was very unclear what data sources were used to populate the model in this study | | |

Title: Economic evaluation of sublingual vs subcutaneous allergen immunotherapy

Author / Year: Pokladnikova / 2008 (24)

Journal: Annals of Allergy, Asthma & Immunology

| Type of economic analysis | Perspective | Countries |
|--|----------------------|--|
| CEA | Health system | Czech Republic |
| Study population | | |
| Adults with at least 2 years of seasonal allergic rhinoconjunctivitis with or without allergic asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT / SCIT / Standard Care | 3 years | RCT 5 years follow up |
| Sample size | Outcome measure | Outcome discount rate |
| 19 SLIT, 23 SCIT, 22 Standard Care | RQLQ | 0% |
| Cost data | Cost year / currency | Cost discount rate |
| Administrative data linked to unit costs | 2002 / Euro | 3% |
| Results | | Sensitivity analysis |
| SLIT and SCIT both performed better on RQLQ than standard care SLIT performed better than SCIT and was cheaper from a health system perspective | | One way deterministic sensitivity analysis performed on costs and discount rates |
| General comments | | |
| <ul style="list-style-type: none"> No incremental cost effectiveness results were provided | | |

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

Author / Year: Petersen / 2005 (23)

Journal: Allergol et Immunopathol

| Type of economic analysis | Perspective | Countries |
|--|-------------------------------------|---|
| CEA | Societal | Denmark |
| Study population | | |
| Patients with grass pollen or mite allergy | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SIT / Standard care | 5 years | Retrospective questionnaire following trial |
| Sample size | Outcome measure | Outcome discount rate |
| 253 | Patient year of improved well being | 5% |
| Cost data | Cost year / currency | Cost discount rate |
| Administrative data | 2002 / DKK | 5% |
| Results | | Sensitivity analysis |
| ICER 2784 DKK per patient year of improved well being | | NA |
| General comments | | |
| <ul style="list-style-type: none"> • Selection bias due to partial response rate to questionnaire not controlled for • Recall bias not controlled for • Outcome measure is not validated and does not capture degree of improvement | | |

Title: Economic evaluation of a tablet based vaccination against hay fever in Denmark

Author / Year: Poulsen / 2008 (25)

Journal: Ugeskr Laeger

| Type of economic analysis | Perspective | Countries |
|--|----------------------|------------------------|
| CUA | Health system | Denmark |
| Study population | | |
| Adults with grass pollen induced rhinotconjunctivitis | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT / Standard care | 9 years | RCT one year follow up |
| Sample size | Outcome measure | Outcome discount rate |
| 493 | EQ5D / QALYs | 3% |
| Cost data | Cost year / currency | Cost discount rate |
| Unclear | ? / DKK | 3% |
| Results | | Sensitivity analysis |
| ICER: 134105 DKK per QALY | | NA |
| General comments | | |
| <ul style="list-style-type: none"> • Based on patients in Denmark, Sweden, England, Germany, Holland with Danish QALY weights and unit costs applied to EQ5D and resource use data • Treatment effect observed in 1 year RCT assumed to persist through 3 years of treatment and 6 years following treatment discontinuation | | |

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

Author / Year: Canonica / 2007 (18)

Journal: Respiratory Medicine

| Type of economic analysis | Perspective | Countries |
|---|----------------------|--|
| CUA | Societal | Spain, Italy, France, Austria |
| Study population | | |
| Patients with a 2 year history of grass pollen induced allergic rhinoconjunctivitis with or without asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT / Standard care | 9 years | RCT 1 year follow up |
| Sample size | Outcome measure | Outcome discount rate |
| Unclear subset of 634 | EQ5D - QALYs | 3 – 5 % depending on country |
| Cost data | Cost year / currency | Cost discount rate |
| RCT patient diary linked to unit costs | 2004 / Euro | 3 – 5 % depending on country |
| Results | | Sensitivity analysis |
| 0.134 incremental QALYs in SLIT patients if SLIT costs 1400 euro per year then ICER would be less than 29000 euro per QALY in all four countries | | Repeated analysis excluding Spanish patients |
| General comments | | |
| <ul style="list-style-type: none"> • Results calculated for France even though trial did not cover France • Unclear exactly what data from the multi country trial was used to calculate these results • Treatment effect observed in 1 year RCT assumed to persist through 3 years of treatment and 6 years following treatment discontinuation | | |

