

4.1.3 Description of the main S&T results/foregrounds

WP1 Common European database and biobank

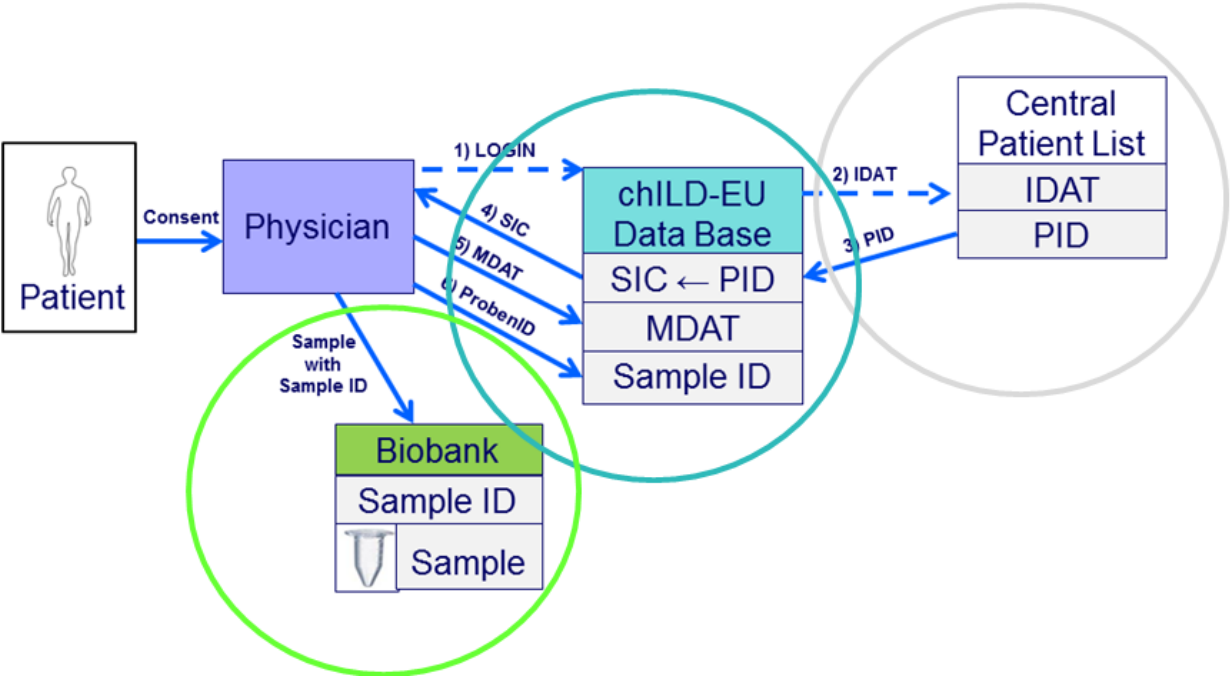


Fig. 1 Data safety concept of the European chILD database and biobank



Fig. 2 Patient information booklet translated into Danish

WP3 Observational cohort – objectively measure and evaluate contemporary management strategies and outcomes

