



HAL
open science

Vérification du critère de réversibilité du VEMS proposé par les recommandations du GINA chez l'enfant asthmatique: VERI-VEMS, une étude rétrospective de cohorte

Anouchka Fillard

► To cite this version:

Anouchka Fillard. Vérification du critère de réversibilité du VEMS proposé par les recommandations du GINA chez l'enfant asthmatique: VERI-VEMS, une étude rétrospective de cohorte. Human health and pathology. 2020. dumas-03109330

HAL Id: dumas-03109330

<https://dumas.ccsd.cnrs.fr/dumas-03109330>

Submitted on 13 Jan 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - ShareAlike 4.0 International License

UNIVERSITE DE MONTPELLIER
FACULTE DE MEDECINE MONTPELLIER-NÎMES

THESE

Pour obtenir le titre de

DOCTEUR EN MEDECINE

Présentée et soutenue publiquement

Par

Anouchka FILLARD

Le 19 octobre 2020

Titre :

" Vérification du critère de réversibilité du VEMS proposé par les recommandations du GINA chez l'enfant asthmatique : Veri-VEMS, une étude rétrospective de cohorte "

Directeur de thèse : Dr Davide CAIMMI

JURY :

Monsieur le Professeur Pascal DEMOLY, Président
Monsieur le Professeur Arnaud BOURDIN, Assesseur
Monsieur le Professeur Stefan MATECKI, Assesseur
Monsieur le Docteur Davide CAIMMI, Assesseur

UNIVERSITE DE MONTPELLIER
FACULTE DE MEDECINE MONTPELLIER-NÎMES

THESE

Pour obtenir le titre de

DOCTEUR EN MEDECINE

Présentée et soutenue publiquement

Par

Anouchka FILLARD

Le 19 octobre 2020

Titre :

" Vérification du critère de réversibilité du VEMS proposé par les recommandations du GINA chez l'enfant asthmatique : Veri-VEMS, une étude rétrospective de cohorte "

Directeur de thèse : Dr Davide CAIMMI

JURY :

Monsieur le Professeur Pascal DEMOLY, Président
Monsieur le Professeur Arnaud BOURDIN, Assesseur
Monsieur le Professeur Stefan MATECKI, Assesseur
Monsieur le Docteur Davide CAIMMI, Assesseur

ANNEE UNIVERSITAIRE 2019 - 2020

PERSONNEL ENSEIGNANT

Professeurs Honoraires

ALLIEU Yves	CALLIS Albert	JAFFIOL Claude	NAVRATIL Henri
ALRIC Robert	CANAUD Bernard	JANBON Charles	OTHONIEL Jacques
ARNAUD Bernard	CHAPTAL Paul-André	JANBON François	PAGES Michel
ASTRUC Jacques	CIURANA Albert-Jean	JARRY Daniel	PEGURET Claude
AUSSILLOUX Charles	CLOT Jacques	JOURDAN Jacques	PELISSIER Jacques
AVEROUS Michel	COSTA Pierre	LAFFARGUE François	POUGET Régis
AYRAL Guy	D'ATHIS Françoise	LALLEMANT Jean Gabriel	PUJOL Henri
BAILLAT Xavier	DEMAILLE Jacques	LAMARQUE Jean-Louis	RABISCHONG Pierre
BALDET Pierre	DESCOMPS Bernard	LAPEYRIE Henri	RAMUZ Michel
BALDY-MOULINIER Michel	DIMEGLIO Alain	LE QUELLEC Alain	RIEU Daniel
BALMES Jean-Louis	DUBOIS Jean Bernard	LESBROS Daniel	ROCHFORDT Henri
BALMES Pierre	DUJOLS Pierre	LOPEZ François Michel	ROUANET DE VIGNE LAVIT Jean Pierre
BANSARD Nicole	DUMAS Robert	LORiot Jean	SAINT AUBERT Bernard
BAYLET René	DUMAZER Romain	LOUBATIERES Marie Madeleine	SANCHO-GARNIER Héléne
BILLIARD Michel	ECHENNE Bernard	MAGNAN DE BORNIER Bernard	SANY Jacques
BLARD Jean-Marie	FABRE Serge	MARY Henri	SEGNARBIEUX François
BLAYAC Jean Pierre	FREREBEAU Philippe	MATHIEU-DAUDE Pierre	SENAC Jean-Paul
BLOTMAN Francis	GALIFER René Benoît	MEYNADIER Jean	SERRE Arlette
BONNEL François	GODLEWSKI Guilhem	MICHEL François-Bernard	SOLASSOL Claude
BOURGEOIS Jean-Marie	GRASSET Daniel	MION Charles	THEVENET André
BRUEL Jean Michel	GUILHOU Jean- Jacques	MION Henri	VIDAL Jacques
BUREAU Jean-Paul	HERTAULT Jean	MIRO Luis	VISIÉ Jean Pierre
BRUNEL Michel	HUMEAU Claude	NAVARRO Maurice	

Professeurs Emérites

ARTUS Jean-Claude	MARES Pierre
BLANC François	MAUDELONDE Thierry
BOULENGER Jean-Philippe	MAURY Michèle
BOURREL Gérard	MILLAT Bertrand
BRINGER Jacques	MONNIER Louis
CLAUSTRES Mireille	MOURAD Georges
DAURES Jean-Pierre	PREFAUT Christian
DAUZAT Michel	PUJOL Rémy
DAVY Jean-Marc	RIBSTEIN Jean
DEDET Jean-Pierre	SCHVED Jean-François
ELEDJAM Jean-Jacques	SULTAN Charles
GROLLEAU RAOUX Robert	TOUCHON Jacques
GUERRIER Bernard	UZIEL Alain
GUILLOT Bernard	VOISIN Michel
LANDAIS Paul	ZANCA Michel

Professeurs des Universités - Praticiens Hospitaliers

PU-PH de classe exceptionnelle

ALBAT Bernard	Chirurgie thoracique et cardiovasculaire
ALRIC Pierre	Chirurgie vasculaire ; médecine vasculaire (option chirurgie vasculaire)
BACCINO Eric	Médecine légale et droit de la santé
BASTIEN Patrick	Parasitologie et mycologie
BLAIN Hubert	Médecine interne ; gériatrie et biologie du vieillissement, médecine générale, addictologie
BONAFE Alain	Radiologie et imagerie médicale
CAPDEVILA Xavier	Anesthésiologie-réanimation et médecine péri-opératoire
CHAMMAS Michel	Chirurgie orthopédique et traumatologique
COLSON Pascal	Anesthésiologie-réanimation et médecine péri-opératoire
COMBE Bernard	Rhumatologie
COTTALORDA Jérôme	Chirurgie infantile
COUBES Philippe	Neurochirurgie
COURTET Philippe	Psychiatrie d'adultes ; addictologie
CRAMPETTE Louis	Oto-rhino-laryngologie
CRISTOL Jean Paul	Biochimie et biologie moléculaire
DE LA COUSSAYE Jean Emmanuel	Médecine d'urgence
DE WAZIERES Benoît	Médecine interne ; gériatrie et biologie du vieillissement, médecine générale, addictologie
DELAPORTE Eric	Maladies infectieuses ; maladies tropicales
DEMOLY Pascal	Pneumologie ; addictologie
DOMERGUE Jacques	Chirurgie viscérale et digestive
DUFFAU Hugues	Neurochirurgie
ELIAOU Jean François	Immunologie
FABRE Jean Michel	Chirurgie viscérale et digestive
FRAPIER Jean-Marc	Chirurgie thoracique et cardiovasculaire
HAMAMAH Samir	Biologie et Médecine du développement et de la reproduction ; gynécologie médicale

HEDON Bernard	Gynécologie-obstétrique ; gynécologie médicale
HERISSON Christian	Médecine physique et de réadaptation
JABER Samir	Anesthésiologie-réanimation et médecine péri-opératoire
JEANDEL Claude	Médecine interne ; gériatrie et biologie du vieillissement, médecine générale, addictologie
JONQUET Olivier	Médecine intensive-réanimation
JORGENSEN Christian	Thérapeutique ; médecine d'urgence ; addictologie
KOTZKI Pierre Olivier	Biophysique et médecine nucléaire
LABAUGE Pierre	Neurologie
LARREY Dominique	Gastroentérologie ; hépatologie ; addictologie
LEFRANT Jean-Yves	Anesthésiologie-réanimation et médecine péri-opératoire
LUMBROSO Serge	Biochimie et Biologie moléculaire
MARTY-ANE Charles	Chirurgie thoracique et cardiovasculaire
MERCIER Jacques	Physiologie
MESSNER Patrick	Cardiologie
MONDAIN Michel	Oto-rhino-laryngologie
MORIN Denis	Pédiatrie
PAGEAUX Georges-Philippe	Gastroentérologie ; hépatologie ; addictologie
PUJOL Pascal	Biologie cellulaire
QUERE Isabelle	Chirurgie vasculaire ; médecine vasculaire (option médecine vasculaire)
RENARD Eric	Endocrinologie, diabète et maladies métaboliques ; gynécologie médicale
REYNES Jacques	Maladies infectieuses, maladies tropicales
RIPART Jacques	Anesthésiologie-réanimation et médecine péri-opératoire
ROUANET Philippe	Cancérologie ; radiothérapie
SOTTO Albert	Maladies infectieuses ; maladies tropicales
TAOUREL Patrice	Radiologie et imagerie médicale
VANDE PERRE Philippe	Bactériologie-virologie ; hygiène hospitalière
YCHOU Marc	Cancérologie ; radiothérapie

PU-PH de 1^{re} classe

AGUILAR MARTINEZ Patricia	Hématologie ; transfusion
ASSENAT Éric	Gastroentérologie ; hépatologie ; addictologie
AVIGNON Antoine	Nutrition
AZRIA David	Cancérologie ; radiothérapie
BAGHDADLI Amaria	Pédopsychiatrie ; addictologie
BEREGI Jean-Paul	Radiologie et imagerie médicale
BLANC Pierre	Gastroentérologie ; hépatologie ; addictologie
BORIE Frédéric	Chirurgie viscérale et digestive
BOULOT Pierre	Gynécologie-obstétrique ; gynécologie médicale
CAMBONIE Gilles	Pédiatrie
CAMU William	Neurologie
CANOVAS François	Anatomie
CAPTIER Guillaume	Anatomie
CARTRON Guillaume	Hématologie ; transfusion
CAYLA Guillaume	Cardiologie
CHANQUES Gérald	Anesthésiologie-réanimation et médecine péri-opératoire
CORBEAU Pierre	Immunologie
COSTES Valérie	Anatomie et cytologie pathologiques
COULET Bertrand	Chirurgie orthopédique et traumatologique
CYTEVAL Catherine	Radiologie et imagerie médicale
DADURE Christophe	Anesthésiologie-réanimation et médecine péri-opératoire
DAUVILLIERS Yves	Physiologie
DE TAYRAC Renaud	Gynécologie-obstétrique, gynécologie médicale
DE VOS John	Histologie, embryologie et cytogénétique
DEMARIA Roland	Chirurgie thoracique et cardio-vasculaire

