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# XXVIII CONGRESSO NAZIONALE SIMRI

*Il respiro: scienza e terapia per la salute del bambino*



Torino, 10-12 ottobre 2024



UNIVERSITÀ DI PAVIA



Fondazione IRCCS  
Policlinico San Matteo

Sistema Socio Sanitario



Regione  
Lombardia

# Asma e AI

**Amelia Licari**

Università di Pavia  
Fondazione IRCCS Policlinico San Matteo

ORIGINALE NETFLIX

# DAREDEVIL

★★★★★ 2016 2 Stagioni **ULTRA HD 4K** 5.1

Privato della vista da bambino, Matt Murdock combatte le ingiustizie come rispettabile avvocato di giorno e nei panni del supereroe Daredevil la notte a Hell's Kitchen.

Charlie Cox, Deborah Ann Woll, Elden Henson  
Serie TV, Serie TV crime, Azione e avventura TV

I più visti su Netflix

Visti di recente

# Meet your DJ

Spotify



# ***AI = Artificial Intelligence***

Ramo della tecnologia che consente ai computer e alle macchine di svolgere **compiti** che normalmente richiederebbero l'intelligenza umana:

- Riconoscimento di immagini
- Comprensione e risposta al linguaggio naturale
- Risoluzione di problemi
- Apprendimento da esperienze passate

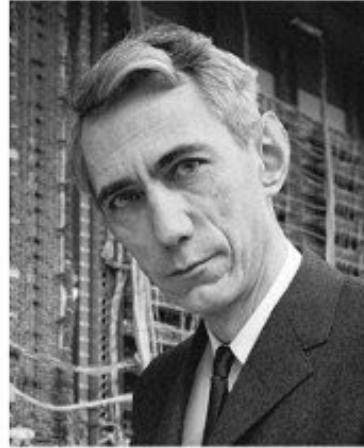
# 1956 Dartmouth Conference: The Founding Fathers of AI



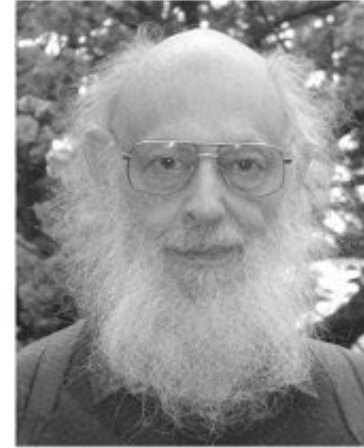
**John MacCarthy**



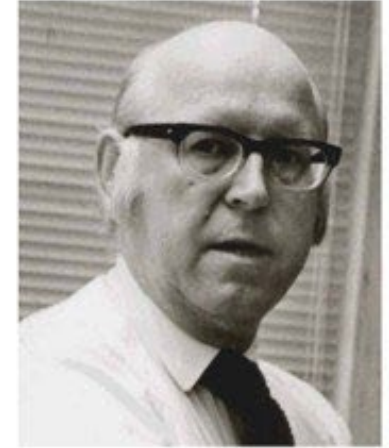
**Marvin Minsky**



**Claude Shannon**



**Ray Solomonoff**



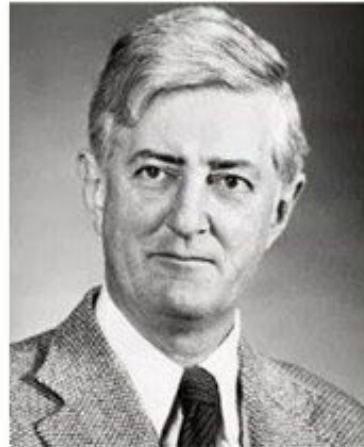
**Alan Newell**



**Herbert Simon**



**Arthur Samuel**



**Oliver Selfridge**



**Nathaniel Rochester**



**Trenchard More**



**John MacCarthy**

A PROPOSAL FOR THE  
DARTMOUTH SUMMER RESEARCH PROJECT  
ON ARTIFICIAL INTELLIGENCE

J. McCarthy, Dartmouth College  
M. L. Minsky, Harvard University  
N. Rochester, I. B. M. Corporation  
C. E. Shannon, Bell Telephone Laboratories



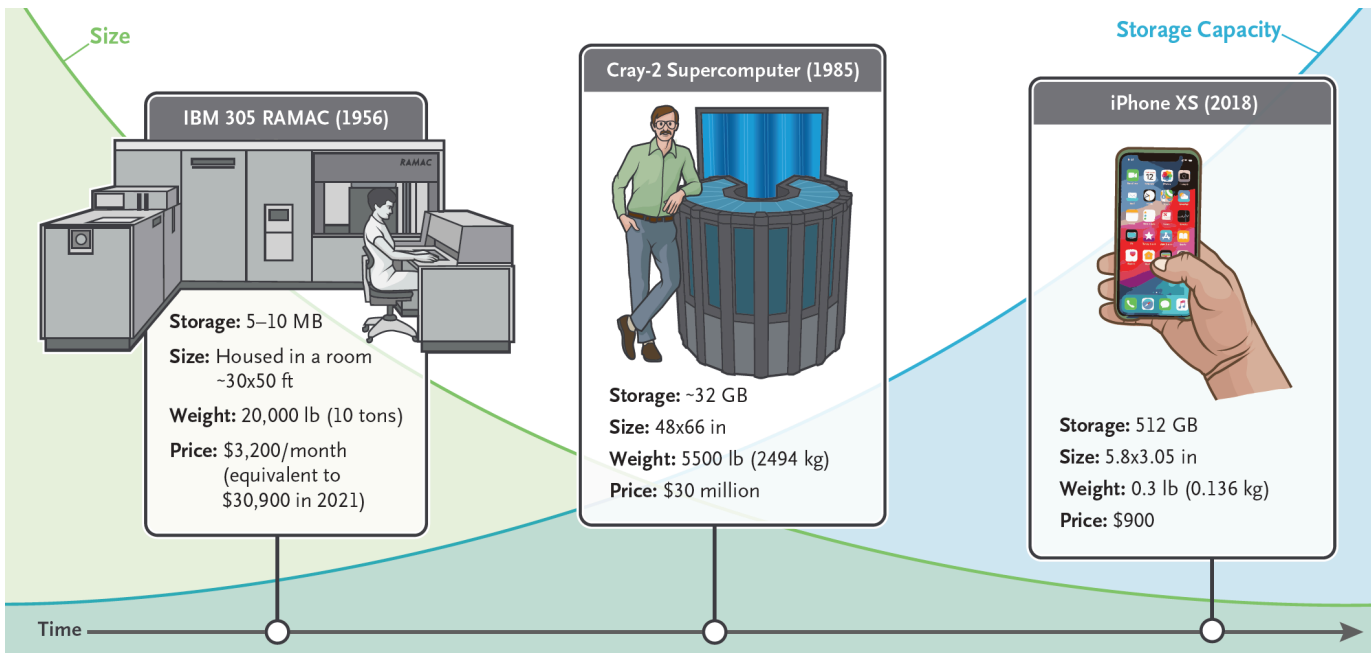
*Dartmouth University*

Aree di studio chiave:

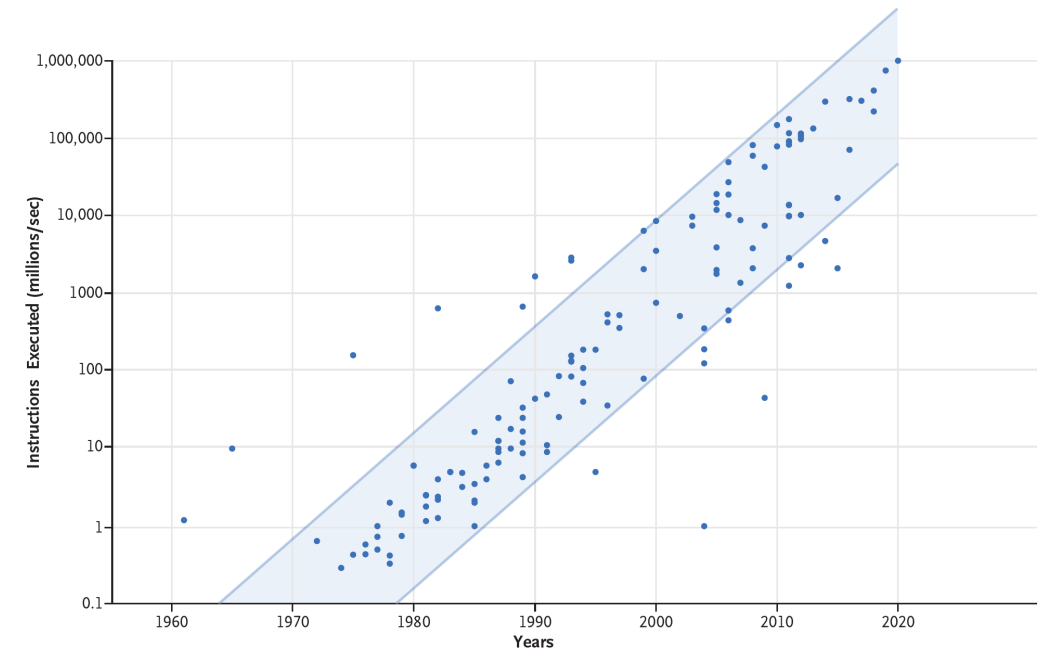
- Automazione dell'apprendimento e della risoluzione di problemi attraverso algoritmi
- Formalizzazione del linguaggio, della comprensione e della logica
- Progettazione di macchine che imitassero il ragionamento umano e la manipolazione dei simboli

# Improvements over 50 Years in the Ability of Computers to Store and Process Data

## Storage capacity



## Speed



# L'Intelligenza Artificiale IMPARA

La parte più importante degli algoritmi di AI sono i DATI utilizzati per il loro sviluppo

E' molto importante tendere alla combinazione di GRANDI QUANTITÀ di dati che siano ETEROGENEI E RAPPRESENTATIVI

I sistemi di AI dovrebbero essere CONTINUAMENTE AGGIORNATI con un flusso continuo di dati perché producano risultati accurati

L'AI è una tecnica adatta a gestire informazioni MULTIMODALI (es. immagini diagnostiche, dati genetici e informazioni cliniche) per la predizione di un singolo esito

# Beyond the Wow Factor: Artificial Intelligence in Pediatrics

April 19, 2023 [Katie Brind'Amour, PhD, MS, CHES](#)



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## AI in Medicine



Artificial Intelligence (AI) has tremendous potential to advance clinical practice and the delivery of patient care. A new Review article series, "AI in Medicine," explores the role of AI technology in clinical medicine and digital health, and examines the promise and pitfalls of its application across the health care continuum.