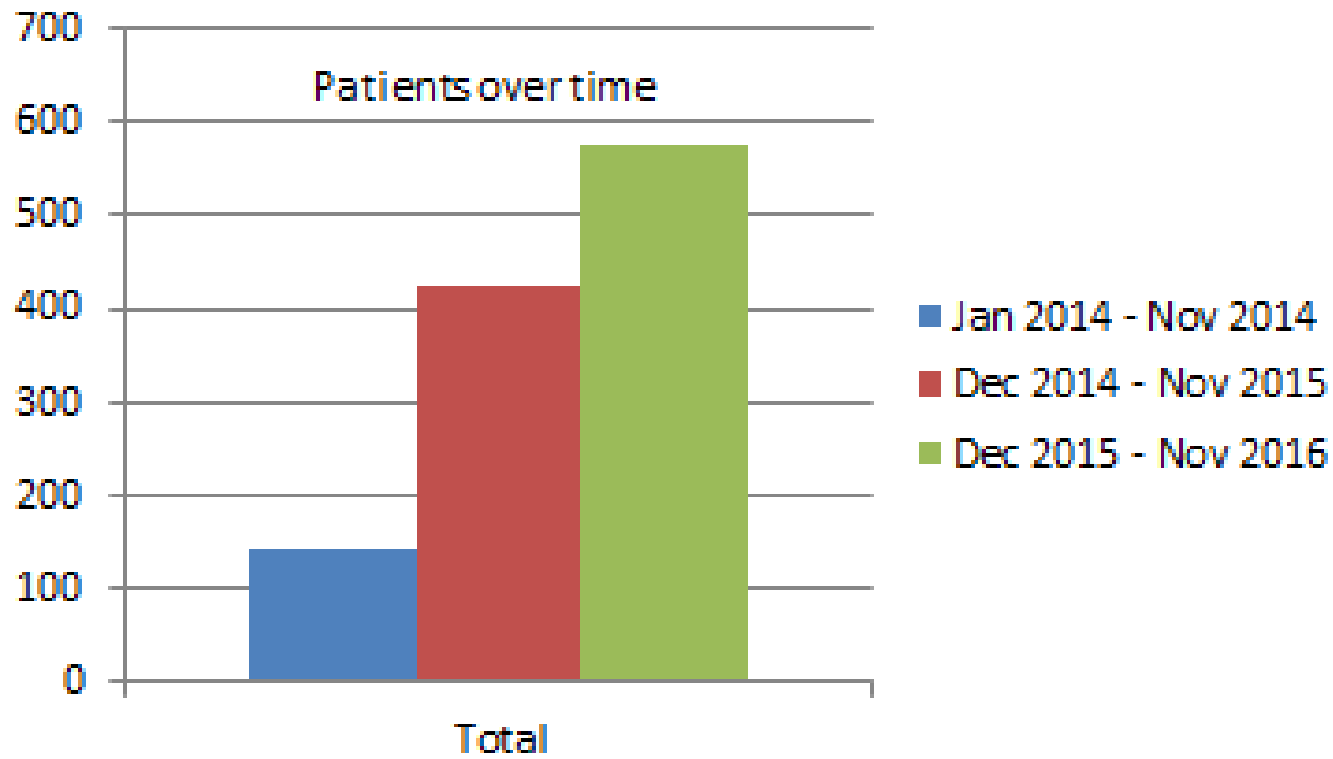


Fig 3: Patients over time in the chILD-EU register from 2014 to 2016

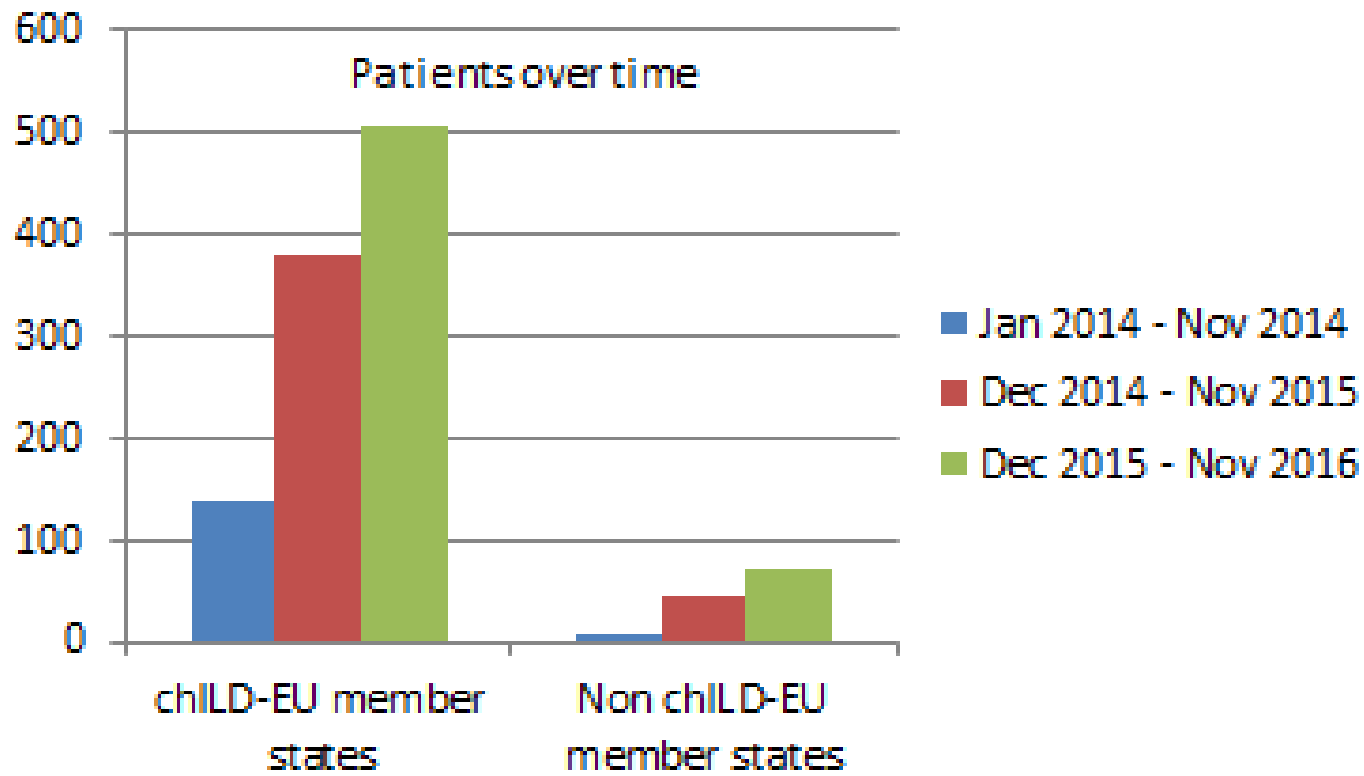


Fig 4: Patients over time in the CHILD-EU member and non-member states