DEREURE Olivier	Dermatologie - vénéréologie
DROUPY Stéphane	Urologie
DUCROS Anne	Neurologie
DUPEYRON Arnaud	Médecine physique et de réadaptation
FESLER Pierre	Médecine interne ; gériatrie et biologie du vieillissement, médecine générale, addictologie
GARREL Renaud	Oto-rhino-laryngologie
GENEVIEVE David	Génétique
HAYOT Maurice	Physiologie
KLOUCHE Kada	Médecine intensive-réanimation
KOENIG Michel	Génétique
LAFFONT Isabelle	Médecine physique et de réadaptation
LAVABRE-BERTRAND Thierry	Histologie, embryologie et cytogénétique
LAVIGNE Jean-Philippe	Bactériologie-virologie ; hygiène hospitalière
LE MOING Vincent	Maladies infectieuses ; maladies tropicales
LECLERCQ Florence	Cardiologie
LEHMANN Sylvain	Biochimie et biologie moléculaire
MARIANO-GOULART Denis	Biophysique et médecine nucléaire
MATECKI Stéfan	Physiologie
MEUNIER Laurent	Dermato-vénéréologie
MOREL Jacques	Rhumatologie
NAVARRO Francis	Chirurgie viscérale et digestive
NOCCA David	Chirurgie viscérale et digestive
PETIT Pierre	Pharmacologie fondamentale ; pharmacologie clinique ; addictologie
PERNEY Pascal	Médecine interne ; gériatrie et biologie du vieillissement, médecine générale, addictologie
PRUDHOMME Michel	Anatomie
PUJOL Jean Louis	Pneumologie ; addictologie
PURPER-OUAKIL Diane	Pédopsychiatrie ; addictologie

TOUITOU Isabelle

Génétique

TRAN Tu-Anh

Pédiatrie

VERNHET Hélène

Radiologie et imagerie médicale

PU-PH de 2ème classe

BOURDIN Arnaud

Pneumologie ; addictologie

CANAUD Ludovic

Chirurgie vasculaire ; médecine vasculaire (option chirurgie vasculaire)

CAPDEVIELLE Delphine

Psychiatrie d'Adultes ; addictologie

CLARET Pierre-Géraud

Médecine d'urgence

COLOMBO Pierre-Emmanuel

Cancérologie ; radiothérapie

COSTALAT Vincent

Radiologie et imagerie médicale

CUVILLON Philippe

Anesthésiologie-réanimation et médecine péri-opératoire

DAIEN Vincent

Ophtalmologie

DORANDEU Anne

Médecine légale et droit de la santé

FAILLIE Jean-Luc

Pharmacologie fondamentale ; pharmacologie clinique ; addictologie

FUCHS Florent

Gynécologie-obstétrique ; gynécologie médicale

GABELLE DELOUSTAL Audrey

Neurologie

GAUJOUX Viala Cécile

Rhumatologie

GODREUIL Sylvain

Bactériologie-virologie ; hygiène hospitalière

GUILLAUME Sébastien

Psychiatrie d'adultes ; addictologie

GUILPAIN Philippe

Médecine Interne, gériatrie et biologie du vieillissement; addictologie

GUIU Boris

Radiologie et imagerie médicale

HERLIN Christian

Chirurgie plastique, reconstructrice et esthétique, brûlologie

HOUEDE Nadine

Cancérologie ; radiothérapie

JACOT William

Cancérologie ; Radiothérapie

JUNG Boris

Médecine intensive-réanimation

KALFA Nicolas

Chirurgie infantile

KOUYOUMDJIAN Pascal	Chirurgie orthopédique et traumatologique
LACHAUD Laurence	Parasitologie et mycologie
LALLEMANT Benjamin	Oto-rhino-laryngologie
LE QUINTREC DONNETTE Moglie	Néphrologie
LETOUZEY Vincent	Gynécologie-obstétrique ; gynécologie médicale
LONJON Nicolas	Neurochirurgie
LOPEZ CASTROMAN Jorge	Psychiatrie d'Adultes ; addictologie
LUKAS Cédric	Rhumatologie
MAURY Philippe	Chirurgie orthopédique et traumatologique
MILLET Ingrid	Radiologie et imagerie médicale
MORANNE Olivier	Néphrologie
MURA Thibault	Biostatistiques, informatique médicale et technologies de la communication
NAGOT Nicolas	Biostatistiques, informatique médicale et technologies de la communication
PANARO Fabrizio	Chirurgie viscérale et digestive
PARIS Françoise	Biologie et médecine du développement et de la reproduction ; gynécologie médicale
PASQUIE Jean-Luc	Cardiologie
PELLESTOR Franck	Histologie, embryologie et cytogénétique
PEREZ MARTIN Antonia	Chirurgie vasculaire ; médecine vasculaire (option médecine vasculaire)
POUDEROUX Philippe	Gastroentérologie ; hépatologie ; addictologie
RIGAU Valérie	Anatomie et cytologie pathologiques
RIVIER François	Pédiatrie
ROGER Pascal	Anatomie et cytologie pathologiques
ROSSI Jean François	Hématologie ; transfusion
ROUBILLE François	Cardiologie
SEBBANE Mustapha	Médecine d'urgence
SIRVENT Nicolas	Pédiatrie
SOLASSOL Jérôme	Biologie cellulaire



STOEBNER Pierre	Dermato-vénérologie
SULTAN Ariane	Nutrition
THOUVENOT Éric	Neurologie
THURET Rodolphe	Urologie
VENAIL Frédéric	Oto-rhino-laryngologie
VILLAIN Max	Ophthalmologie
VINCENT Denis	Médecine interne ; gériatrie et biologie du vieillissement, médecine générale, addictologie
VINCENT Thierry	Immunologie
WOJTUSCISZYN Anne	Endocrinologie-diabétologie-nutrition

PROFESSEURS DES UNIVERSITES

1^{re} classe :

COLINGE Jacques (Cancérologie, Signalisation cellulaire et systèmes complexes)

2^{ème} classe :

LAOUDJ CHENIVESSE Dalila (Biochimie et biologie moléculaire)

VISIER Laurent (Sociologie, démographie)

PROFESSEURS DES UNIVERSITES - Médecine générale

1^{re} classe :

LAMBERT Philippe

2^{ème} classe :

AMOUYAL Michel

PROFESSEURS ASSOCIES - Médecine Générale

CLARY Bernard

DAVID Michel

GARCIA Marc

PROFESSEURS ASSOCIES - Médecine

BESSIS Didier (Dermato-vénérologie)

MEUNIER Isabelle (Ophtalmologie)

MULLER Laurent (Anesthésiologie-réanimation et médecine péri-opératoire)

PERRIGAULT Pierre-François (Anesthésiologie-réanimation et médecine péri-opératoire)

QUANTIN Xavier (Pneumologie)

ROUBERTIE Agathe (Pédiatrie)

VIEL Eric (Soins palliatifs et traitement de la douleur)

Maîtres de Conférences des Universités - Praticiens Hospitaliers

MCU-PH Hors classe

BADIOU Stéphanie	Biochimie et biologie moléculaire
BOULLE Nathalie	Biologie cellulaire
CACHEUX-RATABOUL Valère	Génétique
CARRIERE Christian	Bactériologie-virologie ; hygiène hospitalière
CHARACHON Sylvie	Bactériologie-virologie ; hygiène hospitalière
FABBRO-PERAY Pascale	Epidémiologie, économie de la santé et prévention
GIANSILY-BLAIZOT Muriel	Hématologie ; transfusion
HILLAIRE-BUYS Dominique	Pharmacologie fondamentale ; pharmacologie clinique ; addictologie
PUJOL Joseph	Anatomie
RICHARD Bruno	Médecine palliative
RISPAIL Philippe	Parasitologie et mycologie
SEGONDY Michel	Bactériologie-virologie ; hygiène hospitalière

MCU-PH de 1^{re} classe

BERTRAND Martin	Anatomie
BOUDOUSQ Vincent	Biophysique et médecine nucléaire
BOURGIER Céline	Cancérologie ; Radiothérapie
BRET Caroline	Hématologie biologique
COSSEE Mireille	Génétique
GIRARDET-BESSIS Anne	Biochimie et biologie moléculaire
LAVIGNE Géraldine	Hématologie ; transfusion
LESAGE François-Xavier	Médecine et Santé au Travail
MATHIEU Olivier	Pharmacologie fondamentale ; pharmacologie clinique ; addictologie
MENJOT de CHAMPFLEUR Nicolas	Radiologie et imagerie médicale
MOUZAT Kévin	Biochimie et biologie moléculaire
OLIE Emilie	Psychiatrie d'adultes ; addictologie
PANABIERES Catherine	Biologie cellulaire
PHILIBERT Pascal	Biologie et médecine du développement et de la reproduction ; gynécologie médicale
RAVEL Christophe	Parasitologie et mycologie
SCHUSTER-BECK Iris	Physiologie
STERKERS Yvon	Parasitologie et mycologie
THEVENIN-RENE Céline	Immunologie
TUAILLON Edouard	Bactériologie-virologie ; hygiène hospitalière

MCU-PH de 2^{ème} classe

CHIRIAC Anca	Immunologie
DE JONG Audrey	Anesthésiologie-réanimation et médecine péri-opératoire
DU THANH Aurélie	Dermato-vénérologie
GOUZI Farès	Physiologie



HERRERO Astrid	Chirurgie viscérale et digestive
JEZIORSKI Éric	Pédiatrie
KUSTER Nils	Biochimie et biologie moléculaire
MAKINSON Alain	Maladies infectieuses, Maladies tropicales
PANTEL Alix	Bactériologie-virologie ; hygiène hospitalière
PERS Yves-Marie	Thérapeutique; addictologie
ROUBILLE Camille	Médecine interne ; gériatrie et biologie du vieillissement ; addictologie
SZABLEWSKY	Anatomie et cytologie pathologiques

Maîtres de Conférences des Universités - Médecine Générale

MCU-MG de 1^{re} classe

COSTA David

MCU-MG de 2^{ème} classe

FOLCO-LOGNOS Béatrice

OUDE ENGBERINK Agnès

Maîtres de Conférences associés - Médecine Générale

LOPEZ Antonio

MILLION Elodie

PAVAGEAU Sylvain

REBOUL Marie-Catherine

SERAYET Philippe



Praticiens Hospitaliers Universitaires

BARATEAU Lucie	Physiologie
BASTIDE Sophie	Epidémiologie, économie de la santé et prévention
DAIEN Claire	Rhumatologie
GATINOIS Vincent	Histologie, embryologie et cytogénétique
GOULABCHAND Radjiv	Médecine interne ; gériatrie et biologie du vieillissement ; addictologie
LATTUCA Benoit	Cardiologie
MIOT Stéphanie	Médecine interne ; gériatrie et biologie du vieillissement ; addictologie
PINETON DE CHAMBRUN Guillaume	Gastroentérologie ; hépatologie ; addictologie
SOUCHE François-Régis	Chirurgie viscérale et digestive

REMERCIEMENTS AUX ENSEIGNANTS

À Monsieur le Professeur Pascal DEMOLY

C'est un honneur pour moi que vous présidiez mon jury de thèse.

Votre avis compte énormément pour moi. Merci également de m'avoir fait découvrir cette spécialité merveilleuse qu'est l'allergologie !

À Monsieur le Professeur Arnaud BOURDIN

Un grand merci de faire partie de mon jury, c'est un honneur pour moi que vous jugiez mon travail au vu de votre grande expertise dans le domaine de l'asthme chez l'adulte.

Merci enfin de m'avoir accueilli dans la grande famille de la pneumologie.

À Monsieur le Professeur Stefan MATECKI

Je vous remercie de faire partie de mon jury, ainsi que de m'avoir guidé et aidé dans l'élaboration du projet de ma thèse. J'espère que notre travail pourra apporter une pierre à l'édifice monstrueux, toujours en construction, qu'est l'asthme pédiatrique !