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**Editorial** | Artificial Intelligence and Pediatric Care

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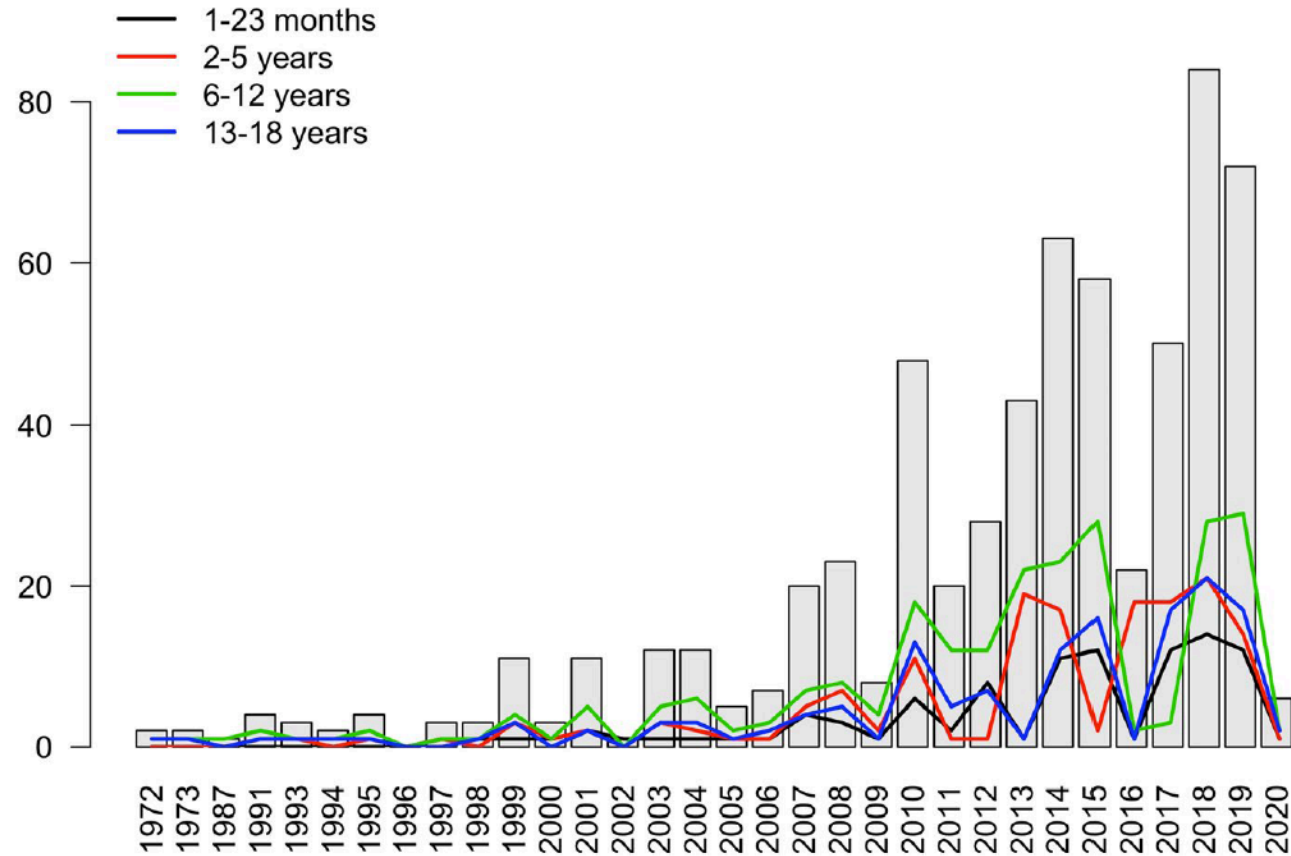
More ▾

July 17, 2023





# Call for Papers on Artificial Intelligence Applied to Pediatric Care

# Artificial intelligence in the diagnosis of pediatric allergic diseases

Giuliana Ferrante<sup>1</sup>  | Amelia Licari<sup>2</sup>  | Salvatore Fasola<sup>3</sup>  | Gian Luigi Marseglia<sup>2</sup>  |  
Stefania La Grutta<sup>3</sup> 



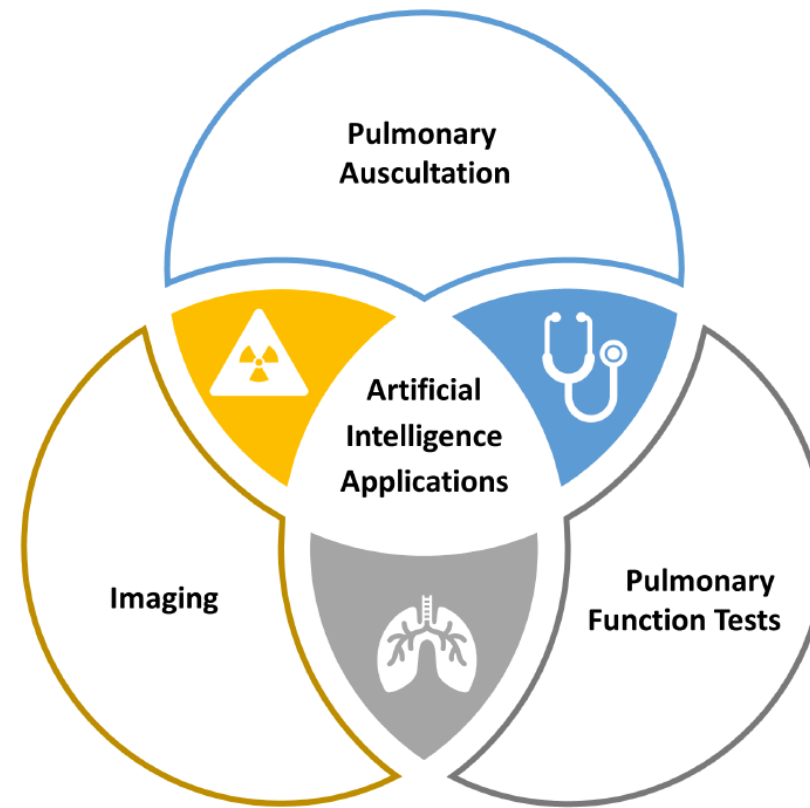
## Artificial intelligence as an emerging diagnostic approach in paediatric pulmonology

Giuliana Ferrante, MD, PhD,<sup>1,2\*</sup>  Amelia Licari, MD,<sup>3\*</sup>   
Gian Luigi Marseglia, MD<sup>3</sup>  and  
Stefania La Grutta, MD, PhD<sup>1,2</sup> 

<sup>1</sup>Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialities "G. D'Alessandro", University of Palermo, Palermo, Italy;

<sup>2</sup>Institute for Biomedical Research and Innovation (IRIB), National Research Council (CNR), Palermo, Italy;

<sup>3</sup>Pediatric Clinic, Department of Clinical, Surgical, Diagnostic and Pediatric Sciences, Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy



## What Is the Impact of Innovative Electronic Health Interventions in Improving Treatment Adherence in Asthma? The Pediatric Perspective

Amelia Licari, MD<sup>a,\*</sup>, Giuliana Ferrante, MD, PhD<sup>b,\*</sup>, Gian Luigi Marseglia, MD<sup>a</sup>, Giovanni Corsello, MD<sup>b</sup>, and Stefania La Grutta, MD, PhD<sup>b,c</sup> Pavia and Palermo, Italy  
doi: 10.1016/j.jaip.2019.08.008

Social robots and therapeutic adherence: A new challenge in pediatric asthma?

Giuliana Ferrante<sup>a,1</sup>, Gianpaolo Vitale<sup>b,1</sup>, Amelia Licari<sup>c,\*</sup>, Laura Montalbano<sup>d</sup>, Giovanni Pilato<sup>b</sup>, Ignazio Infantino<sup>b</sup>, Agnese Augello<sup>b,2</sup>, Stefania La Grutta<sup>d,2</sup>  
doi: 10.1016/j.prrv.2020.11.001

## Digital health interventions in children with asthma

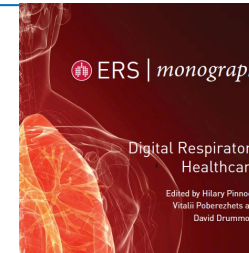
Giuliana Ferrante<sup>1</sup> | Amelia Licari<sup>2</sup> | Gian Luigi Marseglia<sup>2</sup> | Stefania La Grutta<sup>3</sup>  
doi: 10.1111/cea.13793

## Artificial intelligence in the diagnosis of pediatric allergic diseases

Giuliana Ferrante<sup>1</sup> | Amelia Licari<sup>2</sup> | Salvatore Fasola<sup>3</sup> | Gian Luigi Marseglia<sup>2</sup> | Stefania La Grutta<sup>3</sup>  
doi: 10.1111/pai.13419

## Medical assistive robots

Amelia Licari<sup>1,2,3</sup>, Giuliana Ferrante<sup>3,4</sup>, Velia Malizia<sup>3</sup>, Agnese Augello<sup>5</sup> and Stefania La Grutta<sup>3</sup>  
doi:10.1183/2312508X.10000523



## Predicting paediatric asthma exacerbations with machine learning: a systematic review with meta-analysis

Martina Votto<sup>1,2</sup>, Annalisa De Silvestri<sup>3</sup>, Lorenzo Postiglione<sup>1</sup>, Maria De Filippo<sup>1,2</sup>, Sara Manti<sup>4</sup>, Stefania La Grutta<sup>5</sup>, Gian Luigi Marseglia<sup>1,2</sup> and Amelia Licari<sup>1,2</sup>  
doi: 10.1183/16000617.01118-2024

## Machine learning: A modern approach to pediatric asthma

Giovanna Cilluffo<sup>1</sup> | Salvatore Fasola<sup>1</sup> | Giuliana Ferrante<sup>2</sup> | Amelia Licari<sup>3,4</sup> | Giuseppe Roberto Marseglia<sup>5</sup> | Andrea Albarelli<sup>5</sup> | Gian Luigi Marseglia<sup>3,4</sup> | Stefania La Grutta<sup>1</sup>  
doi: 10.1111/pai.13624

## Machine learning-enhanced HRCT analysis for diagnosis and severity assessment in pediatric asthma

Maria De Filippo MD<sup>1,2</sup> | Salvatore Fasola PhD<sup>3</sup> | Federica De Matteis MD<sup>4</sup> | Maria Sole Prevedoni Gorone MD<sup>5</sup> | Lorenzo Preda MD<sup>4,5</sup> | Martina Votto MD, PhD<sup>1,2</sup> | Velia Malizia MD<sup>3</sup> | Gian Luigi Marseglia MD<sup>1,2</sup> | Stefania La Grutta MD, PhD<sup>3</sup> | Amelia Licari MD<sup>1,2</sup>  
doi: 10.1002/ppul.27183