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

Author / Year: Keiding / 2007 (20)

Journal: Current Medical Research and Opinions

| Type of economic analysis | Perspective | Countries |
|---|-----------------------------|--|
| CUA | Health system | Austria, Denmark, Finland, Germany, Netherlands, Sweden |
| Study population | | |
| Adults with clinical history of grass pollen induced seasonal allergic rhinoconjunctivitis | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SCIT / Standard treatment | 9 years | RCT 1 year follow up |
| Sample size | Outcome measure | Outcome discount rate |
| 306 | RQLQ mapped to EQ5D - QALYs | 0% |
| Cost data | Cost year / currency | Cost discount rate |
| Resource use collected in trial with national unit costs applied | 2005 / Euro | 3% |
| Results | | Sensitivity analysis |
| ICER in Euro per QALY Austria 9716; Denmark 2586; Finland 13683; Germany 10300; Netherlands 24519; Sweden 22675 | | One way deterministic analysis on costs described but results not reported |
| General comments | | |
| <ul style="list-style-type: none"> • Treatment effect observed in 1 year RCT assumed to persist through 3 years of treatment and 6 years following treatment discontinuation • Mapping from RQLQ to EQ5D applied to calculate QALYs not standard or validated | | |

Title: Economic evaluation of 5-grass pollen tablets versus placebo in the treatment of allergic rhinitis in adults

Author / Year: Ruggeri / 2013 (28)

Journal: Clinical Drug Investigation

| Type of economic analysis | Perspective | Countries |
|--|-----------------------|--|
| CUA | Health system | Italy |
| Study population | | |
| Patients with grass pollen induced allergic rhinitis | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT / Standard care | 4 years | Posthoc analysis of 2 RCTs |
| Sample size | Outcome measure | Outcome discount rate |
| ? | AAdSS mapped to QALYs | 3% |
| Cost data | Cost year / currency | Cost discount rate |
| SIMAP study updated to 2011 | 2011 / Euro | 3% |
| Results | | Sensitivity analysis |
| At low AAdSS SLIT is dominated by standard care | | PSA showed 99% probability ICER less than 30000 euros per QALY for medium and high AAdSS |
| At medium AAdSS ICER 1024 euros per QALY | | |
| At high AAdSS ICER 1035 euros per QALY | | |
| General comments | | |
| <ul style="list-style-type: none"> • Not clear how AAdSS is converted to QALYs • Cost and effectiveness estimates taken from different studies | | |

Title: Economic evaluation of SQ-standardized grass allergy immunotherapy tablet (GRAZAX) in children

Author / Year: Ronaldson / 2014 (27)

Journal: ClinicoEconomics and Outcomes Research

| Type of economic analysis | Perspective | Countries |
|---|--------------------------------|--|
| CUA | Health system | UK |
| Study population | | |
| 5-16 year olds with grass pollen induced rhinoconjunctivitis with or without asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT / Standard care | 9 years | RCT 1 year follow up |
| Sample size | Outcome measure | Outcome discount rate |
| 253 | Symptom scores mapped to QALYs | 3.5% |
| Cost data | Cost year / currency | Cost discount rate |
| RCT Patient diaries mapped to unit costs | 2008 / GBP | 3.5% |
| Results | | Sensitivity analysis |
| ICER £ 12 168 per QALY | | PSA showed 90% probability of SLIT being cost effective at £30000 per QALY threshold and 60% probability cost effective at £20000 per QALY threshold |
| General comments | | |
| <ul style="list-style-type: none"> • Mapping from symptom scores to QALYs not validated • Treatment effect observed in 1 year RCT assumed to persist through 3 years of treatment and 6 years following treatment discontinuation | | |