À Monsieur le Docteur Davide CAIMMI

Davide, mon directeur de thèse, mais surtout mon ami. Merci de m'avoir donné envie de travailler sur ce sujet palpitant qu'est la pneumo-pédiatrie. Je te dois beaucoup.

AUTRES REMERCIEMENTS

À ma famille :

Maman : À ma meilleur amie, ma confidente infallible (ou presque ! ;)). À toutes les joies et les peines qu'on a partagées ensemble, tous les tourments, car je sais que je ne suis pas forcément facile à vivre tous les jours ! ...C'est dur de synthétiser en quelques lignes tout ce que je voudrais te dire ! Alors je me contenterai de te dire merci pour tout, et surtout de m'avoir permis de devenir la personne que je suis aujourd'hui.

Papa : Mon modèle, le roc de la famille. Merci de nous supporter au quotidien, je sais que bien des fois ça n'a pas été facile d'être au milieu de filles qui se crêpent parfois (souvent ?) le chignon !! A toutes les fois où j'aurais dû t'écouter, et où tu m'as dit « je te l'avais bien dit », sans me juger pour autant. J'espère que tu seras fier de moi.

Lara : Mon petit Pokémon, ma soeur que j'aime par dessus-tout. Dieu sait qu'on a traversé des moments difficiles et que la santé n'a pas toujours été au rendez-vous, mais je suis tellement fière de la grande fille que tu es devenue.

Wallie : Ma grand-mère, ma deuxième maman. Je t'aime et je chérirai à jamais nos jours heureux.

Papi Gérard : A mon grand-père, dentiste mais surtout artiste et libre penseur. Merci pour toutes ses histoires rocambolesques que tu nous as racontées pour nous faire rire !

Mes grand parents paternels et Bruno : Au coté Saint-Gillois de ma famille, merci de votre soutien tout au long de mes études et de m'avoir offert l'asile politique les quelques fois où j'en ai eu besoin !!

Alex : Finalement ensemble après toutes ces années. On en a mis du temps avant de se trouver ! Mais au moins j'espère que maintenant, on ne se lâchera plus. Tellement heureuse de partager ta vie. Je t'aime.

Aux membres de ma belle-famille Florence, Claude, Marc et Ben : Merci de m'avoir si bien accueillie parmi vous !

Ma petite Légende : Tu es partie trop tôt ma puce, je te porte à jamais dans mon coeur... Merci d'avoir ensoleillé mes jours de déprime par ta bouille adorable, tes espiègleries et surtout tes câlineries. Encore maintenant, le simple fait de t'évoquer me met les larmes aux yeux.

Vanille, Hooligan, Titan : Ce n'est pas parce que le temps passe que je vous oublie pour autant... Merci d'avoir partagé notre vie de façon si aimante, ne serait-ce que le temps de quelques (trop courtes) années.

Ibuki : je sais que tu ne sais pas lire, la grosse. Mais je t'aime beaucoup quand même !

Rêveur : On ne se connaît que depuis ce matin, demi-patate/demi-peluche. Mais je sens qu'on va bien s'entendre.

Néo : Oui tu viens en dernier sur la liste, créature maléfique ! Ben écoute, je ne te remercie de rien, en fait... A part de bien faire rire Lara.

À mes chefs :

Du côté pneumo...

Clément : À nos paris foireux et toutes les choses que tu m'as enseigné ! Je t'admire sur beaucoup de plans, s'il te plaît reste toujours aussi agréable et compétent, car c'est ce qui fait ta particularité (je veux dire, en plus des blagues en dessous de la ceinture bien sûr...).

Stephan : Merci pour ta gentillesse incommensurable ! Tu es une des personnes les plus attentionnées et dévouées que je connaisse. Merci également pour ton style vestimentaire « dérangeant » comme tu dis si bien, dédicace spéciale au petit tag rose de tes baskets... Et enfin pour ton fameux « JE L'AIIII JEAN PIERRE !!!! » légendaire, qui est venu ponctuer tellement de fibro (mais pas que !) par la suite !!

Romain : Notre Roro international, sans qui on s'ennuierait dans la file pour manger à l'internat, s'il ne critiquait pas tout le monde sans arrêt. Pour toutes les fois aussi où tu nous as bien fait rire quand tu disais « ça m'énerve !!! » ! Non mais tu fais d'autres trucs cools aussi, je te rassure.

Paul : Même si tu as beaucoup trop squatté la chambre de garde, je ne t'en tiens pas rigueur. Plus sérieusement, vraiment sympa de travailler avec toi !

Margot : Un grand merci pour ta bonne humeur, ton enthousiasme et nos petites sessions « bitchage » qui m'ont bien souvent remontées le moral !!! Même si tu préfères être une moule plutôt qu'une huître (« les vrais le sachent »), tu es vraiment cool comme fille. Et un gros bisou à Bruce, en passant !

Mathilde : On n'a pas énormément travaillé ensemble au final, mais c'était toujours avec plaisir !! Merci d'avoir apporté une cohésion dans cette famille qu'est la pneumo !

Jérémy : À mon confrère biterrois, tuberculologue mais tout d'abord et surtout tabacologue ! Merci pour toutes tes fréquents traits d'humour bien caustiques comme il faut (souvent très drôles il faut l'avouer...) et tous ces moments gênants en staff où on ne savait pas si tu bluffais ou pas...!

Benoit : Solide comme le rock ! (Sauf quand ça se gamèle à vélo...) Merci pour ta gentillesse et ta dévotion ! A nos longs soirs de galère en pneumo A, où on se disait qu'on allait finir plus quand même tôt le lendemain, alors que non !

Anne-Sophie : Merci pour tout ce que tu m'as appris, tu es vraiment un médecin remarquable, tant au niveau des connaissances que sur le plan humain ! Reste comme tu es !

Jean-Pierre : Merci pour tout ce que tu m'as appris notamment au niveau des gestes, mais aussi pour nous avoir appris d'autres choses, moins conventionnelles, comme par exemple les dépigmentations d'endroits qui voient rarement le soleil... Enfin bref !! Toujours un plaisir de travailler avec toi et ta bonne humeur !

Mohammad : Merci pour ta confiance lors des gestes et ton calme imperturbable, tu m'as beaucoup appris ! Merci aussi de m'avoir prêté ta veste pour éviter de mourir de froid durant les pauses café !!

...Et du côté allergeo !

Luciana : à mon amie moitié chinoise, moitié japo-brésilienne (je sais que tu vas râler beaucoup pour ça ! Mais j'assume totalement.) On pourrait disserter des heures sur pourquoi tu es extra, mais je dois faire court, alors soit. Merci pour ton légendaire cri strident appelant « DAVIDE !! », qui résonnera à jamais dans ses couloirs d'allergologie mais aussi dans tous nos esprits. Enfin, et surtout : merci de ne plus jamais préparer de Caïpi. Vraiment, je t'en serais vraiment -VRAIMENT-reconnaissante... Et aussi si tu pouvais effacer toutes les preuves photos ce serait sympa...

Nidhal : A nos fous rires, nos gossips et nos folles soirées ! Tu as été une super chef ! Merci pour tout ! En espérant re-travailler avec toi !

Jean-Luc : Merci pour ta présence apaisante, ta bonne humeur, mais aussi tes histoires de consultations totalement loufoques, tes IgE candida albicans -parce que « ça sert sans doute à rien, mais j'ai trouvé ça marrant » -, et surtout tes fameux mocassins bleus !

Anca : merci pour tout ce que tu nous as appris (surtout avec tes petits schémas) !! Tu es un médecin très compétent que je respecte beaucoup. Au plaisir de travailler avec toi ces deux prochaines années, et d'apprendre de nouvelles choses à ton contact.

Linnéa : nous n'avons pas eu beaucoup l'occasion de travailler ensemble (en même temps, quelle idée saugrenue de vouloir être enceinte pendant mon stage !! ;)) mais ce fut toujours un plaisir !

À l'équipe de pneumo de Béziers : Merci de m'avoir mis le pied à l'étrier lors de mon premier semestre ! J'ai beaucoup appris avec vous, ce qui m'a permis d'être rapidement autonome sur beaucoup de choses. J'ai hâte que nous retravaillions tous ensemble durant ces deux années d'assistantat ! A très vite !

À tous les autres chefs : Merci pour tout ce que vous m'avez appris sur cette longue route qu'est la médecine.

À mes co-internes :

Elodie : Oui je te mets dans les internes, parce que tu resteras pour toujours ma co interne de galère des débuts, ma confidente de pneumo A et B. A tous nos fous rires et nos pleurs !

Agathe et Tiana : Mes co internes depuis toujours ! On a fait un sacré bout de chemin toutes ensemble. Cela a toujours été avec plaisir !

Engi : À ma co interne de mes 6 derniers mois mais aussi à notre maman à tous, merci pour toutes ses années où tu nous as guidé et aidé à grandir !

Evangéline : Petite par la taille, mais grande par la présence ! A ma petite soeur de l'allergologie, avec qui on a passé un superbe semestre.

Marine : Marinette !! Merci pour ta bonne humeur, ton calme et ta gentillesse, ça a été un plaisir de travailler avec toi, tu nous manques maintenant que tu es partie dans cet endroit froid, et inhospitalier qu'est la région parisienne !

Juliette : C'était très « sympaaa » de travailler ensemble !! A nos discussions sur les mecs et le Japon (j'espère quand même qu'on y pourra partir l'an prochain !) !

Maëlle et Arthur : Au plaisir de retravailler avec vous prochainement !

Marion : Ma co interne qui a rejoint le coté obscur de l'allergologie ! Hâte de retravailler avec toi !

Flora et Quentin L. : On a pas souvent travaillé ensemble au final, mais c'était toujours avec grand plaisir !

Zak et Laure : Le binôme de choc, merci pour la cohésion et la bonne humeur que vous avez apporté dans l'équipe !

Zélie : Merci pour ton calme et ta gentillesse ! C'était très agréable de travailler avec toi.

Quentin W. : Le benjamin de notre team hiver 2019, c'était un plaisir de travailler ensemble !

Bénédicte et Gaspard : On n'a pas (encore) eu l'occasion de travailler ensemble, mais bienvenue dans cette grande famille qu'est la pneumologie !!

À mes autres amis :

Marcin : « Mon ami slave » qui lit Proust en buvant du cognac ! Merci pour toutes ces réflexions décalées qui nous font si souvent rire et le fameux hymne du service dont tu es à l'origine !

Bérangère : Parce que l'allergologie sans Bébé, ben ce serait pas drôle. Hâte de voir tes prochaines photos de vacances les doigts de pieds en éventail à Cancun !!

Fabian, Hosam et Aleks : Merci à la dream team pour votre soutien ! Hâte de vivre de nouvelles aventures avec vous !

Elodie et Robin : A nos soirées jeux de société !! Je suis contente d'avoir pu croiser votre route grâce à Alex, vous êtes vraiment des gens bien. Et je ne le dis pas souvent !

Enfin un grand merci à tous nos autres potes, avec qui c'est toujours tellement sympa de passer du temps, merci à vous aussi pour votre soutien !

Mais aussi :

À tous mes petits externes (enfin, presque tous), qui ont dû faire semblant pendant tout leur stage de comprendre ce que je leur expliquais.