# Asma e AI in pediatria oggi

Diagnosi precoce e  
predizione del rischio

Identificazione  
dei fenotipi clinici

*Analisi dei  
Big Data*

*Personalizzazione  
del trattamento*

Monitoraggio  
remoto

Predizione delle  
riacutizzazioni

*Sviluppo di  
farmaci e terapie*

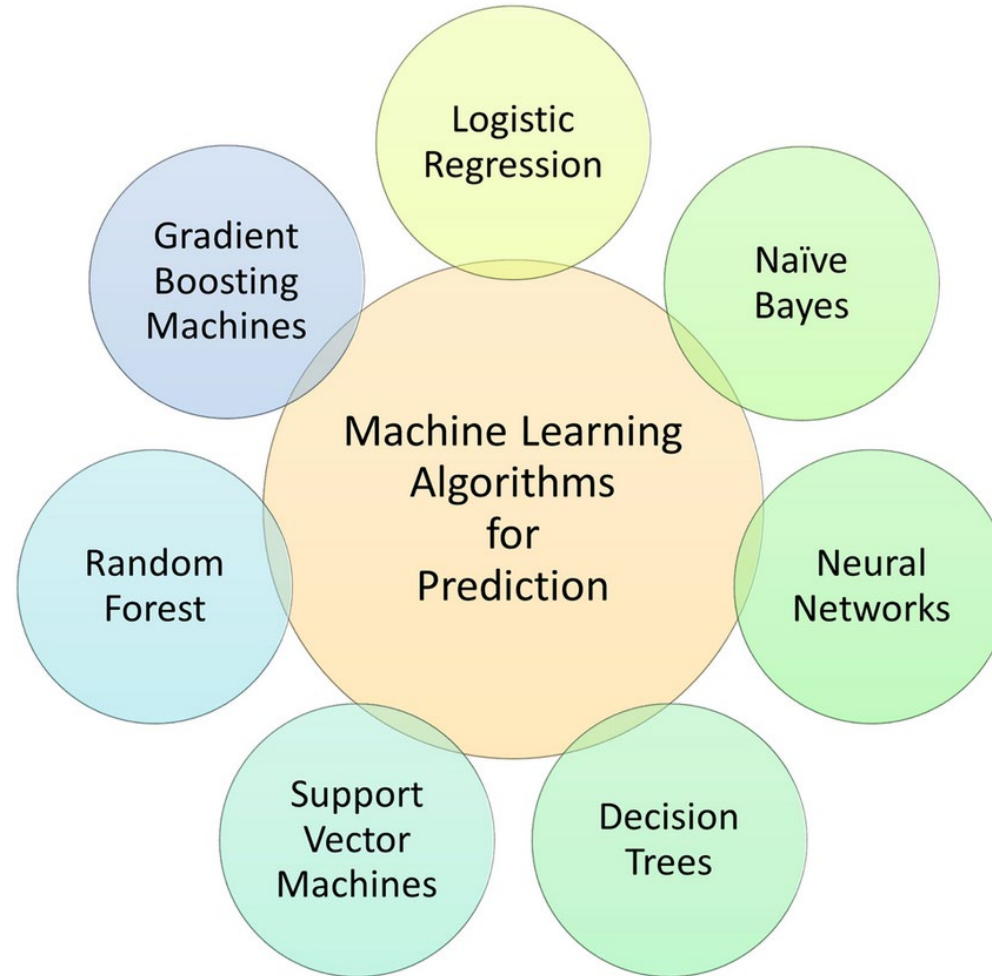
*Supporto  
decisionale clinico*

Analisi di  
immagini

Educazione e coinvolgimento  
del paziente e della famiglia

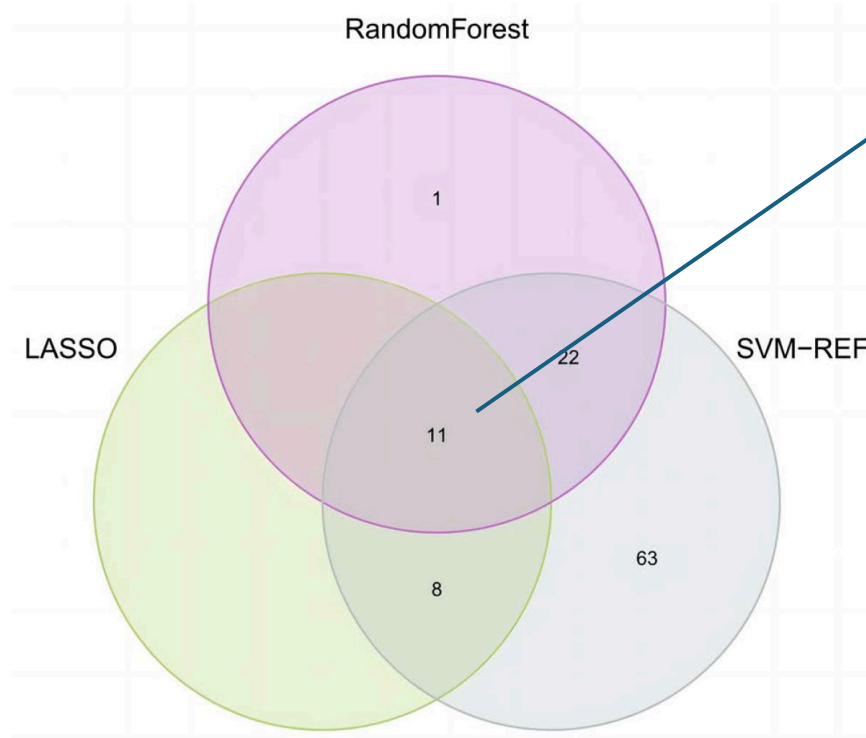
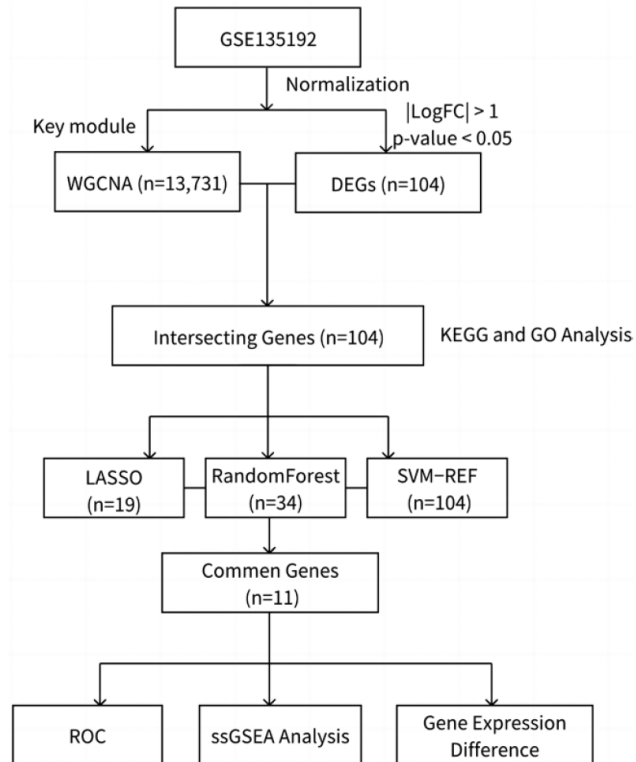


# Diagnosi precoce e predizione del rischio



# Identification of biomarkers associated with pediatric asthma using machine learning algorithms

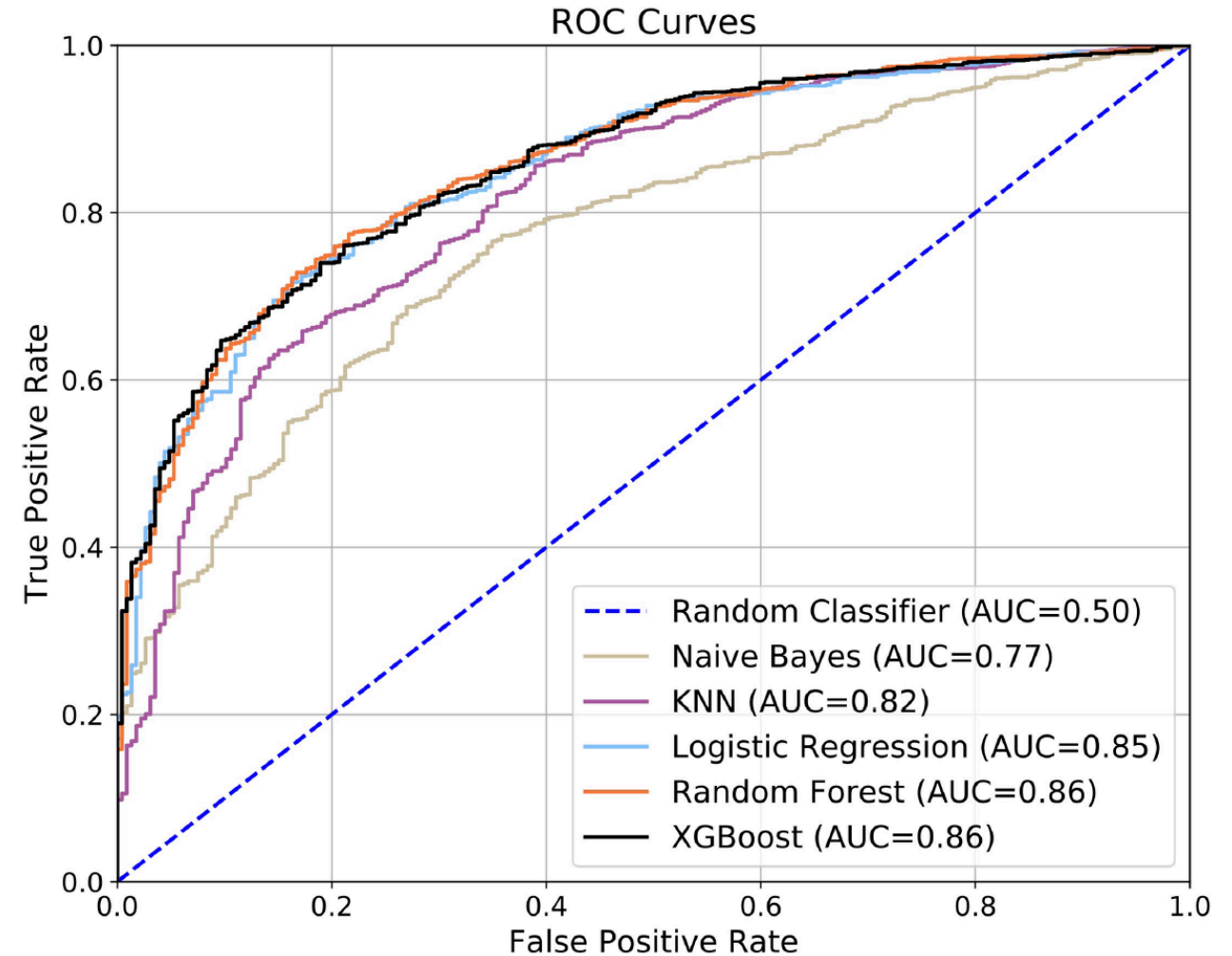
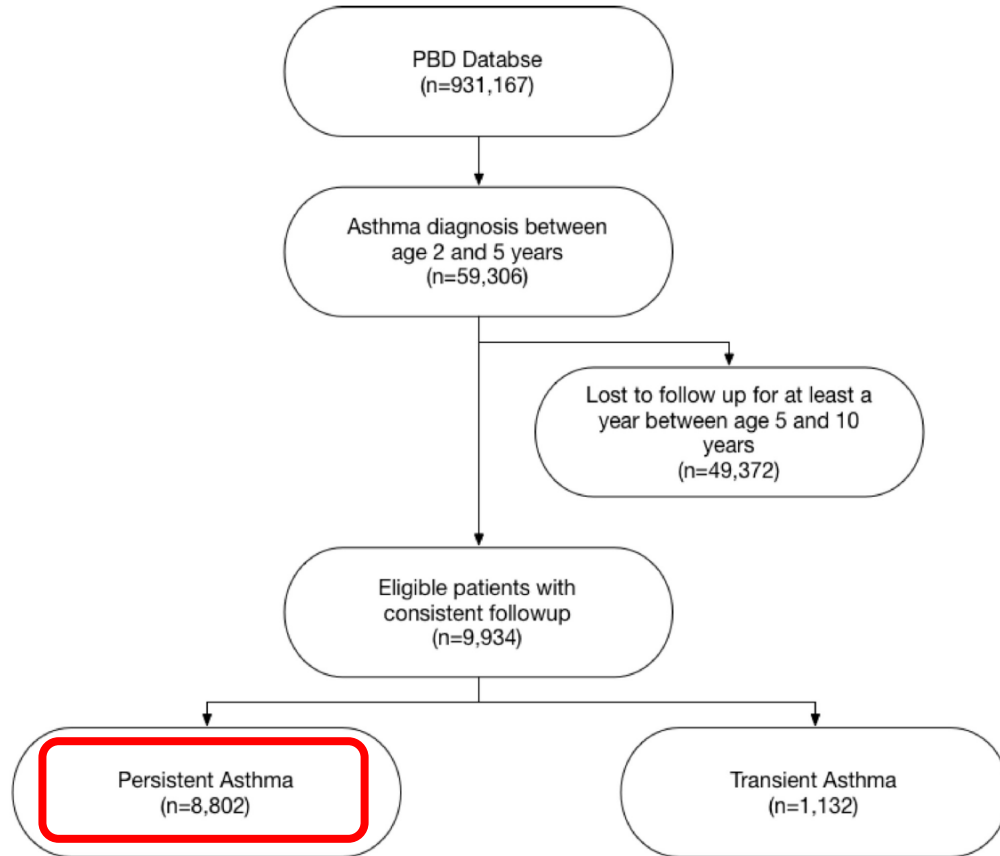
Three machine learning algorithms were used to cross-confirm and analyze gene expression profiles in asthmatic children based on whole transcriptome sequencing.