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

Author / Year: Bachert / 2007 (15)

Journal: Clinical and Experimental Allergy

| Type of economic analysis | Perspective | Countries |
|---|----------------------|--|
| CUA | Health system | UK, Germany, Netherlands, Sweden, Denmark, Norway, Finland |
| Study population | | |
| Patients with grass pollen induced rhinoconjunctivitis | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT / Standard care | 9 years | RCT 1 year follow up |
| Sample size | Outcome measure | Outcome discount rate |
| 493 | EQ5D - QALYs | 3 – 5% depending on country |
| Cost data | Cost year / currency | Cost discount rate |
| RCT patient diary mapped to country specific unit costs | 2005 / Euro | 3 – 5% depending on country |
| Results | | Sensitivity analysis |
| Cost per year of treatment must be below 2200 euros for SLIT to be cost effective at NICE threshold of £20000 per QALY | | NA |
| General comments | | |
| <ul style="list-style-type: none"> • Price of SLIT not given so ICERs not calculated, rather max price for SLIT to be cost effective calculated • Treatment effect observed in 1 year RCT assumed to persist through 3 years of treatment and 6 years following treatment discontinuation | | |

Title: Cost effectiveness analysis of immunotherapy in patients with grass pollen allergic rhinoconjunctivitis in Germany

Author / Year: Westerhout / 2012 (31)

Journal: Journal of Medical Economics

| Type of economic analysis | Perspective | Countries |
|--|----------------------|---|
| CUA | Health system | Germany |
| Study population | | |
| Patients with grass pollen induced rhinoconjunctivitis without asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT (OA) / SLIT (GRZ) / SCIT (ALD) / Standard care | 9 years | Meta-analysis |
| Sample size | Outcome measure | Outcome discount rate |
| NA | QALYs | 3% |
| Cost data | Cost year / currency | Cost discount rate |
| Survey data | 2011 / Euro | 3% |
| Results | | Sensitivity analysis |
| SLIT (OA) dominates SLIT (GRZ) and SCIT (ALD) | | PSA suggests 79% probability SLIT (OA) cost effective at a threshold of £20000 per QALY |
| ICER SLIT (OA) vs Standard care 14728 euros per QALY | | |
| General comments | | |
| <ul style="list-style-type: none"> • Treatment effect observed in 1 year RCT assumed to persist through 3 years of treatment and 6 years following treatment discontinuation • Resource use taken from external survey rather than measured in the underlying studies in meta analysis | | |

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

Author / Year: Berto / 2006 (16)

Journal: Annals of Allergy, Asthma and Immunology

| Type of economic analysis | Perspective | Countries |
|--|-----------------------------|--|
| CEA | Health system | Italy |
| Study population | | |
| Young adults with pollen induced rhinitis with or without allergic asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT / Standard care | 6 years | Retrospective non-random subset selected from clinical study |
| Sample size | Outcome measure | Outcome discount rate |
| 2000 | Number of patients improved | 0% |
| Cost data | Cost year / currency | Cost discount rate |
| Clinical records linked to unit costs | 2002 / Euro | 3% |
| Results | | Sensitivity analysis |
| SLIT is cost saving and more effective than standard care | | Deterministic one way exploration of hospital costs |
| General comments | | |
| <ul style="list-style-type: none"> Potential for selection bias as physicians asked to pick subsets of patients from clinical study for economic evaluation | | |

Title: A systematic review and economic evaluation of subcutaneous and sublingual allergen immunotherapy in adults and children with seasonal allergic rhinitis

Author / Year: Meadows / 2013 (21)

