Disclosure

In relation to this presentation, I declare the following, real or perceived conflicts of interest:

<table>
<thead>
<tr>
<th>Type</th>
<th>Company</th>
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</thead>
<tbody>
<tr>
<td>Employment full time / part time</td>
<td>None</td>
</tr>
<tr>
<td>Research Grant (P.I., collaborator or consultant; pending and received grants)</td>
<td>Mylan</td>
</tr>
<tr>
<td>Other research support</td>
<td>Mylan</td>
</tr>
<tr>
<td>Speakers Bureau / Honoraria</td>
<td>Mylan, Novartis, Sanofi, Teva, Uriach</td>
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<tr>
<td>Ownership interest (stock, stock-options, patent or intellectual property)</td>
<td>Kyomed</td>
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<tr>
<td>Consultant / advisory board</td>
<td>Mylan, Novartis, Sanofi, Teva, Uriach</td>
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A conflict of interest is any situation in which a speaker or immediate family members have interests, and those may cause a conflict with the current presentation. Conflicts of interest do not preclude the delivery of the talk, but should be explicitly declared. These may include financial interests (e.g., owning stocks of a related company, having received honoraria, consultancy fees), research interests (research support by grants or otherwise), organisational interests and gifts.
Next-generation care pathways

1- ICPs in real life

2- The cell phone (The Allergy Diary)

3- Innovation in epidemiology

4- Innovation in management

5- Next-generation care pathways
Next-generation care pathways

1- ICPs in real life
ICPs differ from practice guidelines as

- they are utilized by a **multidisciplinary team**
- have a focus on the quality and co-ordination of care
- ICPs need to have a mechanism for recording **variations/deviations** from planned care
- An ICP is intended to act as a guide to treatment. Clinicians are free to exercise their own professional judgments as appropriate. However, **any alteration to the practice identified within this ICP must be noted as a variance**
- The resulting analysis can be used to **amend the ICP itself** if, for the majority of patients, the practice is different to the pathway
Any alteration to the practice identified with the guideline or ICP must be noted as a variance.

- **ARIA classification**: severity (mild vs moderate/severe) is linked with quality of life (RQLQ)

- **ARIA classification**:
  - Persistence is not associated with RQLQ
  - Persistence is associated with prediction of efficacy
  - Persistence is associated with duration of treatment
  - Persistence is associated with asthma comorbidity

- **Most patients consulting in primary or secondary care**
  - Have moderate/severe disease
  - Receive ICS + antihistamines
ARIA 2016: Care pathways implementing emerging technologies for predictive medicine in rhinitis and asthma across the life cycle

Stepwise care pathways

Integrated care pathways for airway diseases (AIRWAYS-ICPs)

European Innovation Partnership on Active and Healthy Ageing, Action Plan B3 Mechanisms of the Development of Allergy (MedALL, WP10)

GARD (Global Alliance against Chronic Respiratory Diseases, WHO) research demonstration project

Self-care

Patient with rhinitis symptoms

Pharmacist

Incorrect diagnosis

Severity

Improvement

OTC medication

Failure

Check For asthma

YES

General practitioner

Incorrect diagnosis

Severity

Treatment

Improvement

Failure

Specialist

Emergency care (asthma)

Improvement

Failure
MASK mHealth approach for ICPs

Patient with allergic rhinitis symptoms

Goals
1. Develop for each step an mHealth tool
2. cell phone for self-care
3. interoperable tablet for pharmacists and physicians
4. Physicians’s questionnaire
5. Patient’s personal data with maintained privacy (GPDR)
Next-generation care pathways

1- ICPs in real life

2- The cell phone (The Allergy Diary)
The finger approach to manage allergic rhinitis
The Allergy Diary was developed in collaboration between MACVIA-LR and ARIA.

MACVIA-LR (Contre les Maladies Chroniques pour un Vieillissement Actif en Languedoc-Roussillon, France) is a reference site of the European Innovation Partnership on Active and Healthy Ageing aimed at fighting chronic disease.

The ARIA (Allergic Rhinitis and its Impact on Asthma) initiative aims to educate and implement evidenced-based management of allergic rhinitis in conjunction with asthma.

Free on Android and IOS
The General Data Protection Regulation (GDPR), the Data Protection Law Enforcement Directive and other rules concerning the protection of personal data.
Geolocation with respect to personal privacy for the Allergy Diary app - a MASK study


k-anonymity
CHRODIS criteria applied to the MASK (MACVIA-ARIA Sentinel NetworK) Good Practice in allergic rhinitis: a SUNFRAIL report

1- Data storage
   • Crypted transfer of data from user’s smartphone to database
   • Secure database—with restricted access—to store data in E.U. (no transfer outside EU)

2- Data transfer
   • Post treatment of geolocation data to follow GDPR in respect of users' privacy
   • Transfer of data only when protocol detailing analyses is signed
   • Data freely available for MASK participants (per country), fee for others

3- Data analysis
   • Epidemiologic data
   • Assessment of treatment efficacy and adherence
   • Pharmaco-economic impact of allergic diseases (including EQ-5D and work)