Gene	AUC
AK2	0.873
CREBZF	0.814
GZMH	0.796
LARP1B	0.783
NRL	0.792
NUMBL	0.835
PDK4	0.834
PER3	0.796
RXFP1	0.832
SCO2	0.827
VDAC3P1	0.819

**RXFP1**- relaxin receptor 1  
inhibiting airway hyperresponsiveness  
and reversing established fibrosis  
**AK2/PDK4**  
Regulation of the immune responses

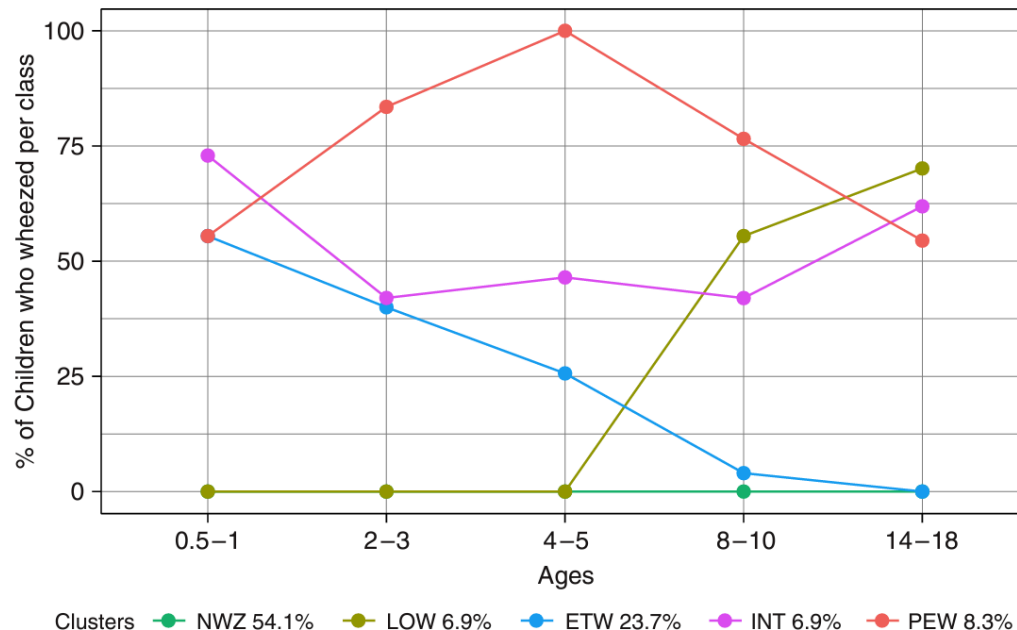
# Personalized prediction of early childhood asthma persistence: A machine learning approach



# Understanding progression from pre-school wheezing to school-age asthma: Can modern data approaches help?

Five UK population-based birth cohorts (7,719 children):

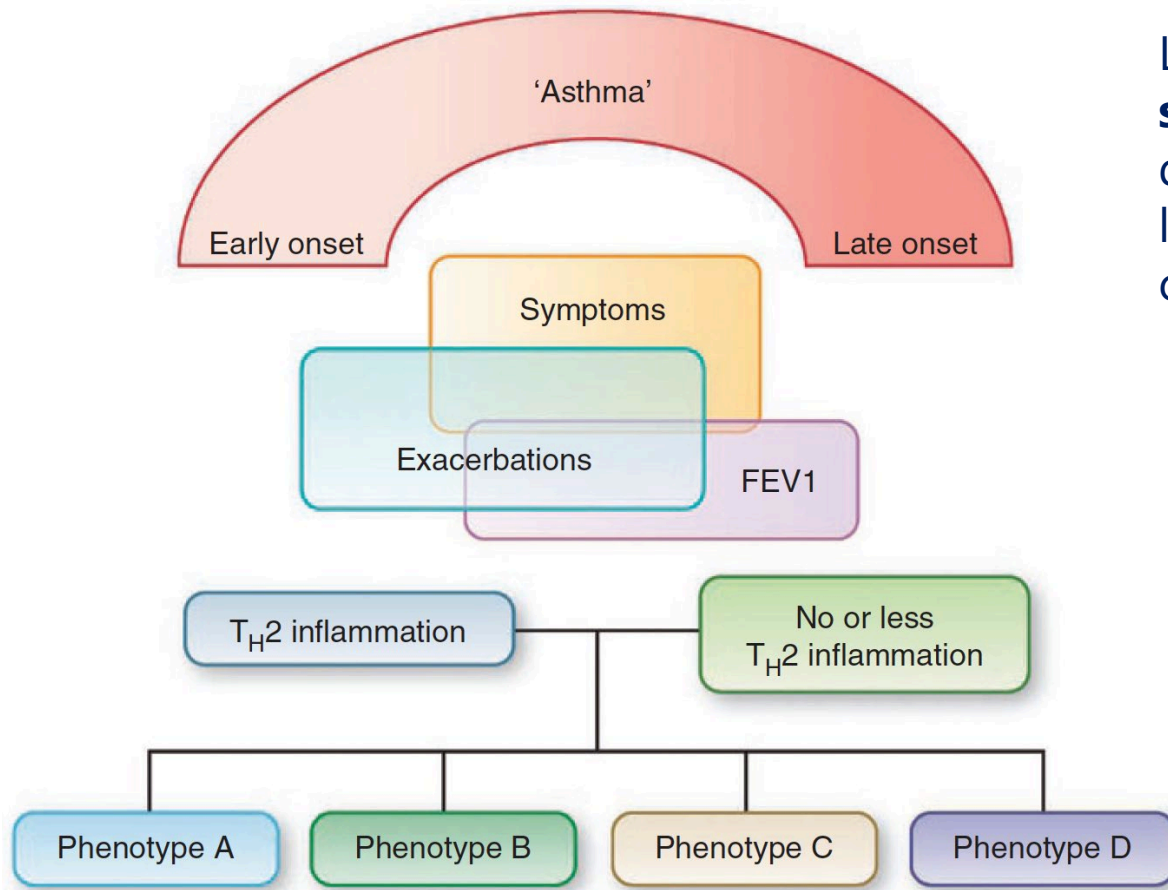
1. ALSPAC (Avon Longitudinal Study of Parents and Children)
2. Ashford
3. IOW (Isle of Wight)
4. SEATON (Aberdeen) cohorts
5. MAAS (Manchester Asthma and Allergy Study)



	Associations with Lung Function in Adolescence*		
	z-Scores for FEV <sub>1</sub> <sup>‡</sup>	z-Scores for FVC <sup>‡</sup>	z-Scores for FEV <sub>1</sub> /FVC <sup>‡</sup>
Never wheeze	Reference	Reference	Reference
Early transient	-0.103 (-0.19 to -0.02)	-0.014 (-0.10 to 0.07)	-0.151 (-0.24 to -0.07)
<i>P</i> value	<b>0.021</b>	0.748	<b>&lt;0.0001</b>
Intermittent	-0.168 (-0.29 to -0.05)	0.054 (-0.06 to 0.17)	-0.379 (-0.49 to -0.27)
<i>P</i> value	<b>0.005</b>	0.37	<b>&lt;0.0001</b>
Persistent	-0.326 (-0.45 to -0.20)	0.079 (-0.05 to 0.21)	-0.707 (-0.83 to -0.59)
<i>P</i> value	<b>&lt;0.0001</b>	0.221	<b>&lt;0.0001</b>
Late onset	-0.003 (-0.13 to 0.13)	0.159 (0.03 to 0.29)	-0.302 (-0.43 to -0.18)
<i>P</i> value	0.959	<b>0.015</b>	<b>&lt;0.0001</b>

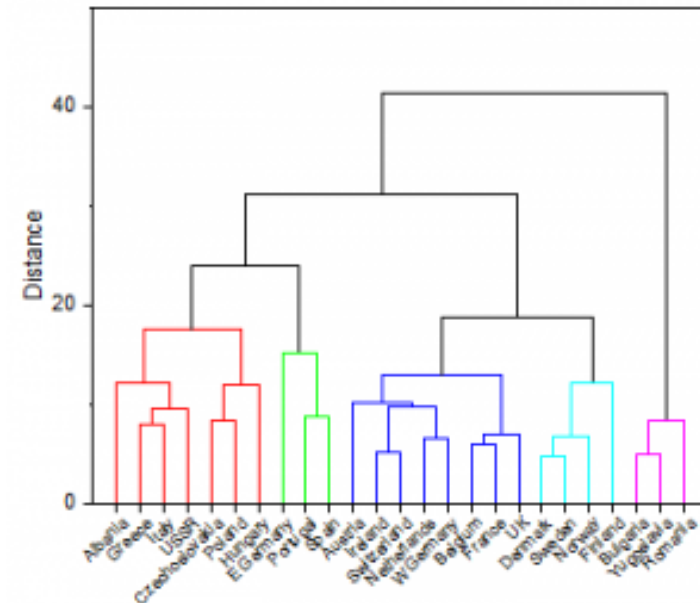
**All wheeze phenotypes were associated with diminished lung function in adolescence and early adulthood, with the greatest impairment in PEW and INT.**

# Identificazione dei fenotipi clinici



## Analisi dei cluster (clustering)

L'analisi dei cluster è una tecnica di **apprendimento non supervisionato** usata per identificare gruppi (cluster) in un dataset. Non ci sono etichette predefinite nei dati, quindi l'obiettivo è scoprire gruppi nascosti basati su determinate caratteristiche o metriche di somiglianza.