Journal: NIHR Health Technology Assessment

| Type of economic analysis | Perspective | Countries |
|--|-----------------------------|------------------------------|
| CUA | Societal | England |
| Study population | | |
| Patients with pollen induced allergic rhinitis with or without allergic asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT / SCIT / Standard care | 6 years | Meta analysis of RCTs |
| Sample size | Outcome measure | Outcome discount rate |
| NA | RQLQ mapped to EQ5D - QALYs | 3.5% |
| Cost data | Cost year / currency | Cost discount rate |
| Resource use from expert opinion with unit costs applied | 2011 / GBP | 3.5% |
| Results | | Sensitivity analysis |
| ICER SLIT vs standard care £37537 per QALY | | NA |
| ICER SCIT vs standard care £29579 per QALY | | |
| ICER SCIT vs SLIT £24404 per QALY | | |
| General comments | | |
| <ul style="list-style-type: none"> Mapping between RQLQ and EQ5D to calculate QALYs not validated | | |

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

Author / Year: Omnes / 2007 (22)

Journal: European Annals of Allergy and Clinical Immunology

| Type of economic analysis | Perspective | Countries |
|--|----------------------------------|------------------------------|
| CEA | Health system | France |
| Study population | | |
| Children over 5 and adults over 16 with dust mite or pollen induced allergic rhinitis | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT / SCIT/ Standard care | 7 years children; 6 years adults | Expert opinion |
| Sample size | Outcome measure | Outcome discount rate |
| NA | Asthma cases avoided | 0% |
| Cost data | Cost year / currency | Cost discount rate |
| Expert opinion | ? / Euro | 0% |
| Results | | Sensitivity analysis |
| ICER vs standard care children dust mite SLIT: 3938; SCIT: 583 ICER vs standard care children dust pollen SLIT: 824; SCIT: 597 ICER vs standard care adults dust mite SLIT: 3158; SCIT: 393 ICER vs standard care adults dust pollen SLIT: 1708; SCIT: 1327 All in Euros per asthma case avoided | | NA |
| General comments | | |
| <ul style="list-style-type: none"> Entire study seems to be based on expert opinion Does not compare treatment with SLIT against SCIT incrementally | | |

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

Author / Year: Bruggenjurgen / 2008 (17)

Journal: Annals of Allergy, Asthma & Immunology

| Type of economic analysis | Perspective | Countries |
|---|-----------------------------|---|
| CUA | Health system | Germany |
| Study population | | |
| Patients with pollen or mite induced allergic rhinitis with or without asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SCIT / Standard care | 15 years | Published study |
| Sample size | Outcome measure | Outcome discount rate |
| NA | QALYs | 3% |
| Cost data | Cost year / currency | Cost discount rate |
| Published study | ? / Euro | 3% |
| Results | | Sensitivity analysis |
| ICER SCIT vs standard care 8308 euros per QALY | | One way deterministic exploration of alternative treatment durations and discount rates |
| General comments | | |
| <ul style="list-style-type: none"> Difficult to assess the validity of cost or utility data as very little detail of studies that this analysis is based on given in the paper | | |

Title: Sublingual or subcutaneous immunotherapy for seasonal allergic rhinitis: an indirect analysis of efficacy, safety and cost

Author / Year: Dranitsaris / 2014 (19)

Journal: Journal of Evaluation in Clinical Practice

| Type of economic analysis | Perspective | Countries |
|--|-----------------------------|--------------------------|
| CEA | Health system | Canada |
| Study population | | |
| Patients with grass induced allergic rhinitis with or without asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SCIT / SLIT (GRX) / SLIT (OA) / Standard care | 1 year | Meta analysis of 20 RCTs |
| Sample size | Outcome measure | Outcome discount rate |
| NA | Symptom control | 0% |
| Cost data | Cost year / currency | Cost discount rate |
| Expert opinion | 2012 / CAD | 0% |
| Results | Sensitivity analysis | |
| SCIT, SLIT(GRX) and SLIT (OA) had similar efficacy in terms of symptom control. Cost of SCIT = 946 CAD; Cost of SLIT (GRX) = 2122 CAD; Cost of SLIT (OA) = 844 SLIT (OA) is as effective as SLIT (GRX) and SCIT but cheaper over 1 year | NA | |
| General comments | | |
| <ul style="list-style-type: none"> Unclear what the allergic rhinitis symptom score represents and if it was comparable between studies Unclear about how much of the cost data was expert opinion as opposed to data from the meta analysis | | |