4- Integration of data
   • Integrated print process from user's smartphone to user or physician’s PC
   • Interoperability of data exported into medical databases: linking to patient’s record
   • Possible integration to contextual data (e.g.: pollution data)
Next-generation care pathways

1- ICPs in real life

2- The cell phone

3- Innovation in epidemiology (research)
Correlation between global and nasal VAS

N = 41,872 days
R = 0.87
N = 16,925 days
20 countries
15 languages

Global VAS: $r=0.82$
Rhinitis: $r=0.77$
Conjunctivitis: $r=0.69$
Asthma: $r=0.60$
Patterns of allergic symptom days (VAS 0-100)

VAS asthma

N= 32,095 days
Rho=0.50
Patterns of allergic symptom days (VAS 0-100)

VAS asthma

A or C Low-R Low
A or C High-R Low
A or C Low-R High
A or C High-R High

N= 32,095 days
Rho=0.50
Patterns of allergic symptom *days* (VAS 0-100)

### VAS asthma

N = 32,095 days  
Rho = 0.50

### VAS eye

N = 32,585 days  
Rho = 0.63
Novel patterns of multimorbidity

Visual Analogue Scale levels depending on allergic multimorbidities

High: VAS ≥50/100

<table>
<thead>
<tr>
<th></th>
<th>VAS Nose</th>
<th>VAS Eye</th>
<th>VAS Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinitis</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>High</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>High</td>
<td></td>
<td>High</td>
</tr>
</tbody>
</table>

Median (25-75th percentile) level:

- Rhinitis: High
- Conjunctivitis: High
- Asthma: High
Allergic multimorbidity MORE COMPLEX than one airway-one disease

Eye symptoms are part of the multimorbidity

The number of diseases is important to consider

Non-allergic multimorbidity is another important component
REVIEW ARTICLE

MeDALL (Mechanisms of the Development of ALLergy): an integrated approach from phenotypes to systems medicine


MeDALL is a collaborative project supported by the European Commission under the Health Cooperation Work Programme of the 7th Framework programme.
# MeDALL novel phenotypes

Garcia-Aymeric et al, Allergy 2015

<table>
<thead>
<tr>
<th></th>
<th>4 years</th>
<th>8 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>Wheezing ever</td>
<td>n=12502 (70%)</td>
<td>n=5157 (30%)</td>
</tr>
<tr>
<td>Wheezing attacks last 12m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wheezing after exercise ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma treatment last 12m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma onset before 2y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchitis/bronchiolitis ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough at night ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sneezing or blocked nose ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sneezing or blocked nose last 12m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itchy watery eyes last 12m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergic rhinitis ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rhinitis onset before 2y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itchy rash ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itchy rash last 12m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itchy rash affecting common areas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itchy rash onset before 2y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eczema ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urticaria ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Food allergy ever</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive to specific IgE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Phenotypes in epidemiologic studies

Boudier, Siroux, Bousquet

Distribution of sensib_respi by Phenotypes

N=840
MeDALL chip
176 allergens
64 allergens > 1%
Phenotypes in epidemiologic studies

N=840
MeDALL chip
176 allergens
64 allergens > 1%

Boudier, Siroux, Bousquet

Portuguese national cohort  Amaral et al
Allergic multi-morbidity is associated with an increased risk of asthma in adults: a population-based case control study

Sanna Toppila-Salmiⁱ,², Sebastien Chanoine³,⁴,⁵ Jussi Karjalainen⁶, Juha Pekkanen⁷,⁸, Jean Bousquet⁹, Valérie Siroux²

Figure 2. Adjusted OR and 95% CI of association between allergic disease(s) with adult onset asthma, according to age groups and the number of allergic diseases. OR values were estimated by conditional logistic regression,
Allergic multimorbidity MORE COMPLEX than one airway-one disease

Eye symptoms are part of the multimorbidity

The number of diseases is important to consider

ICPs will need to consider multimorbidity
Next-generation care pathways

1- ICPs in real life

2- The cell phone

3- Innovation in epidemiology

4- Innovation in management
Limitations of mobile technology studies

- Users self-identified as having AR without confirmation of diagnosis
- No information except age, sex, country, location (Privacy)
- Mobile app users are not representative of the general population
- Adherence is difficult to analyze,
- Users may not report all medications used
- Longitudinal data capture is very challenging:
  - Treatment trajectories are specific for almost each user
  - Most users have gaps in treatment days when they are well-controlled
  - Cross-sectional analysis of days may be performed instead
Adherence to treatment

Bousquet J et al, 2018

N=2850

Adherence:
- ≥ 5 days of VAS reporting
- regular use (70%)
- 70% same treatment

% utilisateurs
Adherence to treatment
Bousquet J et al, 2018

N=2850

Adherence:
- ≥ 5 days of VAS reporting
- regular use (70%)
- 70% same treatment

% utilisateurs

Treatment days

1 to 4
5 to 7
8 to 14
15 to 30

Nonadherent Discontinuous Adherent

Number of treatments reported

1 2 3 ≥4

5 to 7 8 to 14 15 to 30 days

AUTO-MEDICATION
Adherence to treatment

Menditto et al, submitted

- Proportion of medication possession ratio (modified MPR): ratio of days medication reported to days in a given time interval
- Proportion of days covered over a time interval (modified PDC): ratio of days medication reported to days in the time interval between the first and the last record considered
Medical prescriptions (ARIA members)

