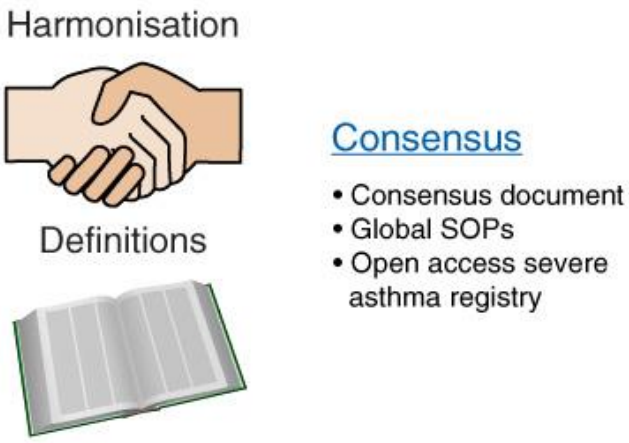
UBIOPRED: Objectives

The project has the following objectives:

- 1) Generating consensus and global standard operating procedures (SOPs)
- 2) Creating adult/paediatric cohorts and biobanks
- 3) Generating phenotype “handprints”
- 4) Validating phenotype “handprints”
- 5) Refining phenotype “handprints” with pre-clinical and human exacerbation models
- 6) Predicting efficacy of intervention
- 7) Refining diagnostic criteria and phenotypes
- 8) Establishing a platform for exchange, education and dissemination

1) Generating consensus and global standard operating procedures (SOPs)



Consensus on diagnostic criteria, clinical subphenotyping and disease outcome measures will be generated during an early consensus meeting. Input to this will be the collective expertise of members of the consortium who are founders/key centres of the major global networks of severe asthma (ENFUMOSA, BIOAIR, GA2LEN, GABRIEL, BTS Severe Asthma, MRC Southampton Severe Asthma and NIH-SARP).

U-BIOPRED is supported by patient organisations, has confirmed EMEA representation on its strategic advisory board and is formally linked to NIH-SARP for global harmonisation. WHO will be involved in the full consensus process. U-BIOPRED SOPs will be derived and extended from the detailed NIH-SARP SOPs.

2) Creating adult/paediatric cohorts and biobanks

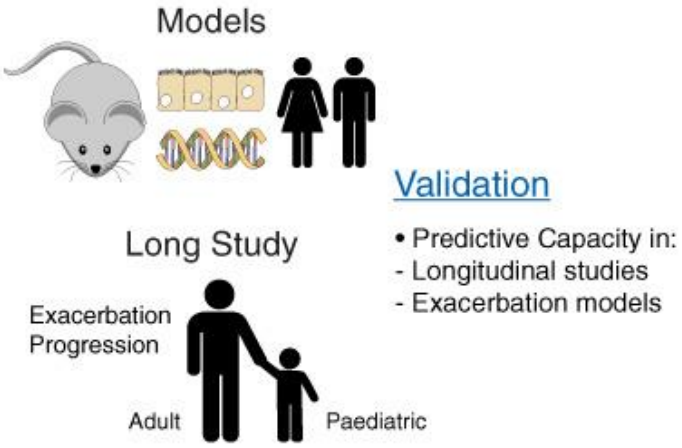
Large adult and paediatric patient registries will be created for cross-sectional and longitudinal cohort studies in well-characterised severe asthmatics and controls (subjects without lung disease, mild asthmatics and COPD patients). This effort will draw upon the considerable experience from past cohorts, such as ENFUMOSA, BIOAIR, the UK and MRC severe asthma cohorts, and the Dutch PARAPLU cohort.

The registries will be available for future studies and will contain standardised protocols and operating procedures for patient-reported outcomes (PRO), physiological measurements, imaging, histology of lower and upper airways, sputum, exhaled breath volatiles, and blood markers, resulting in a high-quality biobank and data suitable for state-of-the-art high-dimensional analyses. Strict quality assurance will be part of all protocols.

3) Generating phenotype "handprints"

An unbiased and innovative systems biology strategy will be used for classifying patients into distinct severe asthma phenotypes. High-dimensional analyses will be integrated into a "handprint" of biomarkers that will be derived from staged sifting of molecular ('omics'), histological, clinical and PRO data. This is a step-change in severe asthma phenotyping, aimed at accelerating discovery of novel diagnostic and therapeutic targets.

4) Validating phenotype "handprints"



The accuracy of the generated handprints to identify severe asthma phenotypes will be validated, using the international guidelines for the evaluation of medical tests (STARD), and their prognostic and predictive ability with regard to:

a) disease progression
b) level of baseline control
c) onset/severity of exacerbations

5) Refining phenotype "handprints" with pre-clinical and human exacerbation models

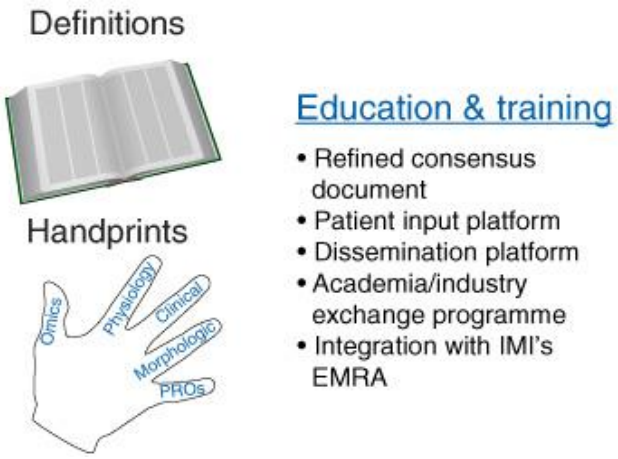
By using an iterative process the handprints will be refined with:
a) pre-clinical animal and in vitro human models in academia and industry
b) human experimental in vivo models of exacerbations and loss of control (rhinovirus inoculation in mild asthma).

This will deliver predictive disease models for drug development.

6) Predicting efficacy of intervention

The handprints will be applied in the prediction of targets relevant to responses to gold-standard and experimental therapeutic interventions in randomised controlled trials using systemic steroids and two proof-of-concept new medicines. This will enable targeting of interventions to well-defined sub-populations of severe asthma, thereby overcoming pre-competitive drug development bottlenecks originating from an inability to predict drug efficacy and to help understand the responder/non-responder therapeutic conundrum.

7) Refining diagnostic criteria and phenotypes



By incorporating the newly established handprints, the criteria for defining, diagnosing and phenotyping severe asthma will be refined. This will enable focused drug development and faster delivery of proof of concept for novel drugs. It will require a renewed, adjusted consensus when finalising the project.

8) Establishing a platform for exchange, education and dissemination

U-BIOPRED will build platforms for professionals (clinicians, scientists, industry, regulators, ERS/ATS and EU), for patients (patient organisations, EFA), and for the public (ELF). All stakeholders can provide input on current and future directions of the consortium and to assist in disseminating findings. The platform will co-ordinate academic-industrial exchange of personnel, also in clinical setting, integrated with IMI's EMRA. The (established) patient platform will be expanded to serve dissemination. The platforms will be established by workshops and supported by a web environment.