Aux infirmières, aux AS, aux secrétaires ainsi qu'au reste de l'équipe de pneumologie et d'allergologie : un plaisir d'avoir travaillé avec tout ce petit monde pendant tout mon internat. Désolée d'avoir été un tel chat noir pendant mes gardes !! Promis c'était pas fait exprès...

Et en avant pour de nouvelles aventures !!!

Table des matières

INTRODUCTION.....	24
MATERIALS AND METHODS	26
A. Study Design	26
B. Population and collected data	26
C. Outcomes of the study	27
D. Statistical analysis.....	27
RESULTS	29
A. Included population	29
B. Primary outcome	29
C. Obstruction criterion and small airways criterion	30
D. Best criteria to predict asthma diagnosis.....	30
E. Subgroup analysis based on asthma severity.....	31
DISCUSSION	33
CONCLUSION	37
REFERENCES	38
FIGURES	41
Figure 1 – Patients included in the study.....	41
Figure 2 – Reversibility criteria ($FEV_1/FVC < 90\%$ and increase in $FEV_1 > 12\%$) after bronchodilation test in all 871 included children.	42
Figure 3 – Best option for cumulative sensitivity of different variables to predict a diagnosis of asthma in children.....	43
TABLES	44
Table 1 – Characteristics of the population included in the study.	44
Table 2 – Sensitivity of the reversibility criteria in children proposed by GINA guidelines for FEV_1 , of bronchial obstruction in children, of the reversibility criteria for FEF_{25-75} , and of the association or either the reversibility of the FEV_1 criterion or the FEF_{25-75} , in the overall population and in the subgroups based on asthma severity patient’s age, and country of origin.	45
Table 3 – Sensitivity of the different clinical criteria in the whole cohort of 871 children, in the subgroup of patients in which normal FEV_1/FVC , in those with $FEV_1/FVC < 90\%$ and an increase in $FEV_1 < 12\%$ after bronchodilation, and in those presenting with reversibility criteria.....	46
Table 4 – Characteristics of the population, per asthma severity.....	47

**VERIFICATION OF FEV₁ REVERSIBILITY CRITERIA ACCORDING TO
GINA RECOMMENDATIONS IN ASTHMATIC CHILDREN:
THE VERI-VEMS RETROSPECTIVE COHORT STUDY**

Glossary:

AIT = Allergen Immunotherapy

BMI = body mass index

FEV₁ = forced expiration volume in 1 second

FVC = forced vital capacity

FEF₂₅₋₇₅ = forced expiratory flow 25-75%

GINA = Global Initiative for Asthma

IgE = Immunoglobulin E

PFT = pulmonary function test

SD = standard deviation

Se = sensitivity

SPT = skin prick test

INTRODUCTION

Asthma is a chronic inflammatory disorder of the bronchi, associated to airflow hyper-reactivity, and possibly leading to acute symptoms, that are reversible either spontaneously or after appropriate bronchodilator treatment^{1,2}. With both prevalence and incidence increasing over the last decades, asthma is a major public health problem³⁻⁵. Almost 300 million people in the world suffer from this disease, and such an evaluation may underestimate the actual prevalence, given the fact that asthma is often underdiagnosed⁴. Many studies have tried to explain the recent increase in prevalence for both asthma and atopic diseases¹, and possible causes may include the « hygiene hypothesis », the use of endocrine disruptor and chemical treatments in agriculture or industry, and the increased pollution of air and waters. Recent studies consider that the strongest risk for developing asthma include an association of both genetic factors and environmental exposures (such as indoor and outdoor allergens, tobacco smoke, air pollution, chemical irritants...)³. The actual consensus consists of a mix of all listed risk factors, making of asthma a multi-factorial disease⁶.

Asthma is a very heterogeneous disorder with multiple clinical phenotypes³. Considering the pediatric population, asthma is the most frequent chronic non-communicable disease, and the leading cause of childhood morbidity, mainly caused by acute exacerbations characterized by breathlessness, wheezing, chest tightness, and/or cough⁷. It is also associated to a high rate of ER visits, hospitalizations, absenteeism from school and presenteeism, and still contributes to many deaths amongst young people even in developed countries^{2,8}. This condition often begins in early childhood, with an earlier onset in males, and initially with intermittent symptoms, especially occurring during viral respiratory tract infections. Other possible triggers include allergies, physical exercise, cold air, extreme emotional arousal, and even some drugs (aspirin, non-steroid anti-inflammatory drugs, or beta-blockers)^{3,9,10}. In pediatrics, known predisposition factors include a family history of asthma, atopy, allergic rhinitis, low birth weight or a history of multiple wheezing episodes during the first two years of life¹¹⁻¹⁵. In children, the disease may express itself through different pathways: while

some patients will have lifelong asthma with active symptoms and progressive lung function loss over time, other children will undergo asthma remission during adolescence¹⁶⁻¹⁸. In this latter group, symptoms may remain quiescent or may relapse in mid-adult life leading clinicians to speculate that the absence of symptoms does not correlate with a full recovery from the disease.

In general, asthma is known to be a chronic disease, tending to present as a life-time condition^{19,20}.

For such reason, an appropriate management with a correct and prompt diagnosis is crucial to control symptoms and therefore reduce asthma burden and increase patients' quality of life. GINA international guidelines advise to perform pulmonary function tests (PFTs) to diagnose asthma, both in children and adults. Diagnostic criteria in children require a FEV₁/FVC ratio lower than 90% and an increase of 12% of their FEV₁ after bronchodilation test, based on what was observed in adults^{4,21-23}. Nevertheless, the bronchodilation test following GINA recommendations, cannot be performed in children younger than 5 years, due to age-related difficulties in achieving test-satisfying controlled expirations^{4,12,24,25}. The increase of the FEF₂₅₋₇₅ after bronchodilation has also been proposed in children to corroborate the diagnosis, but studies seem not to be conclusive^{26,27}. Also, the accuracy of these criteria is debated in children and other possible diagnostic methods have been investigated^{28,29}. Indeed, in clinical practice, clinical signs and response to inhaled therapy are currently considered by pediatricians as the most useful tools to suspect and then diagnose asthma in children^{30,31}.

The aim of the present study was to verify the sensitivity of the reversibility criterion proposed by GINA recommendations (the increase of 12% of the FEV₁), and to look for other variables possibly able to show a satisfying sensitivity for a diagnosis of asthma in children.

MATERIALS AND METHODS

A. Study Design

We conducted a multicenter retrospective cohort study that included data from January 2008 to January 2019. Data were collected at the Pediatric and at the Allergy Unit of the University Hospital of Montpellier, France, and at the Immunology and Allergy Pediatric Unit of the University Hospital of Pavia, Italy.

The study was approved by a local ethical committee, in Montpellier (2019_IRB-MTP_01-06), and validated by the Ethical Committee of the University Hospital of Pavia. The study was registered on ClinicalTrials.gov (ID: NCT03814018).

B. Population and collected data

We included all consecutive children, followed by each center, with a diagnosis of asthma, made by a specialist of pediatric asthma, and who performed a PFT at the time of the diagnosis. Diagnosis of asthma had to be reached between their 5th and their 18th anniversary.

Patients with any documented diagnosis of other obstructive disease (such as cystic fibrosis, or ciliary dyskinesia), cancer, and bronchopulmonary dysplasia were excluded from the study. All those children with a diagnosis of asthma, but who did not perform, for any reason, a PFT at the time of the diagnosis were excluded as well.

In each patient, we collected demographic information (height, weight, age at diagnosis, sex), country of provenance (either France or Italy), PFT results at the time of the diagnosis, asthma severity (based on prescribed treatment and GINA guidelines), clinical information (presented symptoms, treatment efficacy after the first consultation, personal history of bronchiolitis/recurrent wheezing during the first two years of life, qualitative improvement – yes or no – of symptoms due to treatment, judged

by the physician during a follow-up consultation). Presence of atopic comorbidities was evaluated as well, including atopy, defined as sensitization to at least one common respiratory allergen (including *Dermatophagoides pteronissinus*, *Dermatophagoides farinae*, grass, cypress, birch, cat, dog, *Alternaria alternata*); allergic rhinitis, defined as the presence of typical disease symptoms due to exposure to an airborne allergen to which the patients are sensitized; food allergy, defined as the appearance of hypersensitivity symptoms related to consumption of a food allergen to which the patients are sensitized, or a positive food challenge to the culprit food; atopic dermatitis.

C. Outcomes of the study

The primary outcome of this study was to assess the reversibility criterion proposed by GINA guidelines of an increase of 12% of FEV₁ after bronchodilation test.

The secondary end points were: (i) to verify if the definition of obstructive syndrome in children, as proposed by GINA guidelines (FEV₁/FVC < 90%) could be applied in clinical settings; (ii) to evaluate if the reversibility of small airways (FEF₂₅₋₇₅) defined as an increase greater than 30% after bronchodilation test from basal values, is sensible in discriminating asthmatic children; (iii) to assess which spirometric and clinical variables could correlate to the best sensitivity for the diagnosis of asthma; and (iv) to evaluate, in a subgroups analysis, possible correlations between asthma severity and comorbidities.

D. Statistical analysis

Continuous variables were summarized with descriptive statistics (number, mean, SD), while frequency counts and percentages were provided for categorical data. Statistics were computed for patients with available (i.e. non-missing) data. Comparison of patient characteristics was assessed after grouping patients as for asthma severity (persistent severe, persistent moderate, persistent mild,

and intermittent asthma). We used the Student's *t*-test for data in case of continuous variables and the chi-square test for categorical variables. Differences between groups were considered statistically significant if *p*-values were <0.05.

All analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC, USA).

RESULTS

A. Included population

We included a total of 888 children with a diagnosis of asthma reached between January 2008 and January 2019. 17 of them were excluded from the analysis because of missing data (Figure 1).

342 patients were included from the Montpellier University Hospital: 219 of them (64.0%) were males; their mean age at diagnosis was 9.2 years (SD 3.4). 529 patients were included from the Pavia University Hospital: 329 of them (62.2%) were males; their mean age at diagnosis was 9.3 years (SD 3.2). The two populations were not statistically different, when considering their sex and their age (*p-value*: 0.5825 and 0.6605, respectively). Moreover, basal FEV₁ values did not differ between the French and Italian population (1800 mL and 1900 mL, respectively; *p-value*: 0.0728). For all the above reasons, statistical analysis was performed considering the two groups as a single cohort.

An interesting difference between the two populations concerned the prescription of anti-IgE therapy and of Allergen Immunotherapy (AIT): patients were significantly more treated with the monoclonal antibody in the Italian group (5.3% vs. 3.2%; *p-value* < 0.0001), and more AIT treatments were prescribed in the French population (17.0% vs. 8.1%; *p-value* < 0.0001). Another difference concerned sensitization to cypress and birch pollen: in fact, cypress pollen allergy is very common in the Montpellier area, but not in the Pavia area. The opposite consideration is true for birch pollen allergy. We considered these differences very unlikely to influence our objectives.

Characteristics of the children included in the study are shown in Table 1.

B. Primary outcome

The reversibility criterion of an increase of at least 12% of the FEV₁ after bronchodilation test was confirmed in only 266 out of 871 children (Figure 2), with a sensitivity (Se) of 30.4% (Table 2). When

considering children with a $FEV_1/FVC < 90\%$, the reversibility criterion showed a 23.5% sensitivity, being recorded in 205 children only.