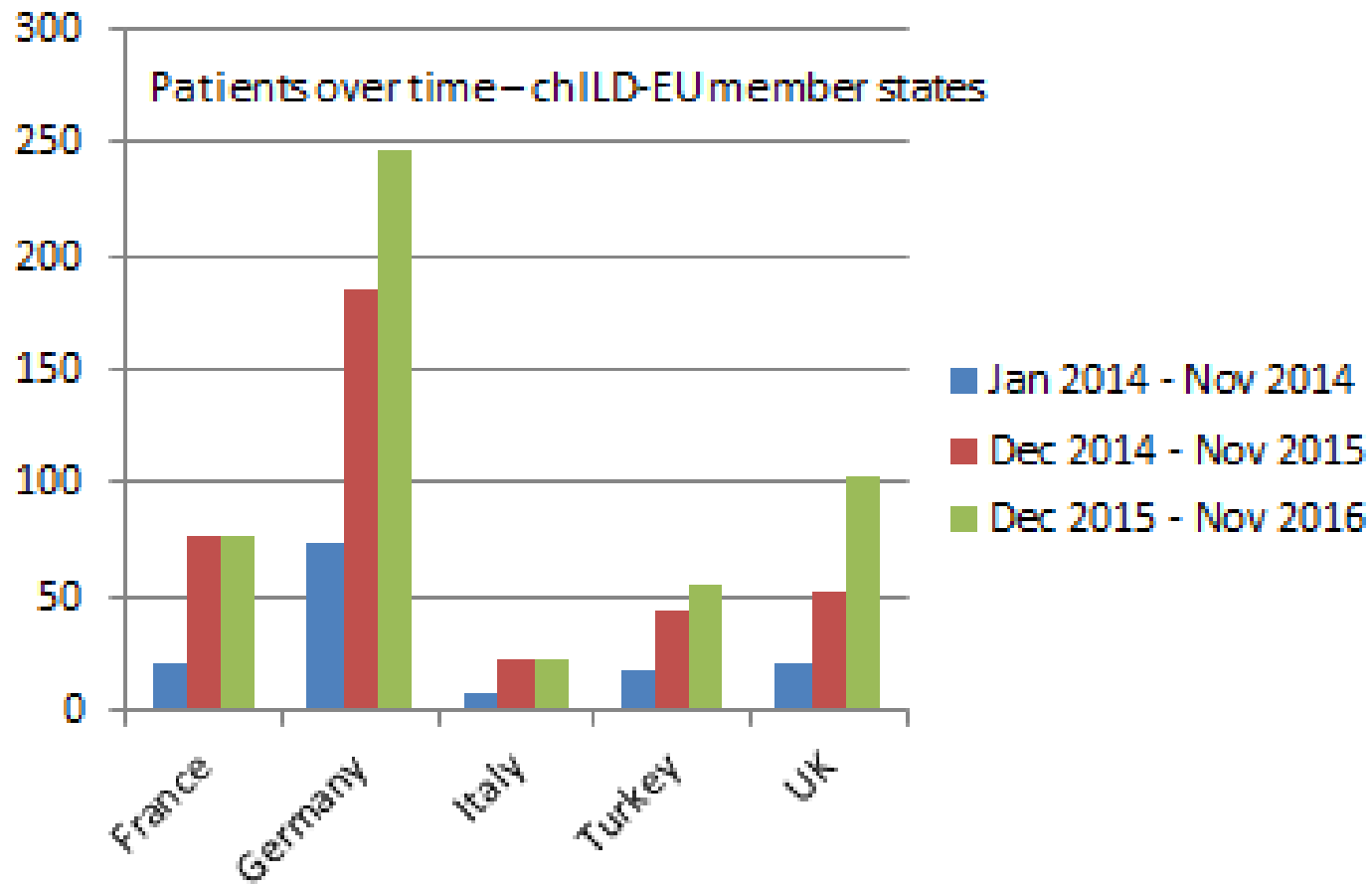


Fig 5: Patients over time in the chILD-EU member states per country

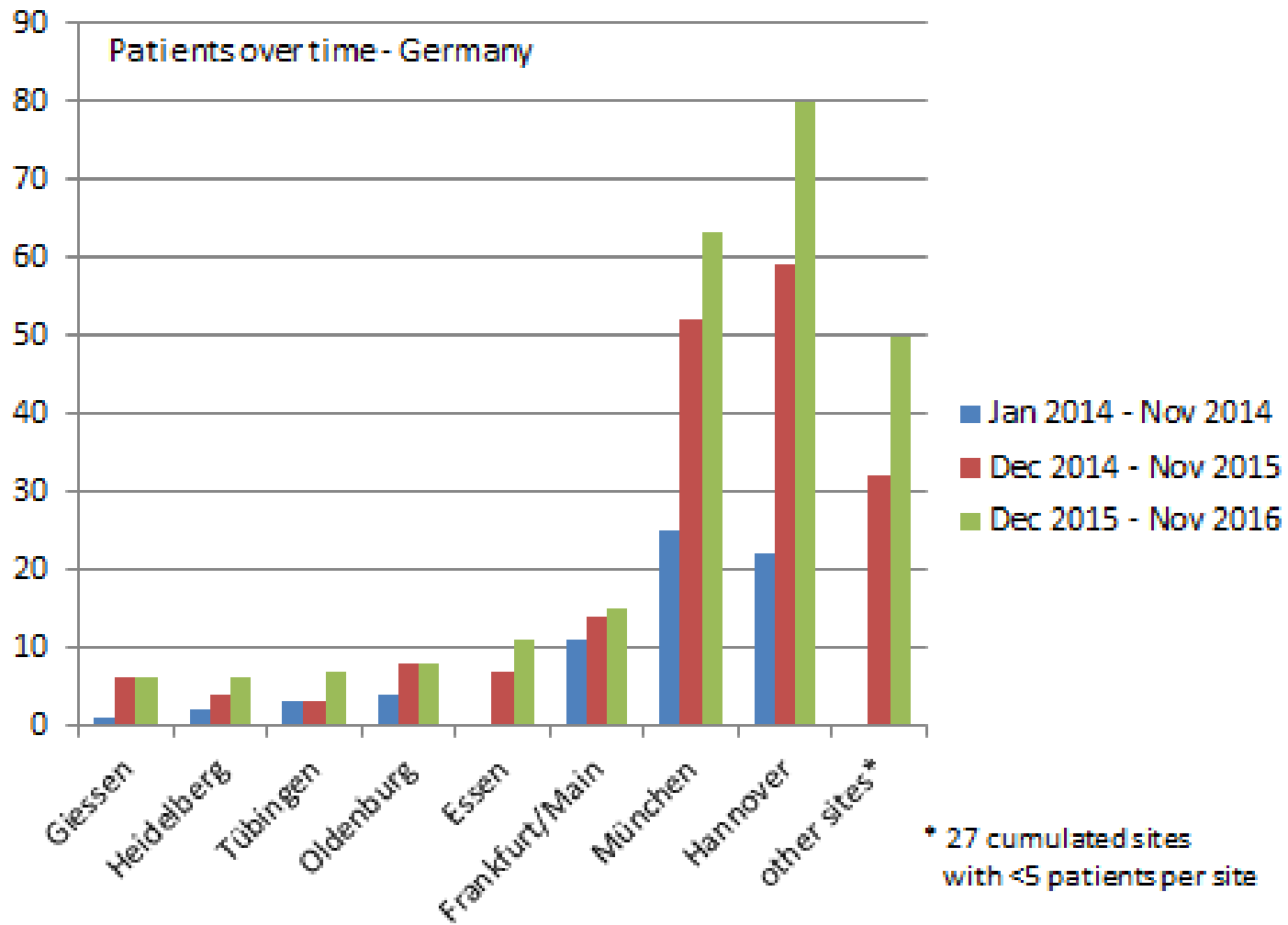


Fig 6: Patients over time in Germany per site