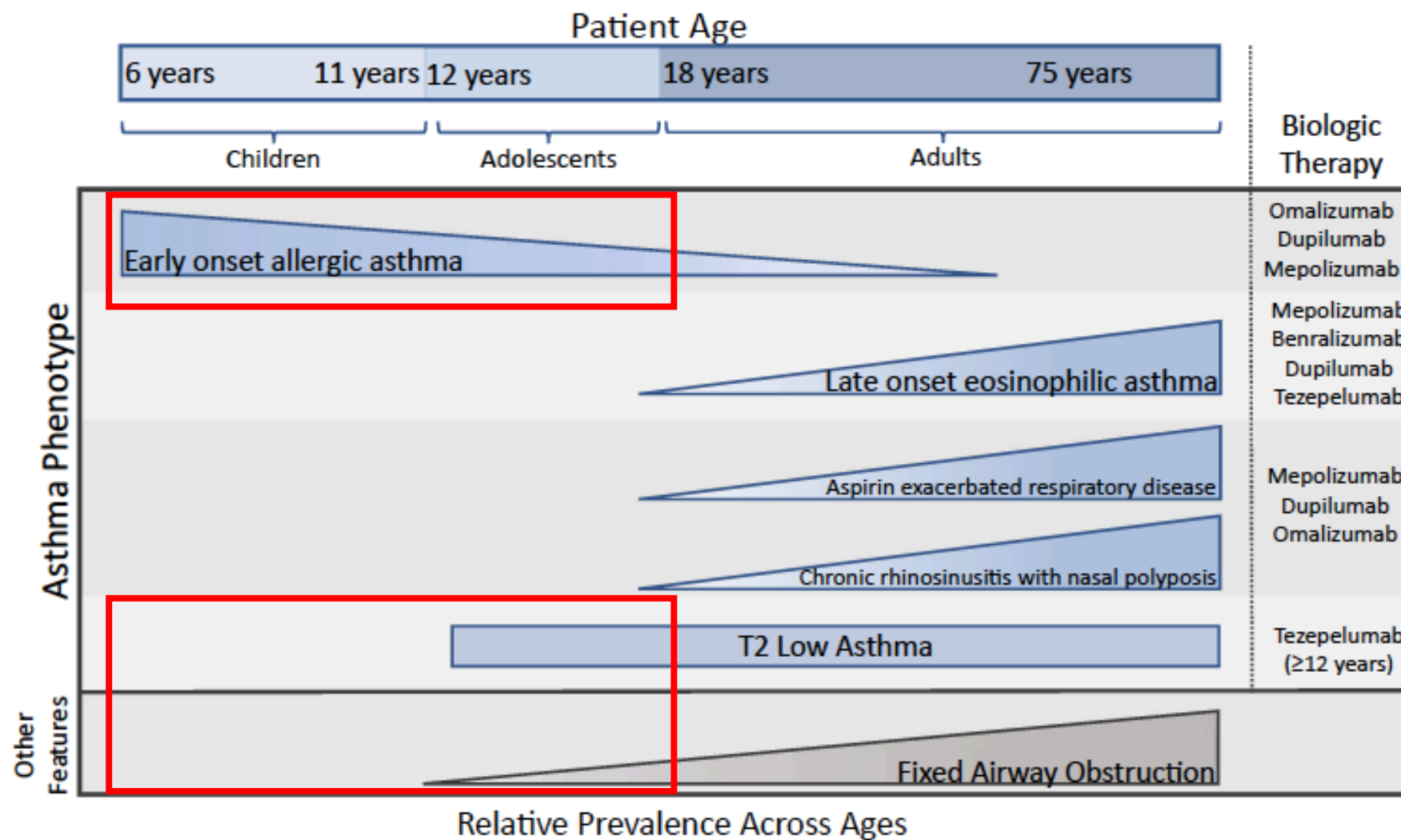
# Identificazione dei fenotipi clinici

ML approach	Study design and participants	Distinctive features of asthma clusters	Clusters identified	Ref.
Hierarchical clustering	Cross-sectional, <u>613</u> asthmatic children	Age of onset, allergic sensitization, severity, and exacerbations in the previous year	<ul style="list-style-type: none"> <li>– Early-onset mild atopic asthma</li> <li>– Early-onset mild non-atopic asthma</li> <li>– Late-onset asthma</li> <li>– Difficult asthma</li> <li>– Exacerbation-prone asthma</li> </ul>	Deliu et al. <sup>1</sup>
k-means clustering	Cross-sectional, <u>351</u> asthmatic children from the Taiwanese Consortium of Childhood Asthma Study	Lung function, symptom frequency, healthcare utilization, percentages of eosinophils and neutrophils in peripheral blood, and serum IgE	<ul style="list-style-type: none"> <li>– Asthma with elevated RBC and wheeze episodes</li> <li>– Neutrophil-predominant asthma</li> <li>– Allergic asthma with preserved pulmonary function</li> <li>– Eosinophil-predominant asthma with poor pulmonary function</li> <li>– Asthma with low wheeze episodes</li> </ul>	Su et al. <sup>2</sup>
LCA	Cross-sectional, <u>2593</u> children with mild to moderate persistent asthma	Demographic features, asthma control, sensitization, type 2 inflammatory markers, and lung function	<ul style="list-style-type: none"> <li>– Multiple sensitization with partially reversible airflow limitation</li> <li>– Multiple sensitization with reversible airflow limitation</li> <li>– Lesser sensitization with reversible airflow limitation</li> <li>– Multiple sensitization with normal lung function</li> <li>– Lesser sensitization with normal lung function</li> </ul>	Fitzpatrick et al. <sup>3</sup>

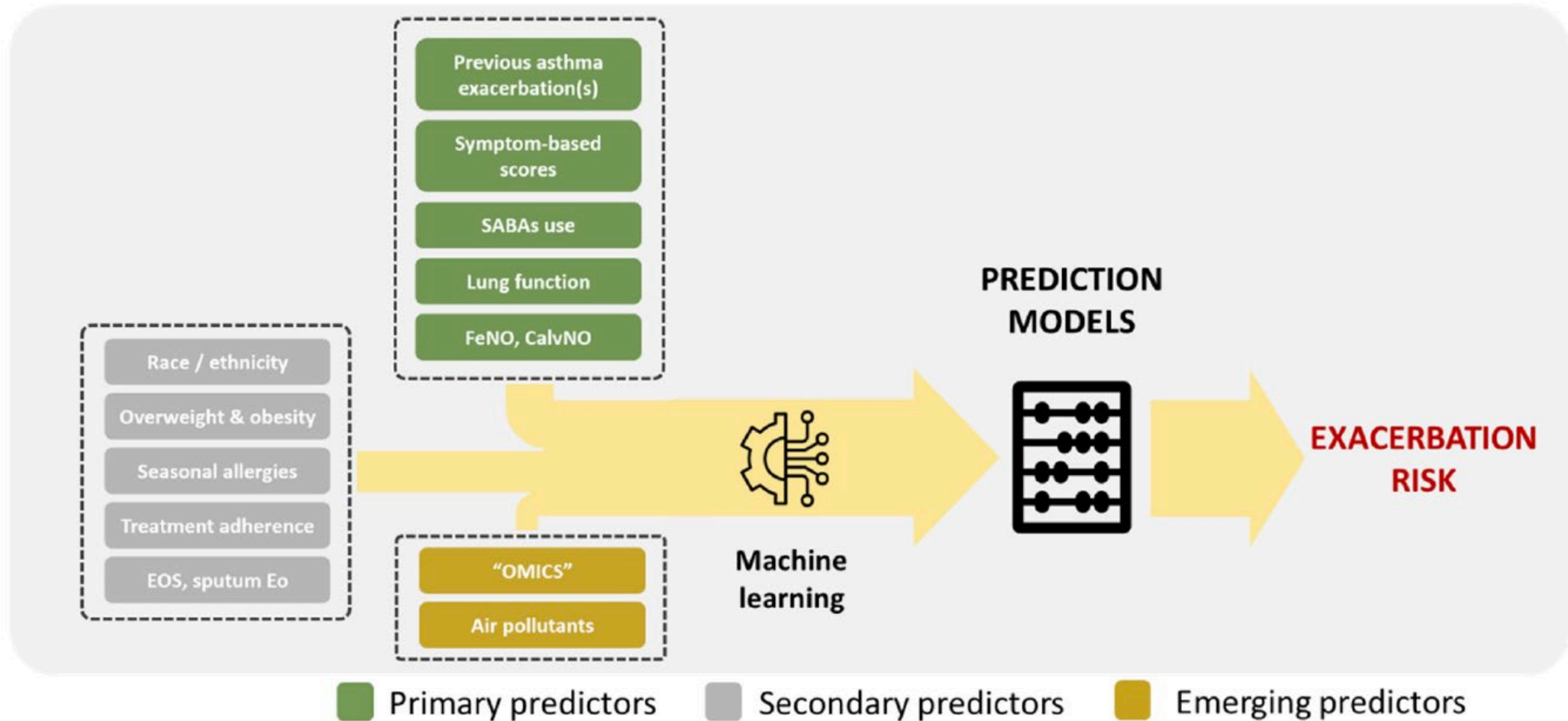
# Identificazione dei fenotipi clinici

	SARP	Asthma Phenotypes in the Inner City (APIC)
Age of cohort	School-age children	Low-income urban children/adolescents
No. of clusters	4	5
Primary distinctions between clusters within each study	<ul style="list-style-type: none"> <li>• Asthma duration</li> <li>• Number of controller medications</li> <li>• Baseline lung function</li> </ul>	<ul style="list-style-type: none"> <li>• Asthma and rhinitis severity</li> <li>• Airway obstruction, baseline bronchodilator response</li> <li>• Allergic sensitization/inflammation</li> </ul>
Notable findings in clusters	<ul style="list-style-type: none"> <li>• Clusters determined as much by the magnitude of allergic sensitization and duration of asthma as by airflow limitation and hyperinflation</li> <li>• All clusters had some degree of atopy, though the magnitude of allergic sensitization differed</li> </ul>	<ul style="list-style-type: none"> <li>• Four clusters had striking parallel relationships between allergic sensitization and indicators of asthma/rhinitis severity</li> <li>• One cluster with comparatively low allergy and modestly impaired pulmonary physiology (remained highly symptomatic)</li> </ul>
Severe asthma	Severe asthma participants existed across all clusters	Severe asthma often co-clustered with highly atopic children