Considering this outcome, there was no significant difference between the two centers (31.0% and 30.1% sensitivity in the French and Italian population, respectively). Moreover, the mean change in FEV_1 after bronchodilation was similar in the two centers as well (8.1% with 13.1% of SD, and 8.3% with 8.8% of SD, respectively; *p-value*: 0.7876).

C. Obstruction criterion and small airways criterion

The obstruction criterion proposed by GINA guidelines for children ($FEV_1/FVC < 90\%$) was valid for 595 children at diagnosis, with a sensitivity of 67.5% overall (Table 2). The mean value of the FEV_1/FVC ratio in the entire cohort was 85% (SD 10%).

The increase of more than 30% in FEF_{25-75} after bronchodilation test was only found in 198 children in our cohort (Se 21.9%), with a mean value of 22.1% (SD 30.0%) (Table 2). Furthermore, older children (>11 years group) were also less likely to achieve this reversibility criterion, compared with patients with less than 7 years of age, or between 7 and 11 years (15.1%, 24.9%, and 23.8%, respectively).

D. Best criteria to predict asthma diagnosis

To assess the variables providing the best sensitivity to predict asthma diagnosis, we included in the analysis both the spirometric criteria ($FEV_1/FVC < 90\%$, change in $FEV_1 > 12\%$, change in $FEF_{25-75} > 30\%$), and the clinical ones (dry cough, tight chest, wheezing, pre-school wheezing, exercise-induced dyspnea, atopy, presence of allergic comorbidities). The best single criterion was the presence of “dry cough” (Se 90.9%). Sensitivity of each criterion is shown in Table 3.

The best two combined criteria were “dry cough and atopy” (Se 98.5%), followed by both “dry cough

and wheezing” or “dry cough and allergic comorbidities” (Se of 97.7%).

Furthermore, the best three criteria to predict asthma were “dry cough, wheezing and atopy”, and “dry cough, wheezing and exercise-induced dyspnea”, with both a sensitivity of 99.5%. The combination of the previously mentioned four criteria (dry cough, wheezing, atopy and exercise-induced dyspnea) was associated to a sensitivity of 100% (Figure 3). In no case, adding spirometric parameters improved the cumulative sensitivity for the diagnosis of asthma. Moreover, when comparing the sensitivity of the different clinical parameters between the subgroup of 383 children with $FEV_1/FVC < 90\%$, but without FEV_1 reversibility and the 205 patients with reversibility criteria, we found no significant difference neither between the groups, nor between each group and the whole cohort of patients (Table 3).

If we consider the follow-up of patients with a diagnosis of asthma, and include the response to the prescribed treatment after the first visit, such criterion was verified in 819 children, and showed therefore the best sensitivity (Se 94.0%), but it cannot be used when first assessing a patient.

E. Subgroup analysis based on asthma severity

The number of included patients significantly differed in each asthma severity subgroup (respectively for severe, moderate, mild persistent and intermittent asthma: 55, 581, 203, 32; all *p-values* $< 0,005$) (Table 4). The small number of patients included in the « intermittent » group could mainly be explained by the fact they are not representative of the average patient consulting at a tertiary University Hospital, and are therefore under-represented, if compared with the general population. Sex and BMI were not statistically different between those four groups (*p-values* $< 0,05$).

The mean improvement in FEV_1 after bronchodilation was higher when the severity was greater: the severe asthma group showed a significantly higher increase in FEV_1 than the moderate asthma group (13.2% (SD 18.2) and 8.9% (SD 10.7), respectively; *p-value*: 0.0084) and the mild group (5.0% (SD 6.9), *p-value* < 0.0001). The same significant difference was also highlighted between the moderate

and the mild group as well ($p\text{-value} < 0.0001$). There was no significant difference when we compared the intermittent group with any other severity group. When we assessed patients presenting an increase of at least 12% in their FEV₁, there was a significant difference ($p\text{-value} < 0.05$) in sensitivity between patients suffering from mild persistent asthma (16.3% of increase in FEV₁, in 33 children) and both moderate persistent asthma (34.3%, $n=199$, $p\text{-value} < 0.0001$) and severe persistent asthma (41.8%, $n=23$, $p\text{-value} < 0.0001$), meaning that, as persistent asthma becomes more severe, the increase in FEV₁ criterion showed a higher sensitivity.

When considering the mean basal obstruction criterion, we found lower values as asthma was more severe. The mean basal FEV₁/FVC was 79.5% (SD 10.5%) in the severe asthma group, 84.1% (SD 9.7%) in the moderate group ($p\text{-value}: 0,0009$), and 87.7% (SD 8.5%) in the mild one ($p\text{-value} < 0.0001$). When we assessed the FEV₁/FVC < 90% criterion per asthma severity, there was a significant difference ($p\text{-value} < 0.005$) between each subgroup, showing that when asthma is more severe, patients present increasing obstructive spirometric values (87.5%, 72.1%, 53.2%, in the mild, moderate, and severe persistent asthma subgroups, respectively).

On the other hand, the mean change in FEF₂₅₋₇₅, was not statistically different between the four severity groups.

Atopy had a significant impact on asthma severity: we found more atopic patients in the severe group (51 patients, 92.7%), compared with the moderate and mild groups (78.3% ($p\text{-value}: 0.0113$) and 73.4% ($p\text{-value}: 0.0023$), respectively). Considering specific respiratory allergens and food allergy, there was no significant difference between the groups.

When analyzing the French vs. the Italian cohort separately, we did not find any difference regarding our outcome results (data not shown).

DISCUSSION

Asthma is a common disease in children and it is probably underdiagnosed. International GINA criteria propose that, in pediatric patients with obstructive signs at PFTs, an increase in FEV₁ of 12% after bronchodilation test is suggestive of a proper diagnosis^{4,28}. Through the present multicenter study, we wanted to assess the applicability of this criterion and its sensitivity in a real-life setting. No study strongly affirms that the 12% threshold is an adequate cut-off value to diagnose asthma in children. Even in the GINA guidelines, this threshold is not justified by clinical trials, but only based on a specialists' agreement. In our study, this reversibility criterion showed a very low sensitivity (30.4%), as a diagnostic tool for asthma in pediatrics. Thus, such a criterion does not seem to be applicable to children, if compared to adults, as previously highlighted in other studies³².

In 2016, Hopp et al. proposed a literature review to search for the evidence that the 12% threshold was appropriate to diagnose asthma in children²⁹. The authors found that most studies reported that a smaller improvement in FEV₁ should be applicable in children, and then suggested an alternative interpretative strategy, which our results support. Several authors indeed searched for a different cut-off to assess reversibility response in pediatrics. Martinez et al. proposed a 9% threshold in children aged 7-14 years as the best option to define the bronchodilation test as positive³³. Using such a threshold (data not shown), in our population including 571 children belonging to this age group, we would find a sensitivity of 41.7% (with 238 children with a reversibility of at least 9%). Kang et al. found that an increase of at least 7.5% in FEV₁ was a better option to diagnose asthma in a cohort of Chinese children (Se 50.7%), while the increase of 12% correlated to a 28.7% sensitivity³⁴, which is even lower than the value found in our study. On the other hand, the cut-off of an increase in FEV₁ of 7.5% proposed by the Authors still shows a low sensitivity, and does not seem appropriate to diagnose asthma in children. Jat et al. affirmed that spirometry is a very useful investigation tool to diagnose asthma in children, if the test is well-performed and patients received adequate training;

nevertheless, they also admitted that the diagnosis should also be based on clinical symptoms and personal history, to be more reliable²⁴.

As for the obstruction threshold FEV₁/CVF of 90%, proposed by several authors, including Quanjer et al., such value should not be used in children to assess airways obstruction, considering the unsatisfying sensitivity of this criterion in our study²³. On the other hand, we showed that, as asthma severity increases, patients tend to present lower FEV₁/FVC ratio, therefore more important bronchial obstruction, and greater increases in FEV₁ after bronchodilation test.

Several authors proposed to evaluate the change in FEF₂₅₋₇₅ after bronchodilation test to diagnose asthma in children, assuming that FEV₁ may be a poor criterion in this age group^{26,27,35,36}. These authors claim that FEF₂₅₋₇₅ could be considered as a more sensitive measure of the small airways obstruction, but, in our study, such criterion showed an even lower sensitivity than FEV₁, to reach a diagnosis.

In a study by Dufetelle et al., the authors proposed two thresholds suggestive of bronchodilator response in asthmatic children³⁷. Based on spirometry z-scores, their preliminary results showed that a 0.42 z-score for FEV₁ and a -0.16 z-score for FEV₁/FVC could indicate bronchoreversibility even in children with normal baseline spirometry. In our cohort, when considering patients presenting with these z-score values (n=279), we found a sensitivity of 32.0% (data not shown). Therefore, these thresholds might be useful to suggest a bronchodilator response in asthmatic children, but their usefulness in diagnosing pediatric asthma seems limited.

As for patients presenting with intermittent asthma, our data showed that this group of patients reported results which were not consistent with those from the other groups. These patients are not representative of the typical patient referring to a tertiary University Hospital. Indeed, they are most likely to be seen outside the hospital, by a general practitioner or a pediatrician, since they do not require a specialized expertise. Further studies in this severity group might be of interest.

A quite surprising observation from our study was that the proportion of patients treated with AIT was not significantly different between severity groups (Table 4), while we were expecting the more

severe group to be the one with patients treated the most with AIT, also considering that children with severe asthma were more atopic. Such aspect could be explained by the fact that AIT is usually prescribed in children not only as a treatment for allergies, but also to prevent the development of further allergen sensitizations and to reduce the burden and the possible aggravation of allergic respiratory diseases (allergic rhinitis, allergic rhino-conjunctivitis, and asthma).

In our study, the best criteria for asthma diagnosis was the response to the prescribed treatment (Se 94.0%): therefore, even in those patients for whom the diagnosis is not sure at the first visit, the follow-up allows to strengthen the doctor's hypothesis. Nevertheless, when focusing on the possibility of diagnosing asthma when evaluating a patient for the first time, the best single clinical predicting criterion was dry cough. When adding three clinical criteria together, such as dry cough, wheezing and atopy or dry cough, wheezing and exercise-induced dyspnea, we reached a very satisfying sensitivity (> 99%), while PFTs values were not providing sufficient support to increase the diagnostic sensitivity. These simple clinical features could therefore be easily and practically used in everyday clinical practice to diagnose asthma in children. These findings are strongly supported by other studies that affirm that a combination of different symptoms seems to be more discriminative than just one or two separate symptoms to reach a diagnosis of pediatric asthma^{12,34,38}. These criteria are simple to assess during a medical consultation and require no specific tool. Therefore, this attitude could simplify the diagnostic process, while showing at the same time a better sensitivity.

The primary strength of this study was the great number of included patients: we present the largest pediatric cohort focusing on this subject, and including both spirometric and clinical parameters. 871 children were indeed included in our analysis, which also enabled us to perform subgroup analysis, based on asthma severity, with satisfying group sizes. Also, our multi-centric approach, including patients from two centers from different countries, France and Italy, allowed us to gather a cohort with data coming from physicians with different backgrounds, and could bring us to speculate that our results could also be extended and applied to other countries and/or settings.

Our study presents some limitations as well. We present a retrospective cohort study, based on information found in patients' files: for such reason, we had a few missing data for 17 patients, which nevertheless represented less than 2% of our entire cohort. Also, we included asthmatic children only, and a prospective study including any patients consulting for possible asthma could help strengthen our results and provide further insights. Finally, we did not have data assessing F_ENO in our population. However, in a study by Murray et al., the authors showed that F_ENO is the most sensitive objective test to diagnose asthma in children, with a low 44% sensitivity³⁸. Nevertheless, we should consider two different aspects: firstly, our data come from real-life settings, and F_ENO measurements are not routinely evaluated by pediatricians, and therefore such data are not systematically included in patients' chart; secondly, this parameter still shows a lower sensitivity if compared with those found by our study.