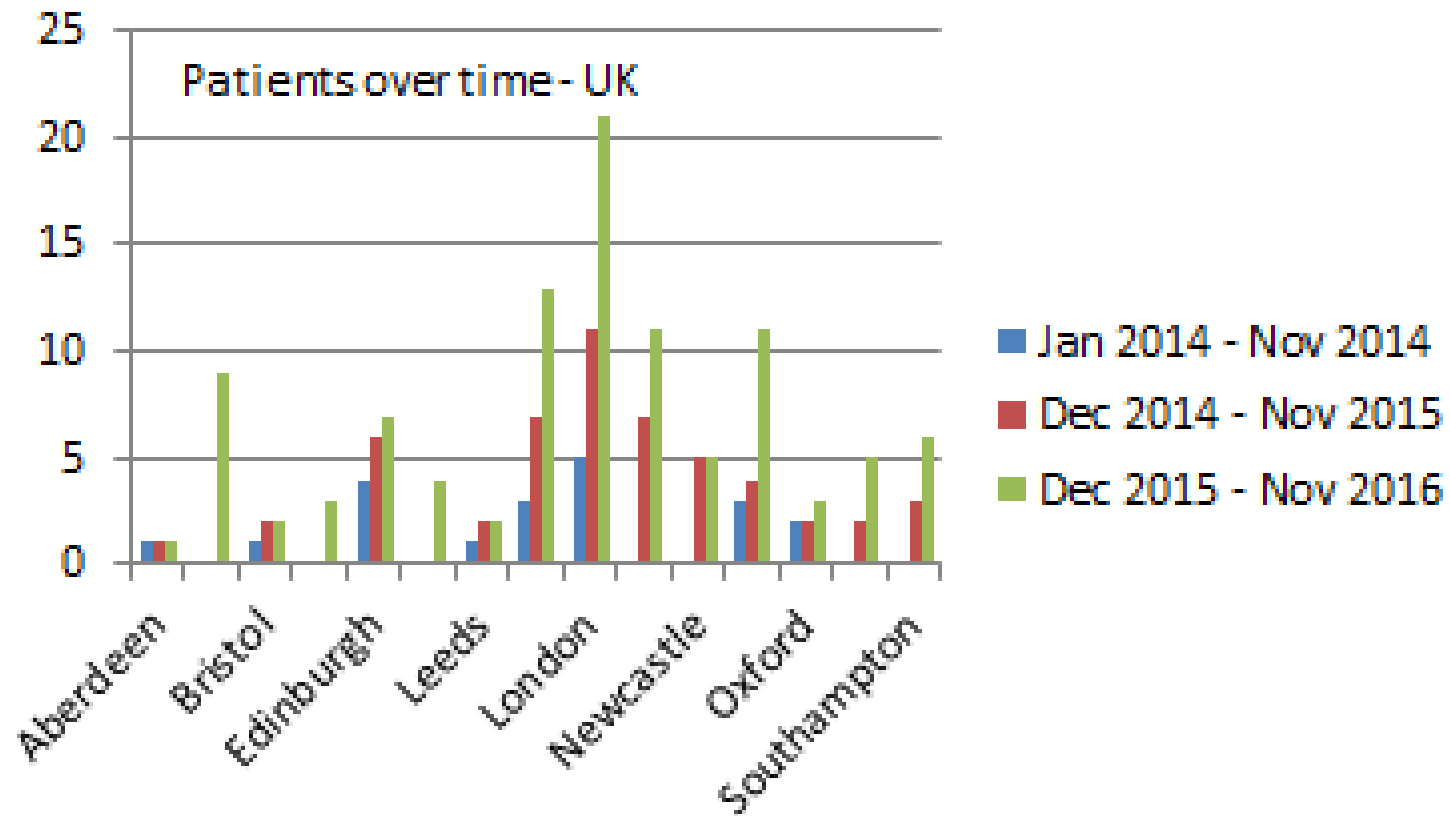


Fig 7: Patients over time in United Kingdom per site

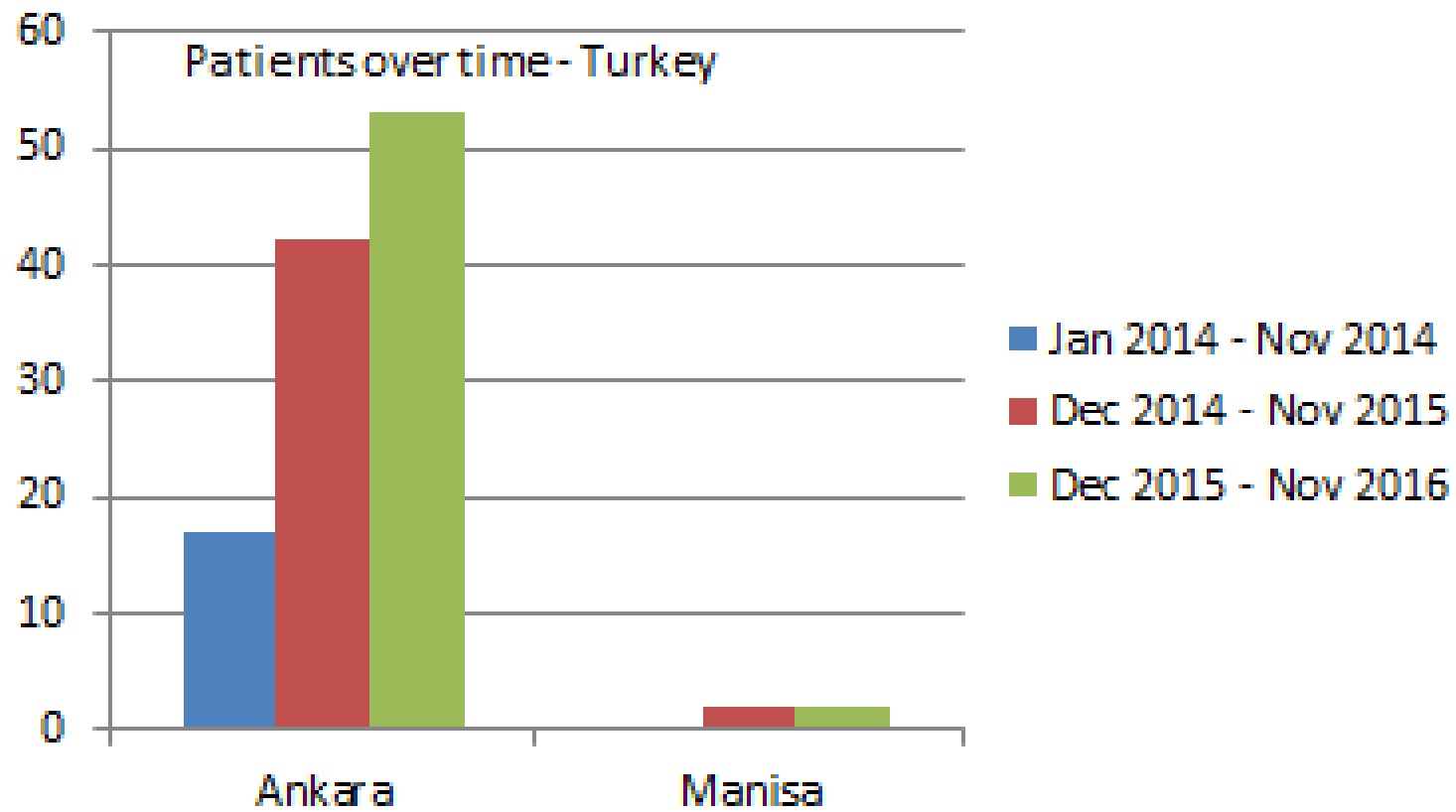


Fig 8: Patients over time in Turkey per site