Title: Cost-effectiveness of grass pollen SCIT compared with SLIT and symptomatic treatment

Author / Year: Reinhold / 2016 (26)

Journal: Allergo Journal International

| Type of economic analysis | Perspective | Countries |
|---|--|-----------------------|
| CEA | Health insurer | Germany |
| Study population | | |
| 29 year old patients with seasonal grass-allergic rhinoconjunctivitis and no asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT (OA) vs SCIT (Allergovit) vs symptomatic treatment | 9 years | RCT |
| Sample size | Outcome measure | Outcome discount rate |
| ? | Utility mapped to QALY | 3% |
| Cost data | Cost year / currency | Cost discount rate |
| Administrative data | 2013/euro | 3% |
| Results | Sensitivity analysis | |
| SCIT dominates SLIT and has an ICER of 11 000 euros per QALY against symptomatic treatment | Probabilistic and deterministic sensitivity analysis conducted | |
| General comments | | |
| <ul style="list-style-type: none"> This is a model based analysis that incorporates multiple different datasets and explores a number of different assumptions in sensitivity analysis Unexplored assumption that 3 years of treatment give continued constant treatment effect for 9 years | | |

Title: Health economic comparison of SLIT allergen and SCIT allergoid immunotherapy in patients with seasonal grass-allergic rhinoconjunctivitis in Germany

Author / Year: Verheggen / 2015 (30)

Journal: Clinical and Translational Allergy

| Type of economic analysis | Perspective | Countries |
|--|---|---|
| CEA | Payer's perspective | Germany |
| Study population | | |
| 29 year old patients with seasonal grass-allergic rhinoconjunctivitis and no asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT vs blended mix of current SCIT treatments | 9 years | RCT |
| Sample size | Outcome measure | Outcome discount rate |
| ? | QALYs mapped from Rhinitis Symptom Utility Index (RSUI) | 3% |
| Cost data | Cost year / currency | Cost discount rate |
| Administrative data | 2013/euros | 3% |
| Results | | Sensitivity analysis |
| ICER of SLIT vs SCIT is 12,593 euro per QALY with a probability of being cost effective at 20,000 euro per QALY of 76% | | Probabilistic and deterministic sensitivity analysis as well as scenario analysis performed |
| General comments | | |
| <ul style="list-style-type: none"> • This is a model based analysis that incorporates multiple different datasets and explores a number of different assumptions in sensitivity analysis • Comparator is a mix of SCIT treatments rather than one specific treatment • Unexplored assumption that 3 years of treatment give continued constant treatment effect for 9 years | | |

Data extraction of Asthma studies

Title: Influence of subcutaneous specific immunotherapy on drug costs in children suffering from allergic asthma

Author / Year: Reinhold / 2013 (32)

Journal: Clinical and Translational Allergy

| Type of economic analysis | Perspective | Countries |
|--|--------------------------------|--|
| CEA | Health system | Germany |
| Study population | | |
| Children and adolescents with mite induced allergic asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SCIT / Standard Care | 3 years | RCT 3 year mean follow up |
| Sample size | Outcome measure | Outcome discount rate |
| 65 | Mean morning peak flow (l/min) | 0% |
| Cost data | Cost year / currency | Cost discount rate |
| RCT – patient diary | 2009 / Euro | 0% |
| Results | | Sensitivity analysis |
| ICER: 11 Euros per l/min mean morning peak flow | | Bootstrapping performed but not used in cost effectiveness results |
| General comments | | |
| <ul style="list-style-type: none"> • No hospital costs included • 5 SCIT and 1 non-SCIT patients excluded because of “outlier” levels of costs | | |

Data extraction of Asthma and Rhinitis studies

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

Author / Year: Nasser / 2008 (14)