We believe that our results bring an important contribution to current knowledge on asthma diagnosis in children. The results strongly suggest that spirometric reversibility values, along with other data such as obstruction criterion, even though essentials for the follow-up of pediatric asthmatic patients, have a very unsatisfying sensitivity for the diagnosis of asthma in children.

CONCLUSION

Our data strongly affirm that PFTs, even though essentials for the follow-up of pediatric asthmatic patients, have a low sensitivity for the diagnosis of asthma. Clinical symptoms, on the other hand, show a very high sensitivity. For such reason, any physicians could diagnose asthma in children, without needing to perform PFTs to confirm their diagnosis. Therefore, we would like to stress that general practitioners and pediatricians could diagnose asthma in children, through carefully evaluating the clinical history and the symptoms presented by patients, while asthmatic patients presenting with severe forms or needing a follow-up require a more complete assessment in specialized centers.

REFERENCES

1. Caimmi D, Marseglia A, Pieri G, Benzo S, Bosa L, Caimmi S. Nose and lungs: one way, one disease. *Ital J Pediatr.* 2012;38:60.
2. Pedersen SE, Hurd SS, Lemanske RF, Becker A, Zar HJ, Sly PD, et al., Global Initiative for Asthma. Global strategy for the diagnosis and management of asthma in children 5 years and younger. *Pediatr Pulmonol.* 2011;46:1–17.
3. Papi A, Brightling C, Pedersen SE, Reddel HK. Asthma. *Lancet.* 2018;391:783–800.
4. Global Strategy for Asthma Management and Prevention. GINA MAIN REPORT. 2020. Available from: <https://ginasthma.org/gina-reports/> (last access on September 25th, 2020).
5. National Heart, Lung, and Blood Institute. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. National Heart, Lung, and Blood Institute, Bethesda (MD), USA. 2007.
6. Marks GB, Mahrshahi S, Kemp AS, Tovey ER, Webb K, Almqvist C, et al. Prevention of asthma during the first 5 years of life: a randomized controlled trial. *J Allergy Clin Immunol.* 2006;118:53–61.
7. Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. *N Engl J Med.* 1995;332:133–8.
8. Kuehni CE, Strippoli MPF, Low N, Brooke AM, Silverman M. Wheeze and asthma prevalence and related health-service use in white and south Asian pre-schoolchildren in the United Kingdom. *Clin Exp Allergy.* 2007;37:1738–46.
9. Chen E, Langer DA, Raphaelson YE, Matthews KA. Socioeconomic status and health in adolescents: the role of stress interpretations. *Child Dev.* 2004;75:1039–52.
10. Sedaghat AR, Matsui EC, Baxi SN, Bollinger ME, Miller R, Perzanowski M, et al. Mouse Sensitivity is an Independent Risk Factor for Rhinitis in Children with Asthma. *J Allergy Clin Immunol Pr.* 2016;4:82–8.
11. Sly PD, Boner AL, Björkstén B, Bush A, Custovic A, Eigenmann PA, et al. Early identification of atopy in the prediction of persistent asthma in children. *Lancet.* 2008;372:1100–6.
12. Pedersen S. Preschool asthma--not so easy to diagnose. *Prim Care Respir J.* 2007;16:4-6.
13. Woodcock A, Lowe LA, Murray CS, Simpson BM, Pipis SD, Kissen P, et al, on behalf of the NAC Manchester Asthma and Allergy Study Group. Early life environmental control: effect on symptoms, sensitization, and lung function at age 3 years. *Am J Respir Crit Care Med.* 2004;170:433–9.
14. Bufford JD, Gern JE. Early exposure to pets: good or bad? *Curr Allergy Asthma Rep.* 2007;7:375–82.
15. Ownby DR, Johnson CC, Peterson EL. Exposure to dogs and cats in the first year of life and risk of allergic sensitization at 6 to 7 years of age. *JAMA.* 2002;288:963–72.
16. Hallas HW, Chawes BL, Rasmussen MA, Arianto L, Stokholm J, Bønnelykke K, et al. Airway obstruction and bronchial reactivity from age 1 month until 13 years in children with asthma: A prospective birth cohort study. *PLoS Med.* 2019;16:e1002722.
17. Morgan WJ, Stern DA, Sherrill DL, Guerra S, Holberg CJ, Guilbert TW, et al. Outcome of asthma and wheezing in the first 6 years of life: follow-up through adolescence. *Am J Respir Crit Care Med.* 2005;172:1253–8.
18. Grol MH, Gerritsen J, Vonk JM, Schouten JP, Koëter GH, Rijcken B, et al. Risk factors for growth and decline of lung function in asthmatic individuals up to age 42 years. A 30-year follow-up study. *Am J Respir Crit Care Med.* 1999;160:1830–7.

19. Sears MR, Greene JM, Willan AR, Wiecek EM, Taylor DR, Flannery EM, et al. A longitudinal, population-based, cohort study of childhood asthma followed to adulthood. *N Engl J Med.* 2003;349:1414–22.
20. Grol MH, Postma DS, Vonk JM, Schouten JP, Rijcken B, Koëter GH, et al. Risk factors from childhood to adulthood for bronchial responsiveness at age 32-42 yr. *Am J Respir Crit Care Med.* 1999;160:150–6.
21. Graham BL, Steenbruggen I, Miller MR, Barjaktarevic IZ, Cooper BG, Hall GL, et al, on behalf of the American, Thoracic Society and the European Respiratory Society. Standardization of Spirometry 2019 Update An Official American Thoracic Society and European Respiratory Society Technical Statement. *Am J Respir Crit Care Med.* 2019;200:e70–88.
22. Quanjer PH, Borsboom GJ, Brunekreef B, Zach M, Forche G, Cotes JE, et al. Spirometric reference values for white European children and adolescents: Polgar revisited. 1995;19:135–42.
23. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, et al., the ERS Global Lung function Initiative. Multi-ethnic reference values for spirometry for the 3-95 year age range: the global lung function 2012 equations. *Eur Respir J.* 2012;40:1324–43.
24. Jat KR. Spirometry in children. *Prim Care Respir J.* 2013;22:221–9.
25. Crenesse D, Berlioz M, Bourrier T, Albertini M. Spirometry in children aged 3 to 5 years: reliability of forced expiratory maneuvers. *Pediatr Pulmonol.* 2001;32:56–61.
26. Kanchongkittiphon W, Gaffin JM, Kopel L, Petty CR, Bollinger ME, Miller R, et al. Matsui and Wanda Phipatanakul. The Association of FEF_{25–75} and Bronchodilator reversibility with Asthma Control and Asthma Morbidity in Inner City Children with Asthma. *Ann Allergy Asthma Immunol.* 2016;117:97–9.
27. Rao DR, Gaffin JM, Baxi SN, Sheehan WJ, Hoffman EB, Phipatanakul W. The utility of forced expiratory flow between 25% and 75% of vital capacity in predicting childhood asthma morbidity and severity. *J Asthma.* 2012;49:586–92.
28. NICE guideline. Asthma: diagnosis, monitoring and chronic asthma management. 2017. Available from: www.nice.org.uk/guidance/ng80 (last access on September 25th, 2020).
29. Hopp RJ, Pasha MA. A literature review of the evidence that a 12% improvement in FEV₁ is an appropriate cut-off for children. *J Asthma.* 2016;53:413–8.
30. Bacharier LB, Strunk RC, Mauger D, White D, Lemanske RF, Sorkness CA. Classifying asthma severity in children: mismatch between symptoms, medication use, and lung function. *Am J Respir Crit Care Med.* 2004;170:426–32.
31. Sharma S, Litonjua AA, Tantisira KG, Fuhlbrigge AL, Szeffler SJ, Strunk RC, et al., Childhood Asthma Management Program Research Group. Clinical Predictors and Outcomes of Consistent Bronchodilator Response in the Childhood Asthma Management Program. *J Allergy Clin Immunol.* 2008;122:921–8.
32. Viložni D, Hakim F, Livnat G, Ofek M, Bar-Yoseph R, Bentur L. Assessment of Airway Bronchodilation by Spirometry Compared to Airway Obstruction in Young Children with Asthma. *Can Respir J.* 2016;2016:5394876.
33. Pardos Martínez C, Fuertes Fernández-Espinar J, Nerín De La Puerta I, González Pérez-Yarza E. Cut-off point for a positive bronchodilation test. *Esp Pediatr.* 2002;57:5–11.
34. Kang XH, Wang W, Cao L. A clinical study to determine the threshold of bronchodilator response for diagnosing asthma in Chinese children. *World J Pediatr.* 2019;15:559–64.
35. Simon MR, Chinchilli VM, Phillips BR, Sorkness CA, Lemanske RF, Szeffler SJ, et al., Childhood Asthma Research and Education Network of the National Heart, Lung, and Blood Institute. Forced expiratory flow between 25% and 75% of vital capacity and FEV₁/forced vital capacity ratio in relation to clinical and physiological parameters in asthmatic children with normal FEV₁ values. *J Allergy Clin Immunol.* 2010;126:527–34.

36. Ciprandi G, Cirillo I. Forced expiratory flow between 25% and 75% of vital capacity may be a marker of bronchial impairment in allergic rhinitis. *J Allergy Clin Immunol.* 2011;127:549.
37. Dufetelle E, Bokov P, Delclaux C, Beydon N. Should reversibility be assessed in all asthmatic children with normal spirometry? *Eur Respir J.* 2018;58:1800373.
38. Murray C, Foden P, Lowe L, Durrington H, Custovic A, Simpson A. Diagnosis of asthma in symptomatic children based on measures of lung function: an analysis of data from a population-based birth cohort study. *Lancet.* 2017;1:114–23.

FIGURES

Figure 1 – Patients included in the study.