- % physicians
- N = 201

- mild
- moderate/severe pollen
- moderate/severe indoor

- ≥ 2 weeks
- allergic season
Letters

The allergic allergist behaves like a patient

Responses Obtained during the Meeting

- Total number of respondents to a generic questionnaire on allergy: 248
- Number of respondents answering the question: “How many of you have allergic rhinitis?”: 102
- Number of respondents answering the question: “How many of you use a regular medication during the entire pollen season?”: 0
Medical prescriptions (ARIA members)

There is a major disconnection between physicians’ prescriptions and patients’ behavior.

Guidelines are not used by patients.

Allergic physicians behave like patients.
## Treatments received in MAST

**Bousquet J et al, Allergy 2018**

<table>
<thead>
<tr>
<th>Days</th>
<th>N= 1628</th>
<th>N= 1252</th>
<th>N= 1368</th>
<th>N= 1102</th>
<th>N= 1293</th>
</tr>
</thead>
</table>

**Graph**: The graph shows the VAS level (median, 25-75) for different treatments. The treatments include monotherapy and co-medication. The data points are represented by bars, with error bars indicating the variability. The untreated days are highlighted with a blue box.
Treatments received in MASK
Bousquet J et al, Allergy 2018

Days
N= 1628  N= 1252  N= 1368  N= 1102  N= 1293
• When patients are well they do not take a medication
• They increase their medications to be controlled
• But some patients cannot be controlled
• These observations do not accord with guidelines
Next-generation care pathways

1- ICPs in real life
2- The cell phone
3- Innovation in epidemiology
4- Innovation in management
5- Next-generation care pathways
Next-generation integrated care pathways for allergic rhinitis and asthma multi-morbidity

A model for non-communicable diseases

POLLAR (eit Health)
GARD demonstration project (WHO Alliance)
ARIA-Euforea-Ga2len 2019

ACAAI
EAACI
EFA
ERS
ERS (Rhinology)
IPCRG
POLLAR
EHH
RNSA and MedUni Vienna

RSCN of the European Innovation Partnership on Active and Healthy Ageing

az WAO
Patient with rhinitis symptoms

Self-care

Pharmacist

Incorrect diagnosis
Severity
OTC medication
Improvement
Failure
Check For asthma
YES

General practitioner

Incorrect diagnosis
Severity
Treatment
Improvement
Failure

Specialist

Emergency care (asthma)

Patient participation, health literacy and self-care through technology assisted ‘patient activation’

ARIA in the pharmacy

Next-generation ARIA-WAO guidelines

Goals

1. Develop for each step a document with a 4-pages pocket-guide
2. Include mHealth for each step
3. From one step to the next one
4. When to go to the next step
5. Stepwise approach for management
6. Develop machine learning to optimize ICPs
Transfer of data to HCP

**Goals**

1. Patient’s personal data with privacy
2. The patient cannot send to the HCP any electronic form
3. The patient can show his/her data

*By Bousquet et al, Allergy 2018*
Embedding environment in next-generation ICPs

**Goals**
1. Embedding environmental data
2. Prevention of symptoms and asthma (self-care)
3. Assess if severity of symptoms is associated with allergens or pollution
4. Predict emergency care visits
5. Develop machine learning to optimize ICPs
• MASK (Mobile Airways Sentinel Network) has been selected by DG SANTE as a Good Practice in the field of **digitally-enabled, integrated, person-centred care**.

• In the context of implementing the **Communication on the digital transformation of health and care**, specifically in relation to chapter 5 – "digital tools for citizen empowerment and for person-centred care", DG SANTE supports the scaling-up and wider implementation of good practices.

• DG SANTE in collaboration with the Commission's Joint Research Centre will organise a "marketplace" workshop with The Joint Research Centre in Ispra. for representatives from Member States and other countries participating in the 3rd Health Programme to **learn more about a selected number (12) of good practices and key policy initiatives** in the domain of digitally-enabled, integrated, person-centred care, with a view to **possible transfer and replication** of the presented practices.
The Airways Diary (with COPD)

- IPAG questionnaire
- Daily evaluation
  - VAS Dyspnea
  - VAS Exercise
  - Pulmonary function

Multimorbidity App

- For diagnosed disease NOT for screening
- Based on The Airways Diary
- Diseases: those commonly associated with COPD
- User with a diagnosis of the disease
- Simple questionnaire for the diagnosis of the disease
- Risk factors
- Daily evaluation
  - Most important symptom
  - Objective measurements

Home services

- Alert system
- Pilot study completed
- Major clinical alerts
- Clinical alerts
- Social alerts

Pilot study in 500 patients completed