# Identificazione dei fenotipi clinici



# Predizione delle riacutizzazioni



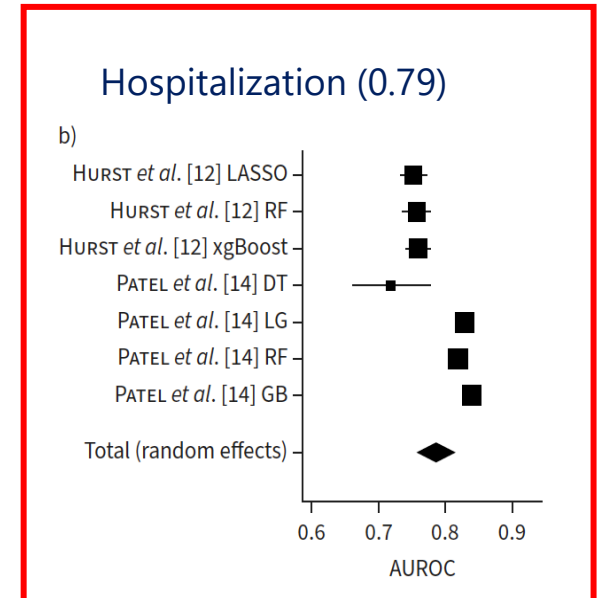
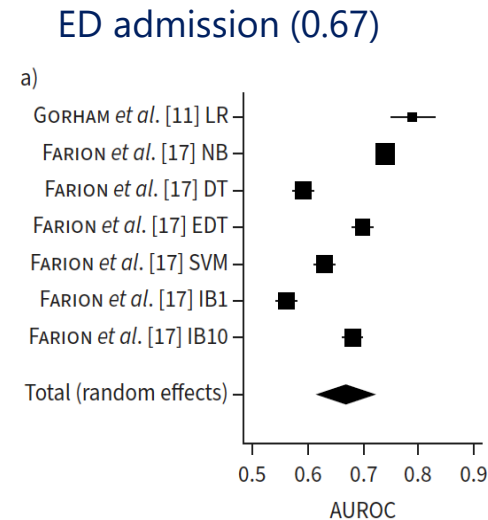


# Predicting paediatric asthma exacerbations with machine learning: a systematic review with meta-analysis

- **Study characteristics:** Seven studies included; 17 ML-based models were analyzed.
- **Types of Models:** Logistic regression, random forests, and gradient boosting were the most common algorithms.
- **Predictors:** Age, past asthma-related admissions, inhaled steroid use, and air quality were common predictors.

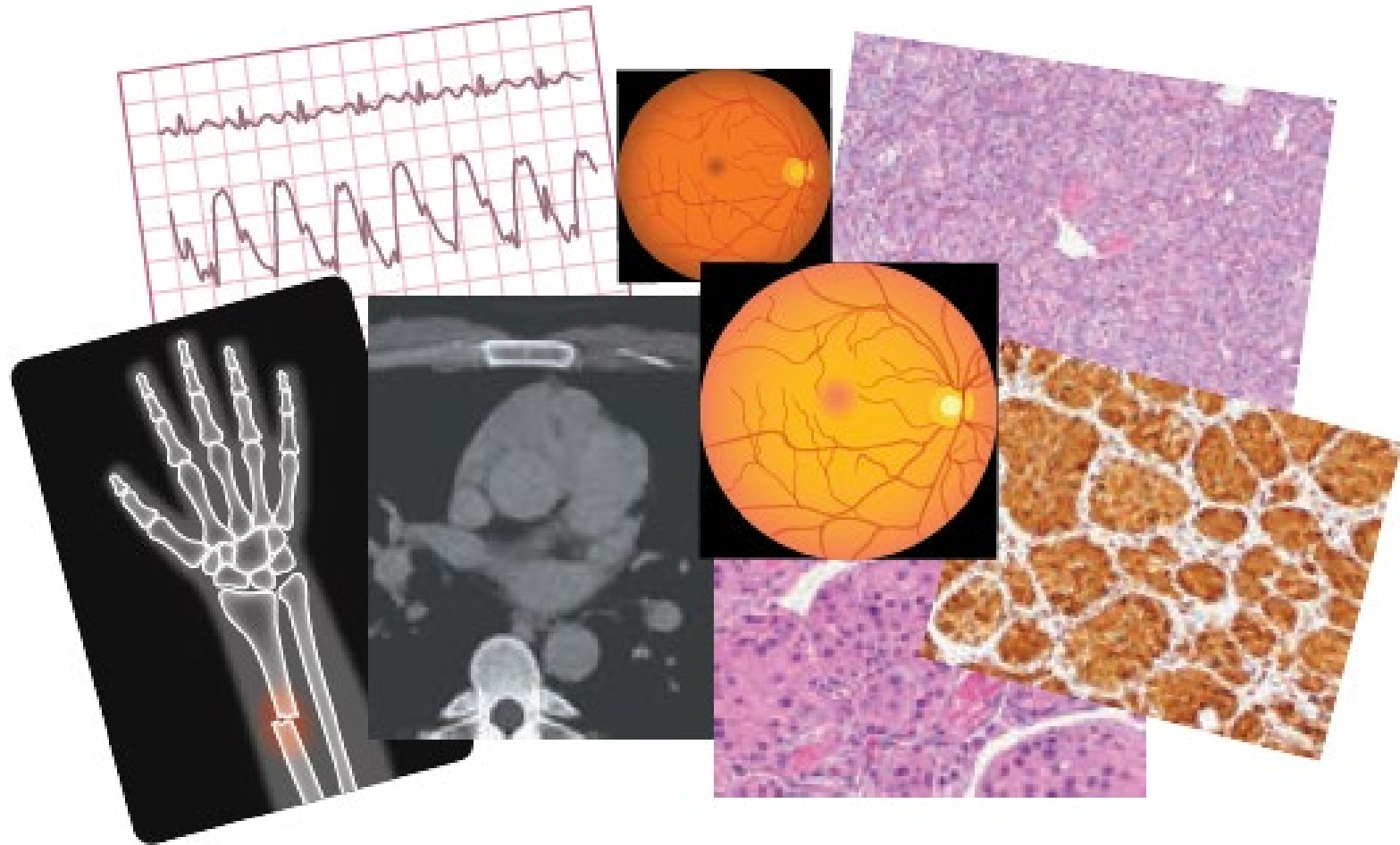
► **Strengths of ML Models:** Potential to improve early identification of high-risk children.

► **Limitations:** High heterogeneity between studies; lack of standardized asthma diagnostic criteria across studies; need for further validation of ML models.



*ML algorithms show promise for predicting pediatric asthma exacerbations, particularly hospitalizations, but require further validation before clinical implementation.*

# *Analisi di immagini*



# Pediatric severe asthma: high-resolution ct features

Maria De Filippo, Salvatore Fasola, Martina Votto, Maria Sole Prevedoni Gorone, Gian Luigi Marseglia, Stefania La Grutta, Amelia Licari



Chest high-resolution computed tomography (HRCT) is conditionally recommended to rule out conditions that mimic or coexist with severe asthma in children.



- **Retrospective case-control study** compared children with **SA** (as defined by ERS/ATS guidelines) to age- and sex-matched controls without asthma (**C**).
- 20 children with **SA** (40% females, mean age 10.4 years) and 21 **C** (48% females, mean age 11.4 years).
- Chest HRCT examinations were performed using a **64-section multidetector CT scanner** (Aquilion Toshiba One) at full inspiration (total lung capacity) following a dedicated low-dose volumetric protocol.
- **Software:** COPD (Chronic Obstructive Pulmonary Disease) application within IntelliSpace Portal release 9 (Philips Medical Systems Best, the Netherlands).

ClinicalTrials.gov ID: NCT05140889

This study is a part of the research project "Integrating deep learning CT-scan model, biological and clinical variables to predict severity of asthma in children" (BREATHE, protocol number 0003233/22) funded by the 5x1000, Ricerca Corrente, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy.

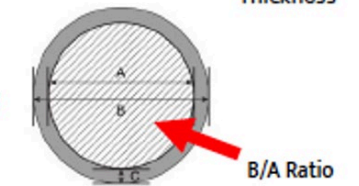
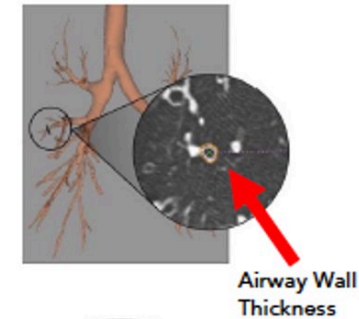
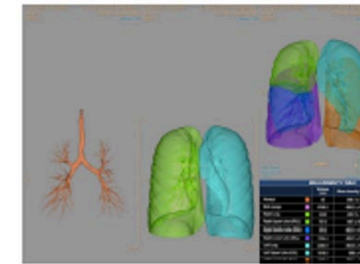
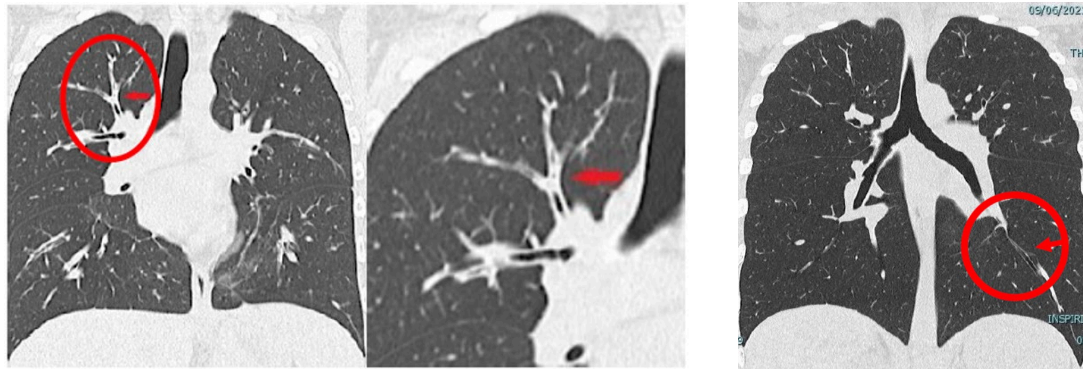


# Pediatric severe asthma: high-resolution ct features

Maria De Filippo, Salvatore Fasola, Martina Votto, Maria Sole Prevedoni Gorone, Gian Luigi Marseglia, Stefania La Grutta, Amelia Licari

	C	SA	P
Bronchial thickening (BT)	0.0	0.9	<0.001
Airway wall thickness percentage (AWT%)	34.8	43.9	<0.001
Bronchiectasis grading (BG) score	0.0	0.2	0.016
Bronchiectasis severity grading (BS) score	0.0	0.2	0.016
Mucus plugging	0.0	6	0.009
Centrilobular emphysema	0.0	6	0.009

- The percentage of airway wall thickness (**AWT%**) was calculated as follows: **AWT% = [(Do-Di)/Do] x 100**; outer (Do) and inner (Di) diameters.