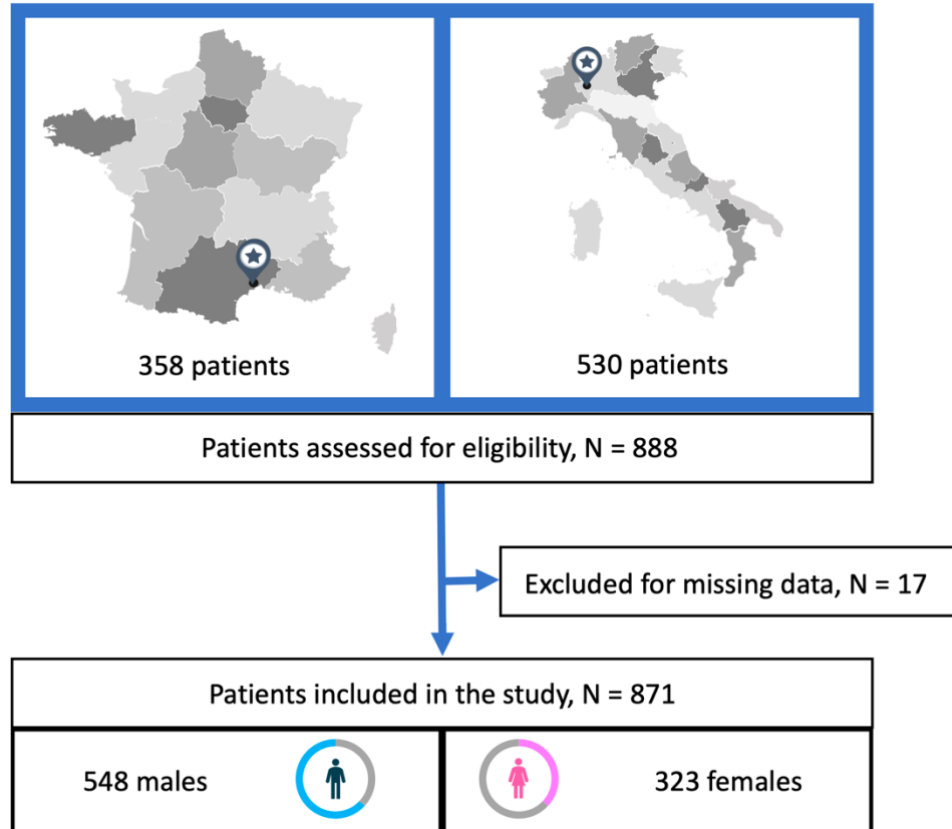
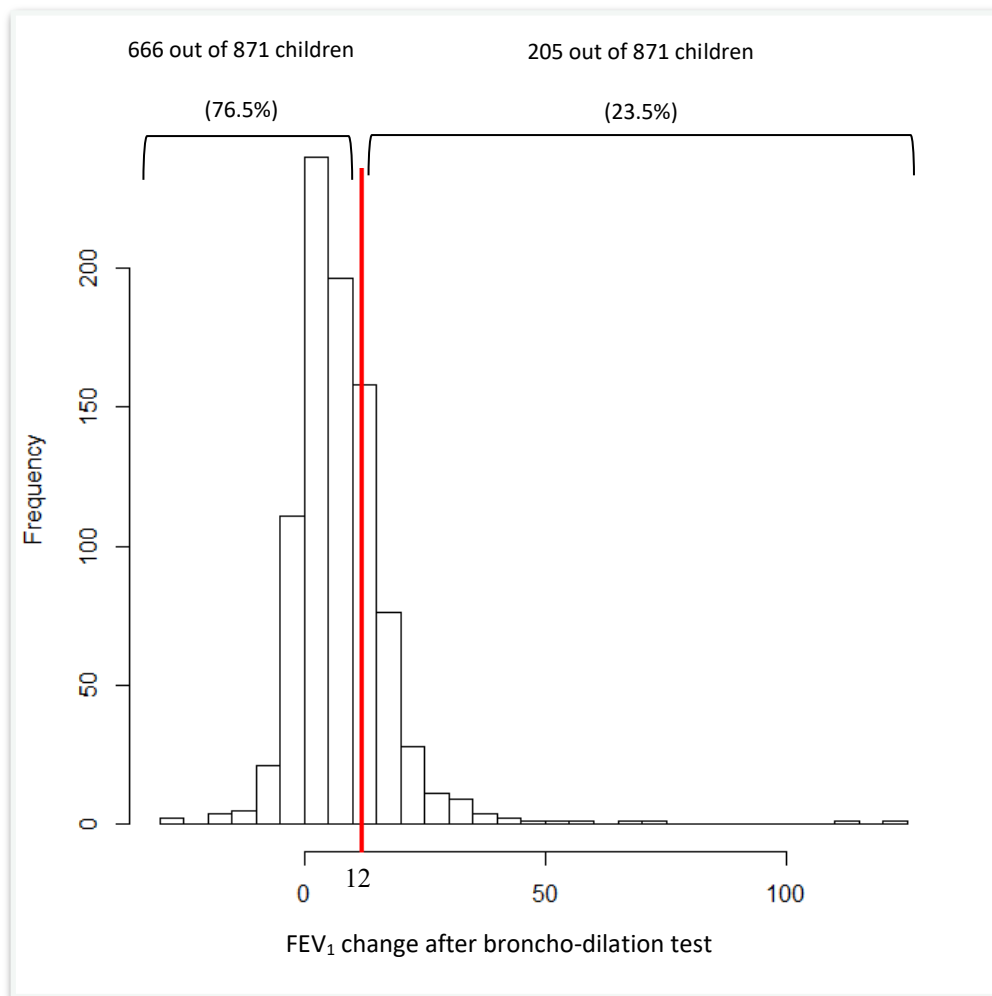
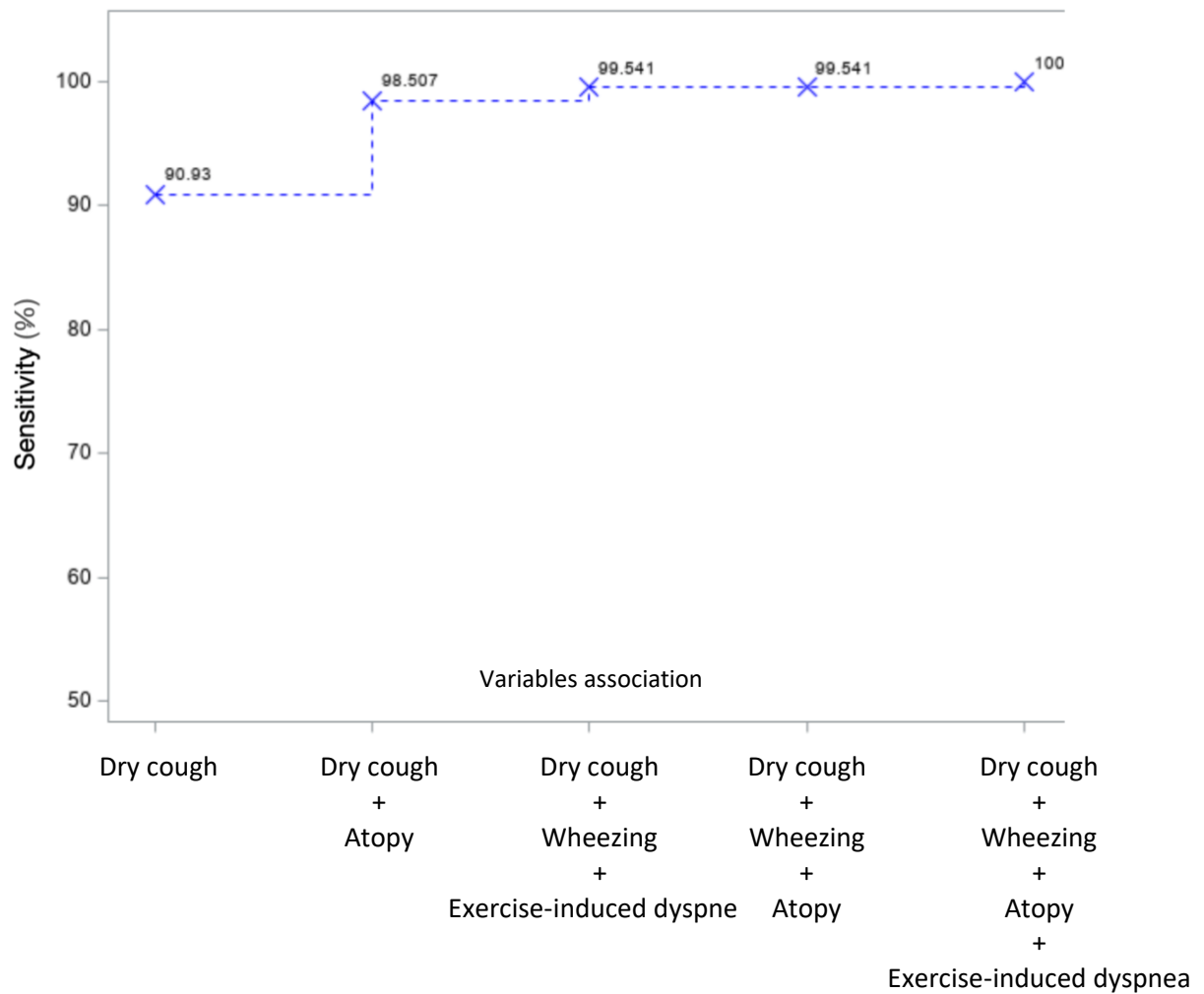


Figure 2 – Reversibility criteria ($FEV_1/FCV < 90\%$ and increase in $FEV_1 > 12\%$) after bronchodilation test in all 871 included children.



The line shows the 12% cut-off proposed by GINA guidelines. All children on the left of the line would be considered as non-asthmatics following current recommendations.

Figure 3 – Best option for cumulative sensitivity of different variables to predict a diagnosis of asthma in children.



TABLES

Table 1 – Characteristics of the population included in the study.

	Overall	France	Italy
General information			
Number of patients, n (%)	871 (100%)	342 (39.3)	529 (60.7)
Males, n (%)	548 (62.9%)	219 (64.0)	329 (62.2)
Age, mean (SD)	9.2 (3.3)	9.2 (3.4)	9.3 (3.2)
BMI, mean (SD)	18.1 (3.7)	17.6 (3.3)	18.5 (3.8)
Results of PFTs			
Basal FEV ₁ , in liters, mean (SD)	1.9 (0.80)	1.8 (0.79)	1.9 (0.81)
Mean Change in FEV ₁ after bronchodilation, % (SD)	8.2 (10.7)	8.1 (13.1)	8.3 (8.8)
Mean basal FEV ₁ /FVC, % (SD)	84.9 (9.7)	86.1 (11.3)	84.0 (8.5)
Mean Change in FEF ₂₅₋₇₅ after bronchodilation, % (SD)	22.1 (30.0)	20.0 (38.9)	23.4 (22.3)
Prescription of biotherapies			
Patients treated with Anti-IgE, n (%)	39 (4.5)	11 (3.2)	28 (5.3)
Patients treated with AIT, n (%)	101 (11.6)	58 (17.0)	43 (8.1)
Clinical symptoms			
Any of the below evocative symptom, n (%)	868 (99.7)	339 (99.1)	528 (100)
Patients presenting with dry cough, n (%)	791 (90.8)	322 (94.1)	469 (88.7)
Patients presenting with wheezing n (%)	553 (63.5)	138 (40.3)	415 (78.5)
Patients presenting with exercise-induced dyspnea, n (%)	410 (47.1)	193 (56.4)	217 (41.0)
Patients presenting with tight chest, n (%)	149 (17.1)	40 (11.7)	109 (20.6)
Patients with a history of pre-school wheezing, n (%)	315 (36.2)	119 (34.8)	196 (37.1)
Patients with symptoms improvement after treatment, n (%)	819 (94.0)	295 (86.3)	524 (99.1)
Atopic comorbidities			
Patients presenting with any atopic comorbidity, n (%)	713 (81.9)	289 (84.5)	424 (80.2)
Patients suffering from Allergic Rhinitis, n (%)	605 (69.5)	210 (61.4)	395 (74.7)
Patients suffering from food allergy, n (%)	108 (12.4)	28 (8.2)	80 (15.1)
Patients suffering from atopic dermatitis, n (%)	193 (22.2)	65 (19.0)	128 (24.2)
Atopic patients, n (%)	678 (77.8)	244 (71.4)	434 (82.0)
Atopic sensitization			
Patients sensitized to house dust mites, n (%)	471 (54.1)	151 (44.2)	320 (60.5)
Patients sensitized to grass, n (%)	407 (46.7)	111 (32.5)	296 (56.0)
Patients sensitized to cypress, n (%)	109 (12.5)	103 (30.1)	6 (1.1)
Patients sensitized to birch, n (%)	135 (15.5)	37 (10.8)	98 (18.5)
Patients sensitized to animal dander, n (%)	314 (36.1)	108 (31.6)	206 (38.9)
Patients sensitized to molds, n (%)	175 (20.1)	54 (15.8)	121 (22.9)

Legend – BMI: Body Mass Index; SD: Standard Deviation; FEV₁: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; FEF₂₅₋₇₅: mean Forced Expiratory Flow between the 25% and 75% of the FVC; AIT: Allergen Immunotherapy.