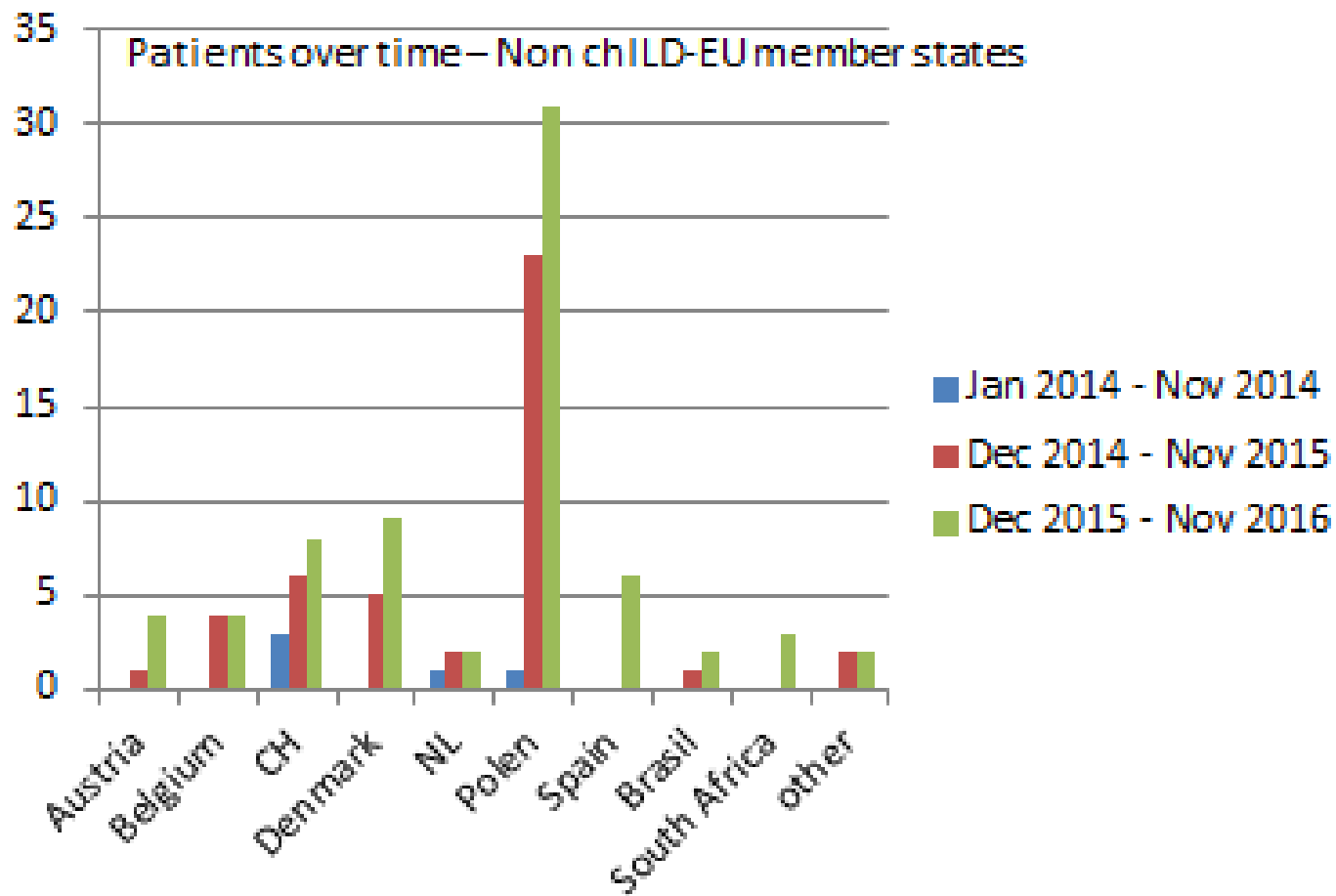


Fig 9: Patients over time in the Non chILD-EU member states per country

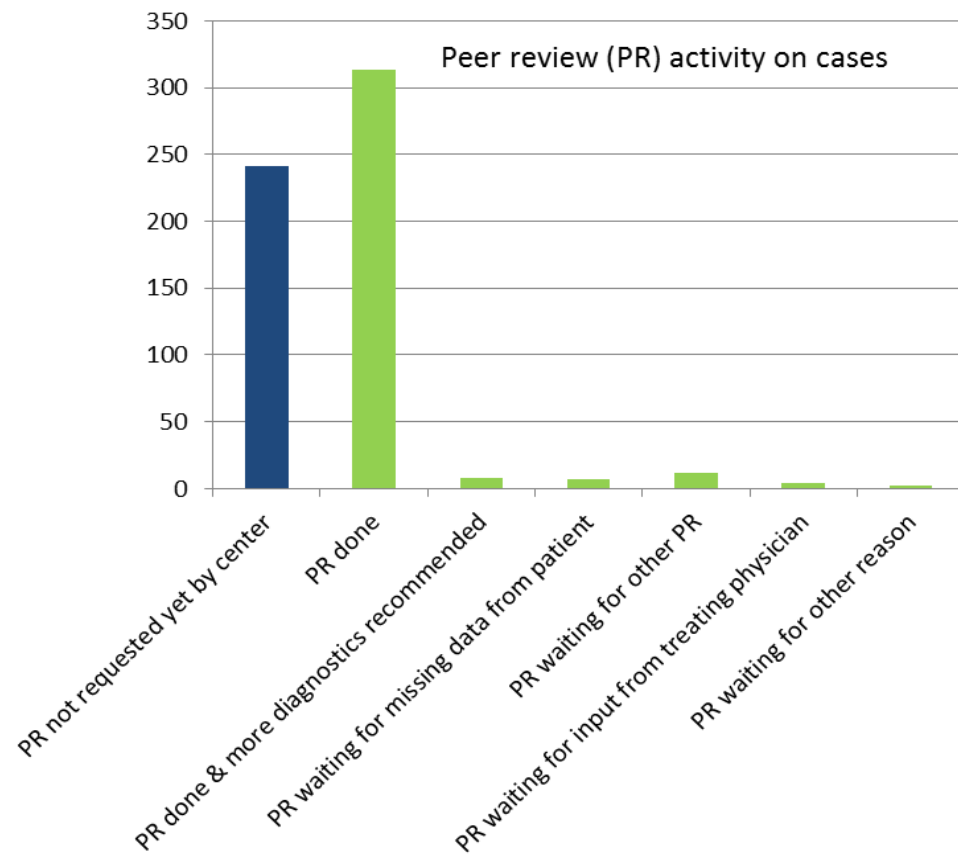


Fig 10: Peer review activity on cases