Journal: Allergy

| Type of economic analysis | Perspective | Countries |
|--|----------------------|---|
| CUA | Health system | UK |
| Study population | | |
| Patients suffering from grass pollen induced rhinoconjunctivitis co-existing with asthma | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT (Grazax) / Standard Care | 9 years | RCT 1 year follow up |
| Sample size | Outcome measure | Outcome discount rate |
| 151 | EQ5D - QALYs | 3.5% |
| Cost data | Cost year / currency | Cost discount rate |
| RCT patient diary linked to unit costs | 2005 / GBP | 3.5% |
| Results | | Sensitivity analysis |
| ICER £8816 per QALY | | One way sensitivity analysis to explore impact of changing time horizon |
| General comments | | |
| <ul style="list-style-type: none"> • results based on patients in UK, Germany, the Netherlands, Denmark, Sweden, Spain, Austria and Italy • treatment effect assumed to persist through 3 years of treatment and 6 years following treatment discontinuation | | |

Title: Economic evaluation of sublingual immunotherapy vs symptomatic treatment in allergic asthma

Author / Year: Ariano / 2009 (13)

Journal: Annals of Allergy, Asthma & Immunology

| Type of economic analysis | Perspective | Countries |
|--|----------------------|-----------------------------|
| CEA | Health system | Italy |
| Study population | | |
| Patients with dust mite induced allergic asthma and rhinitis | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| SLIT / Standard Care | 5 years | RCT 5 year follow up |
| Sample size | Outcome measure | Outcome discount rate |
| 70 | VAS symptom score | 0% |
| Cost data | Cost year / currency | Cost discount rate |
| RCT patient diary and unit costs | ? / Euros | 0% |
| Results | | Sensitivity analysis |
| Overall costs lower in SLIT patients and lower symptom score | | NA |
| General comments | | |
| <ul style="list-style-type: none"> • very little detail provided of the analysis performed • no real economic analysis or interpretation of the results provided | | |

Data extraction of Insect Venom Allergy study

Title: A systematic review of the clinical effectiveness and cost-effectiveness of Pharmedin® for the treatment of bee and wasp venom allergy

Author / Year: Hockenhull / 2012 (33)

Journal: NIHR HTA

| Type of economic analysis | Perspective | Countries |
|---|---|--|
| CUA | Health System | England |
| Study population | | |
| General population as well as high risk of sting subset of population | | |
| Intervention / Comparator | Time horizon | Effectiveness data |
| PhVIT + HAD + AAI / HAD + AAI / avoidance advice only | 10 years | Subset of RCT and survey data |
| Sample size | Outcome measure | Outcome discount rate |
| 337 | Systemic reaction or death following sting converted to QALYs | 3.5% |
| Cost data | Cost year / currency | Cost discount rate |
| Administrative data and reference costs | ? / GBP | 3.5% |
| Results | | Sensitivity analysis |
| PhVIT + HAD + AAI is cost saving and more effective when compared to either HAD + AAI or avoidance advice only for patients likely to be stung more than five times a year. In the general population the ICER for PhVIT + HAD + AAI against HAD + AAI is > £ 18 million per QALY and against avoidance advice only is > £ 7.6 million | | Extensive sensitivity analysis on wide range of model parameters |
| General comments | | |
| <ul style="list-style-type: none"> • Very little data available to base the model on • Extensive use of sensitivity and scenario analysis to explore all plausible assumption and demonstrate the robustness of the findings | | |

APPENDIX 2: PRISMA CHECKLIST

| Section/topic | # | Checklist item | Reported on page # |
|------------------------------------|----|---|--------------------|
| TITLE | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 147 |
| ABSTRACT | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 149 |
| INTRODUCTION | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 150 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 150 |
| METHODS | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 151 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 150 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 150 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 150 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 150 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 150 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 150 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 150 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 150-1 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis. | 150-1 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 150 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A |

| Section/topic | # | Checklist item | Reported on page # |
|-------------------------------|----|--|--------------------|
| RESULTS | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 151 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | Table 1, 163-5 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Table2a-e 163-5 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 163-5 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | N/A |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | Table 2 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A |
| DISCUSSION | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 165 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 165 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 166 |
| FUNDING | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 166 |

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.