Table 2 – Sensitivity of the reversibility criteria in children proposed by GINA guidelines for FEV₁, of bronchial obstruction in children, of the reversibility criteria for FEF₂₅₋₇₅, and of the association or either the reversibility of the FEV₁ criterion or the FEF₂₅₋₇₅, in the overall population and in the subgroups based on asthma severity and patient’s age.

	Overall	Based on severity				Based on patient's age		
		Persistent severe asthma	Persistent moderate asthma	Persistent mild asthma	Intermittent asthma	< 7 years	7-11 years	> 11 years
Number of patients	871	55	581	203	32	221	432	218
Sensitivity of reversibility criteria: increase of FEV ₁ > 12% in patients with FEV ₁ /FVC < 90%	23.5%	38.2%	27.4%	10.8%	9.4%	18.6%	27.5%	20.6%
Sensitivity of reversibility criteria: increase of FEV ₁ > 12%	30.4%	41.8%	34.3%	16.3%	31.3%	32.1%	32.4%	24.8%
Sensitivity of obstruction criteria: FEV ₁ /FVC < 90%	67.5%	87.3%	72.1%	53.2%	43.8%	48.0%	26.5%	76.6%
Sensitivity of reversibility criteria: increase of FEF ₂₅₋₇₅ > 30%	21.9%	25.5%	23.8%	16.7%	15.6%	24.9%	23.8%	15.1%
Sensitivity of reversibility of either FEV ₁ or FEF ₂₅₋₇₅	36.7%	50.9%	40.1%	23.2%	37.5%	43.0%	37.5%	28.9%

Legend: FEV₁: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; FEF₂₅₋₇₅: mean Forced Expiratory Flow between the 25% and 75% of the FVC.

The *p-value* was statistically significant (<0.05):

- for the reversibility criterion (increase of 12% in FEV₁ in patients with FEV₁/FVC < 90%): between the severe group and the mild and intermittent ones; between the moderate group and the mild and intermittent ones; between the <7 years group and the 7-11 years one;
- for the FEV₁ criterion: between mild asthma and any other severity group;
- for the obstruction criterion: between severe and any other severity group; between moderate and any other severity group; between the <7 years group and any other group;
- for the FEF₂₅₋₇₅ criterion: between severe and mild; between moderate and mild; between the >11 years group and any other group;
- for either the FEV₁ criterion or the FEF₂₅₋₇₅ criterion: between severe and mild; between moderate and mild; between the >11 years group and any other group.

Table 3 – Sensitivity of the different clinical criteria in the whole cohort of 871 children, in the subgroup of patients in which normal FEV₁/FVC, in those with FEV₁/FVC < 90% and an increase in FEV₁ < 12% after bronchodilation, and in those presenting with reversibility criteria.

Clinical criteria	In the whole cohort (N = 871)		Patients with FEV ₁ /FVC ≥ 90% (N = 283)		Patients with FEV ₁ /FVC < 90% and increase in FEV ₁ < 12% after bronchodilation (N = 383)		Patients with FEV ₁ /FVC < 90% and increase in FEV ₁ ≥ 12% after bronchodilation (N = 205)	
	Number of patients (n)	Sensitivity (%)	Number of patients (n)	Sensitivity (%)	Number of patients (n)	Sensitivity (%)	Number of patients (n)	Sensitivity (%)
Dry cough	792	90.9%	250	88.3%	350	91.4%	192	93.7%
Wheezing	553	63.5%	162	57.2%	251	65.5%	140	68.3%
Exercise-induced dyspnea	410	47.1%	122	43.1%	187	48.8%	102	49.8%
Tight chest	149	17.1%	32	11.3%	73	19.1%	44	21.5%
Pre-school wheezing	315	36.2%	108	38.2%	134	35.0%	73	35.6%
Atopy	678	77.8%	202	71.4%	306	79.9%	170	82.9%
Allergic comorbidities	713	81.9%	219	77.4%	320	83.6%	174	84.9%

We found a significant difference between the whole cohort and the subgroup of patients with normal FEV₁/FVC for the tight chest (*p-value* 0.0198) and atopy (*p-value* 0.0264) criteria.

Table 4 – Characteristics of the population, per asthma severity.

Asthma severity	Persistent severe asthma	Persistent moderate asthma	Persistent mild asthma	Intermittent asthma	Statistical difference between groups, <i>p-value</i>						
					Between severe and moderate asthma	Between severe and mild asthma	Between severe and intermittent asthma	Between moderate and mild asthma	Between moderate and intermittent asthma	Between mild and intermittent asthma	
General information											
Number of patients, n (%)	55 (6.3)	581 (66.7)	203 (23.3)	32 (3.7)	< 0.0001	< 0.0001	0.0014	< 0.0001	< 0.0001	< 0.0001	< 0.0001
Males, n (%)	34 (61.8)	375 (64.5)	122 (60.1)	17 (53.1)	0.6867	0.8170	0.4273	0.2577	0.1903	0.4557	0.4557
Age, mean (SD)	9.6 (3.3)	9.4 (3.2)	8.6 (3.2)	10.3 (3.6)	0.6588	0.0422	0.3588	0.0022	0.1244	0.0065	0.0065
BMI, mean (SD)	18.6 (3.8)	18.2 (3.7)	17.9 (3.5)	17.3 (2.8)	0.4448	0.1977	0.0955	0.3136	0.1761	0.3566	0.3566
Results of PFTs											
Mean Change in FEV ₁ after bronchodilation, % (SD)	13.2 (18.2)	8.9 (10.7)	5.0 (6.9)	7.2 (8.9)	0.0084	< 0.0001	0.0847	< 0.0001	0.3782	0.1094	0.1094
Mean basal FEV ₁ /FVC, n (SD)	79.5 (10.5)	84.1 (9.7)	87.7 (8.5)	89.4 (10.4)	0.0009	< 0.0001	0.0001	< 0.0001	0.0028	0.3095	0.3095
Mean Change in FEF ₂₅₋₇₅ after bronchodilation, % (SD)	23.9 (23.8)	23.1 (32.5)	19.6 (24.5)	16.2 (21.1)	0.8588	0.2465	0.1334	0.1615	0.2358	0.4585	0.4585
Prescription of biotherapies											
Patients treated with Anti-IgE, n (%)	37 (67.3)	2 (0.3)	0	0	< 0.0001	N/A	N/A	N/A	N/A	N/A	N/A
Patients treated with AIT, n (%)	5 (9.1)	64 (11.0)	28 (13.8)	4 (12.5)	0.6609	0.3544	0.6146	0.2898	0.7946	0.8429	0.8429
Atopic comorbidities											
Patients presenting with any atopic comorbidity, n (%)	47 (85.5)	493 (84.9)	149 (73.4)	24 (75.0)	0.9053	0.0634	0.2248	0.0003	0.1354	0.8429	0.8429
Patients suffering from Allergic Rhinitis, n (%)	42 (76.4)	418 (71.9)	128 (63.1)	17 (53.1)	0.4839	0.0648	0.0253	0.0177	0.0224	0.2829	0.2829
Patients suffering from food allergy, n (%)	6 (10.9)	75 (12.9)	23 (11.3)	4 (12.5)	0.6707	0.9301	0.8225	0.5582	0.9464	0.8470	0.8470
Patients suffering from atopic dermatitis, n (%)	14 (25.5)	140 (24.1)	34 (16.8)	5 (15.6)	0.8222	0.1411	0.2846	0.0301	0.2723	0.8738	0.8738
Atopic patients, n (%)	51 (92.7)	455 (78.3)	149 (73.4)	23 (71.9)	0.0113	0.0023	0.0085	0.1518	0.3922	0.8565	0.8565
Patients sensitized to house dust mites, n (%)	35 (63.6)	318 (54.7)	104 (51.2)	14 (43.8)	0.2041	0.1016	0.0713	0.3890	0.2248	0.4315	0.4315

Legend: BMI: Body Mass Index; SD: Standard Deviation; FEV₁: Forced Expiratory Volume in 1 second; FVC: Forced Vital Capacity; FEF₂₅₋₇₅: mean Forced Expiratory Flow between the 25% and 75% of the FVC; N/A: not applicable; AIT: Allergen Immunotherapy

SERMENT

- En présence des Maîtres de cette école, de mes chers condisciples et devant l'effigie d'Hippocrate, je promets et je jure, au nom de l'Être suprême, d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la médecine.
- Je donnerai mes soins gratuits à l'indigent et n'exigerai jamais un salaire au-dessus de mon travail.
- Admis (e) dans l'intérieur des maisons, mes yeux ne verront pas ce qui s'y passe, ma langue taira les secrets qui me seront confiés, et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.
- Respectueux (se) et reconnaissant (e) envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.
- Que les hommes m'accordent leur estime si je suis fidèle à mes promesses.
Que je sois couvert (e) d'opprobre et méprisé (e) de mes confrères si j'y manque.

RÉSUMÉ

Introduction : L'asthme est la maladie chronique la plus fréquente chez l'enfant et un diagnostic robuste est crucial afin d'optimiser la prise en charge des patients et d'améliorer « le fardeau de la maladie ». Pour poser le diagnostic d'asthme chez l'enfant, les recommandations du GINA proposent une amélioration de 12% du VEMS après le test de broncho-dilatation, mais en pratique clinique, ce critère est rarement présent chez ces patients. L'objectif de cette étude était d'évaluer la sensibilité de ce critère de réversibilité et de trouver des variables capables de montrer une grande sensibilité pour prédire le diagnostic d'asthme.

Méthodes : VERI-VEMS était une étude multicentrique internationale rétrospective incluant tous les enfants consécutifs (de 5 à 18 ans), avec un diagnostic d'asthme posé par un médecin spécialiste de l'asthme. Les résultats des EFR au moment du diagnostic ont été relevés pour chaque patient. Le critère de jugement principal était de vérifier si le critère de réversibilité proposé par le GINA était corrélé chez les enfants avec le diagnostic d'asthme.

Résultats : 871 ont été inclus au total. Le critère de réversibilité de 12% du VEMS montrait une sensibilité de seulement 30,4%. Par ailleurs, en évaluant tous les critères spirométriques et cliniques, les trois meilleurs critères diagnostiques étaient « toux sèche, sifflements et atopie » et « toux sèche, sifflements et dyspnée à l'effort », avec une sensibilité atteignant 99.5%, alors que les paramètres spirométriques ne présentaient pas d'intérêt dans le calcul de la sensibilité cumulée pour le diagnostic.

Conclusion : Les EFR ont une sensibilité insuffisante pour le diagnostic de l'asthme chez l'enfant, bien qu'ils soient essentiels pour le suivi. L'association de symptômes cliniques devrait être considérée comme le gold standard pour effectuer ce diagnostic en pédiatrie.

Mots clés : Asthme, Diagnostic d'Asthme, Enfant, Épreuves Fonctionnelles Respiratoires, Symptômes cliniques, GINA