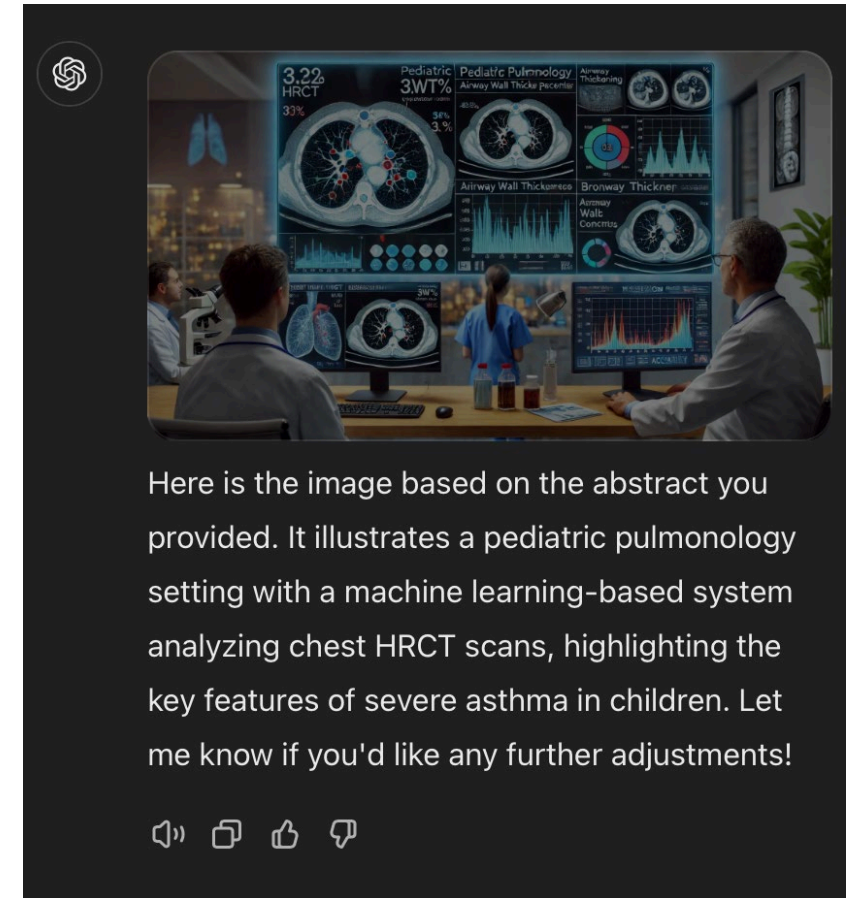


ClinicalTrials.gov ID: NCT05140889

This study is a part of the research project "Integrating deep learning CT-scan model, biological and clinical variables to predict severity of asthma in children" (BREATHE, protocol number 0003233/22) funded by the 5x1000, Ricerca Corrente, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy.



# Machine learning-enhanced HRCT analysis for diagnosis and severity assessment in pediatric asthma



Here is the image based on the abstract you provided. It illustrates a pediatric pulmonology setting with a machine learning-based system analyzing chest HRCT scans, highlighting the key features of severe asthma in children. Let me know if you'd like any further adjustments!



# Machine learning-enhanced HRCT analysis for diagnosis and severity assessment in pediatric asthma

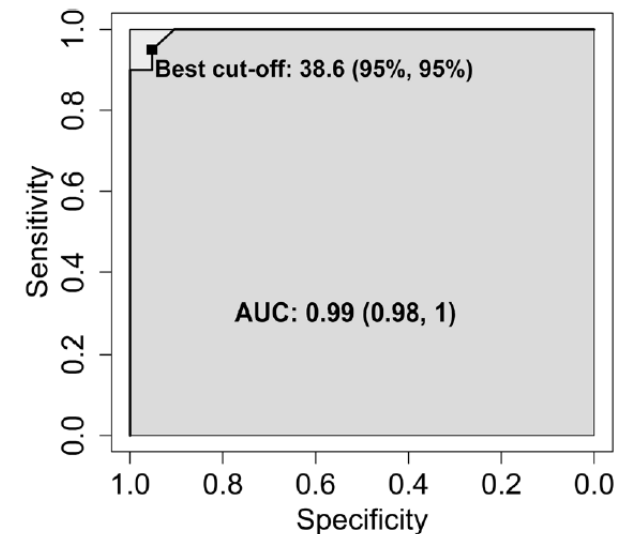
The study aimed to develop a machine learning (ML) model classifying severe asthma cases based on radiological findings.

	Classification tree		Random Forest		AWT% $\geq$ 38.6	
	Training set	Cross-validated	Training set	Cross-validated	Training set	Cross-validated
Sensitivity	95%	90%	95%	95%	95%	90%
Specificity	100%	90%	100%	100%	95%	90%
Accuracy	98%	90%	98%	98%	95%	90%

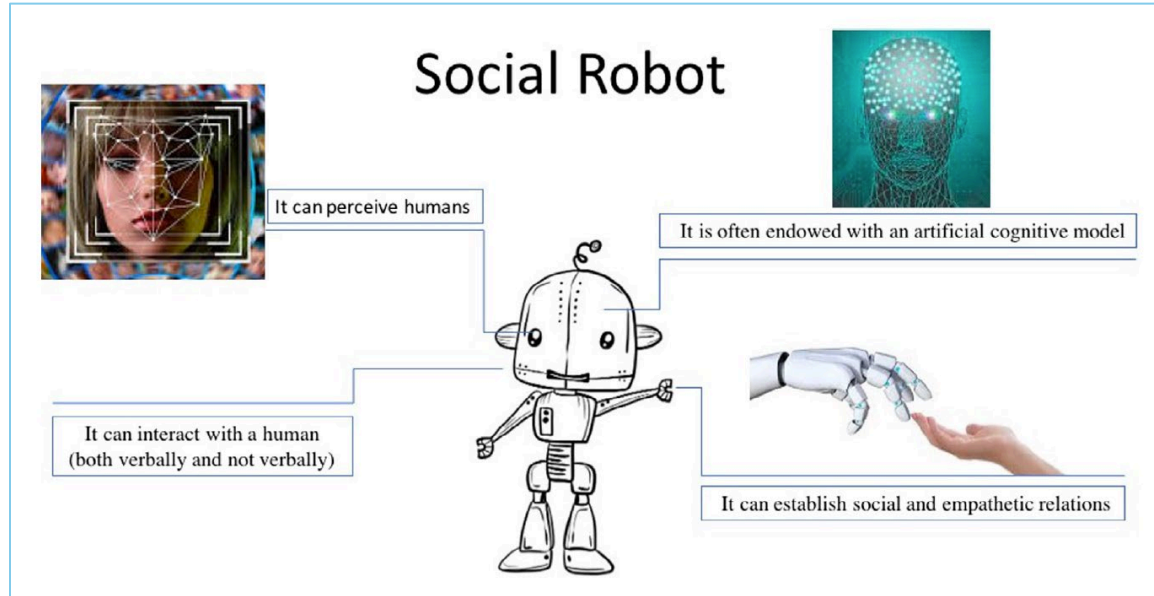
Using **airway wall thickness percentage AWT%** as the predictor in conventional ROC analysis, an **AWT%  $\geq$  38.6** emerged as the **optimal classifier for discriminating severe asthmatics from controls, with 95% sensitivity, specificity, and overall accuracy.**

*ClinicalTrials.gov (NCT0514088)*

**Statistical analysis:** classification trees, random forests, and conventional ROC analysis to identify the most significant imaging features that mark **SA** from **C**.



# Educazione e coinvolgimento del paziente e della famiglia

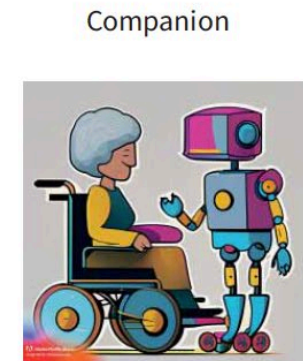
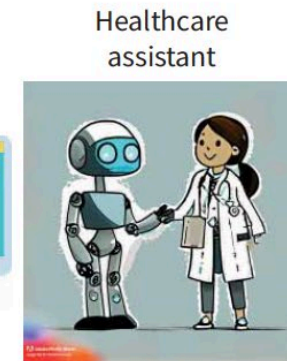
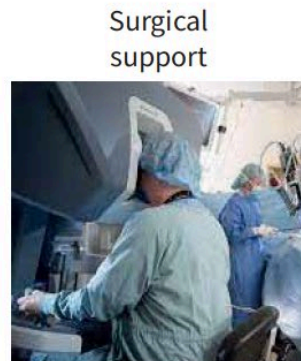


A **social robot** is an autonomous or semi-autonomous robot that interacts and communicates with humans by following the behavioral norms expected by the people with whom the robot is intended to interact.

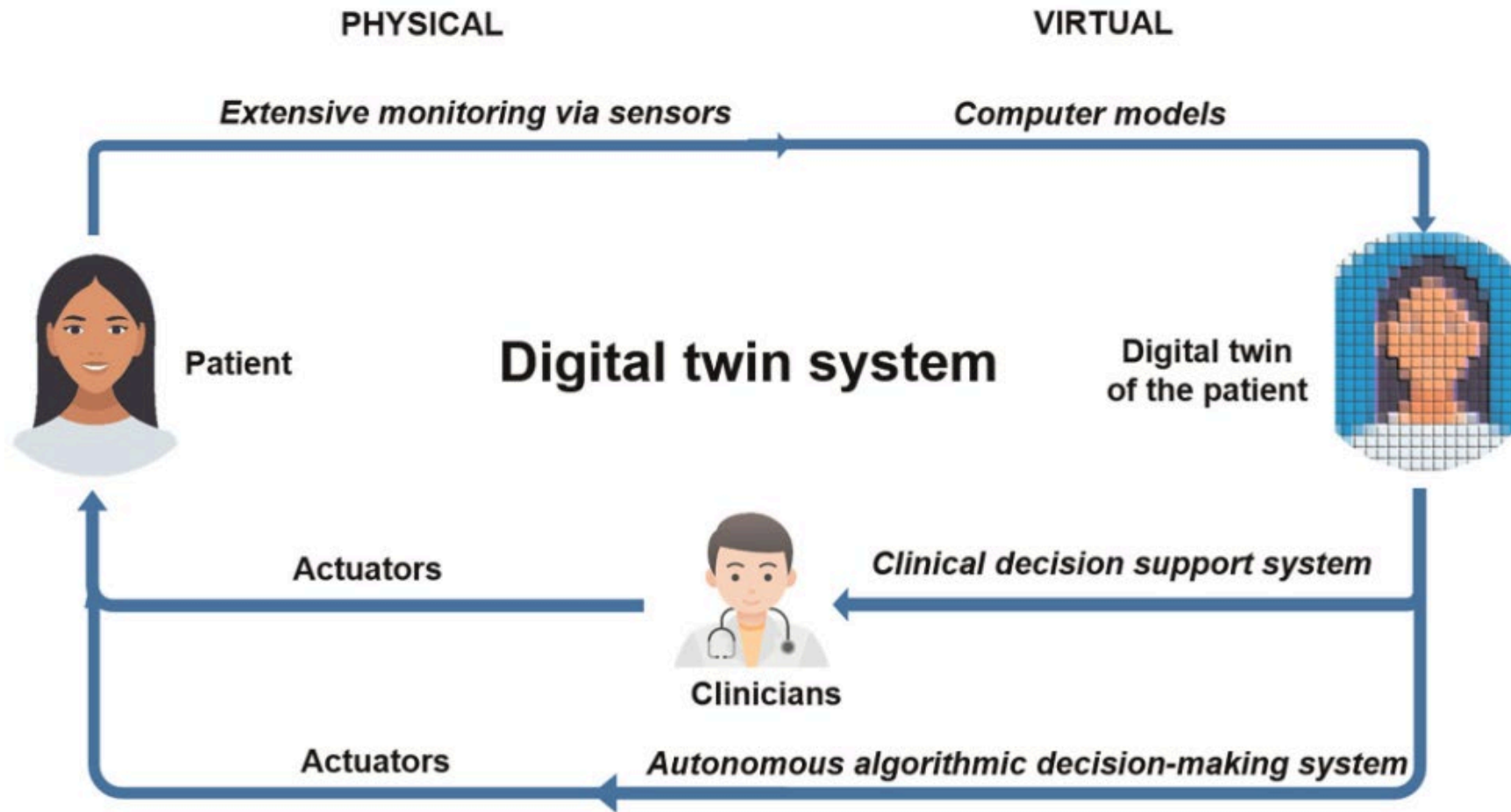
*Ferrante G, et al. Paediatr Respir Rev. 2021 Dec;40:46-51*



**It can be employed in healthcare contexts to perform assistive functionalities**



# Educazione e coinvolgimento del paziente e della famiglia



*Drummond D, Roukema J, Pijnenburg M. Home monitoring in asthma: towards digital twins. Curr Opin Pulm Med. 2023 Jul 1;29(4):270-276.*

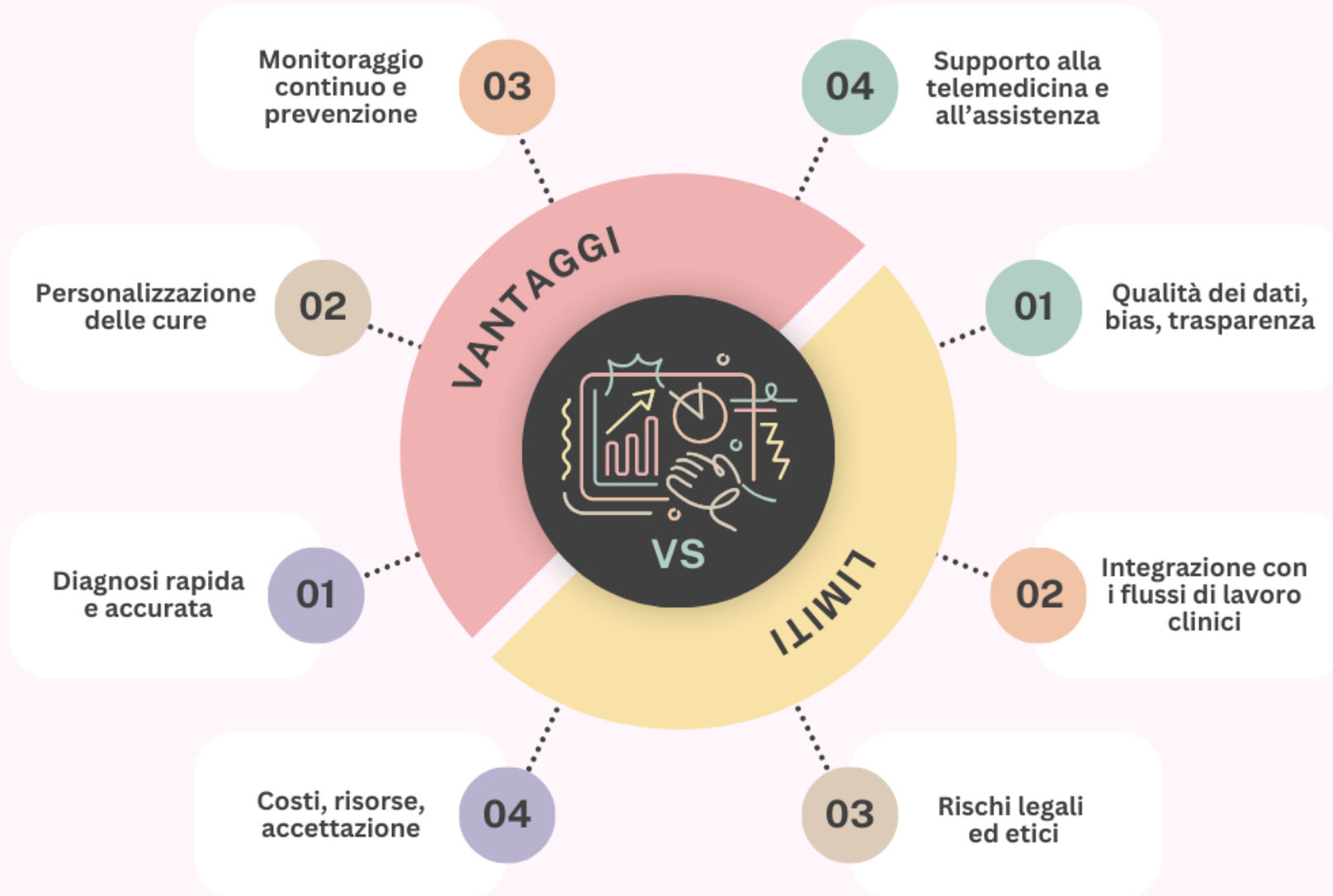
# Educazione e coinvolgimento del paziente e della famiglia

Animation created to show children what the interface of the digital twinning system might look like

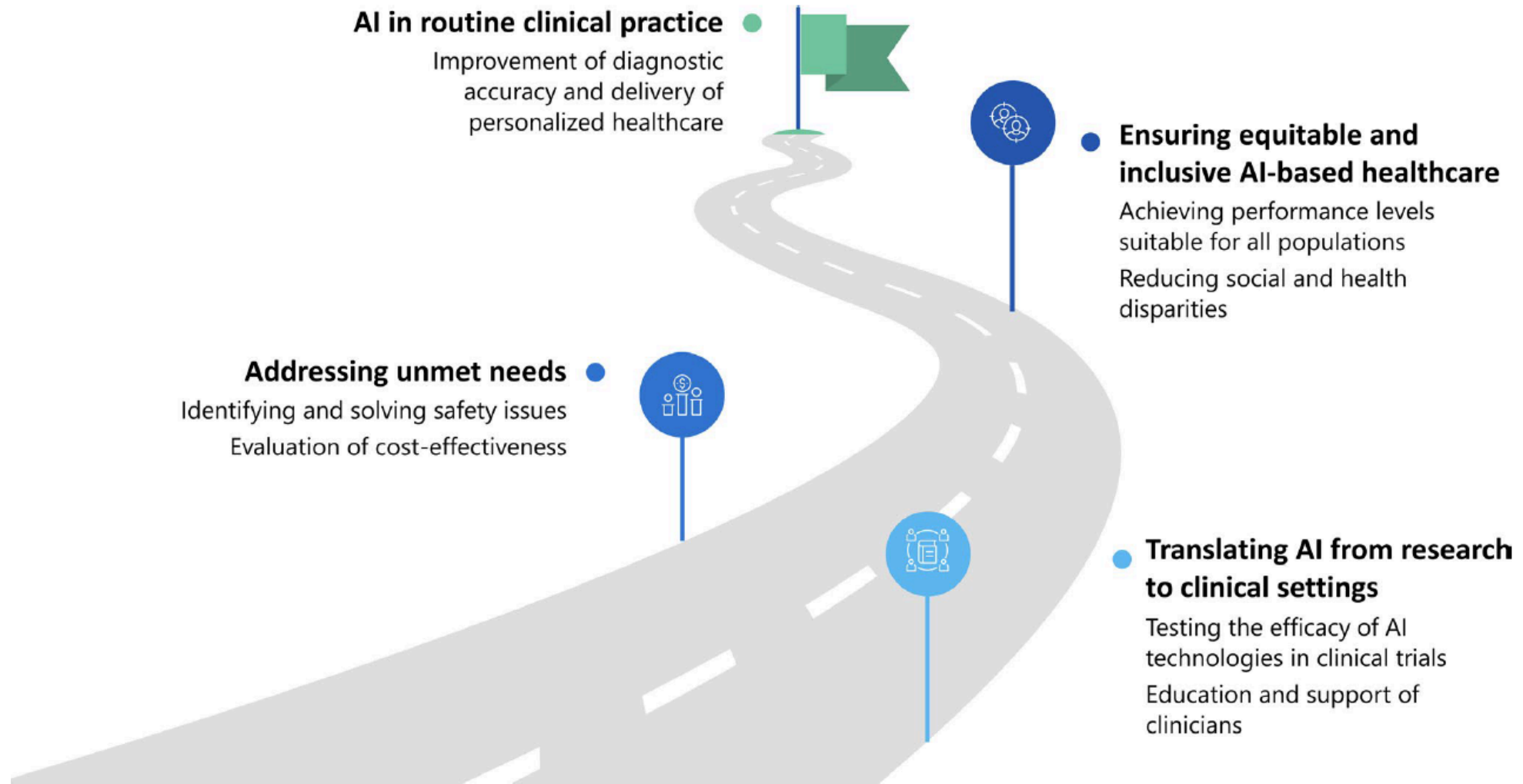


Gonsard A, et al. Children's views on artificial intelligence and digital twins for the daily management of their asthma: a mixed-method study. *Eur J Pediatr.* 2023 Feb;182(2):877-888.

# Vantaggi e Limiti dell'AI in Pediatria



# Prospettive future



# Promoting implementation research into sustainable, equitable, connected digital respiratory care in diverse healthcare systems.



<https://www.ersnet.org/science-and-research/ongoing-clinical-research-collaborations>



- I Build a multidisciplinary research network
- II Create an EU-wide repository of respiratory healthcare technologies
- III Scope published research on implementation of digital respiratory care
- IV Develop position papers on societal infrastructure and core outcomes for trials
- V Secure future funding for research into digital respiratory health

<https://www.simri.it/evento/tecnologie-digitali-innovative-per-lassistenza-respiratoria-pediatrica/>



## *Pediatric Digital Technologies for Respiratory Care: PeDiTCare*

- ❖ To develop a national multidisciplinary network that promotes research on the implementation of digital healthcare in childhood respiratory diseases
- ❖ To map the knowledge and use of digital technologies across Italian pediatric pulmonology centers
- ❖ To implement digital respiratory healthcare in pediatric pulmonology
- ❖ To publish a summary document through the creation of a national research network