peer reviews per site

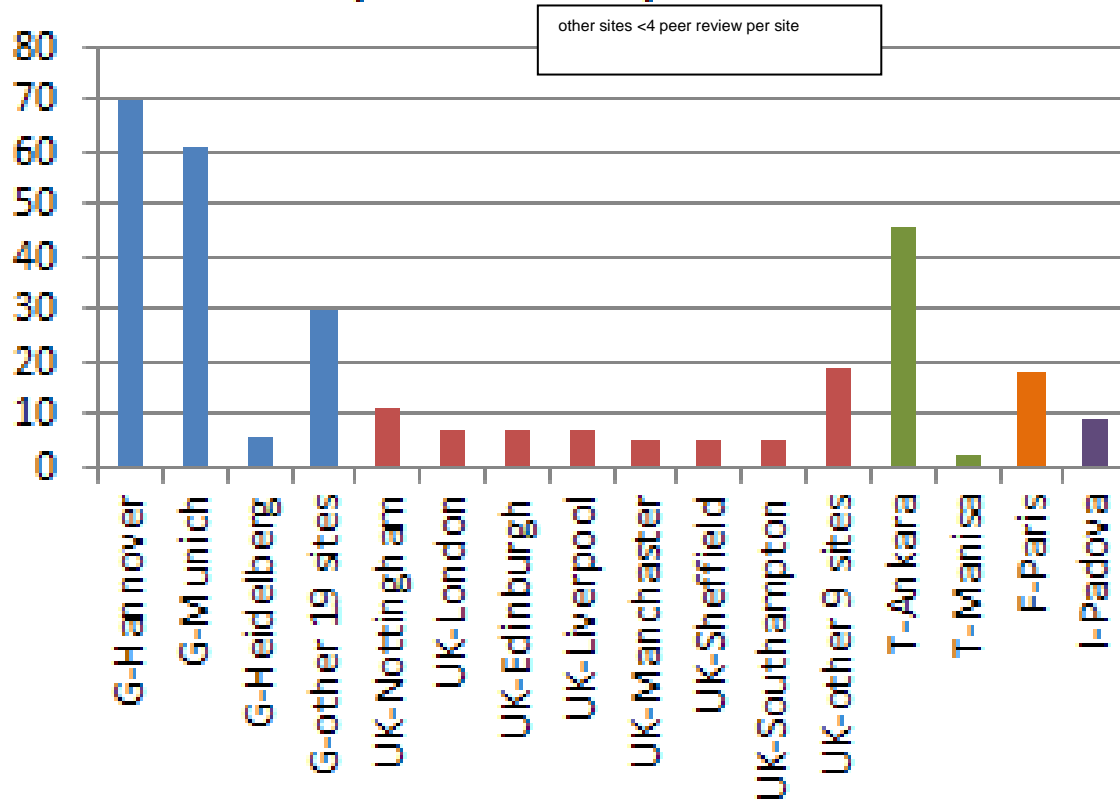


Fig 11: Peer reviews per site

Final list of acute exacerbation criteria

1. Increase in respiratory rate $\geq 20\%$ from baseline
2. Increase or development in/of dyspnoea
3. Newly developing or increased abnormalities on chest imaging
4. Onset/increase of/in oxygen demand to attain the individual baseline saturation (at rest and/or during exercise)
5. Need for an additional level of ventilatory support (in addition to oxygen)

6. Decrease in spirometry in children able to perform the tests ($\geq 10\%$ from baseline for vital capacity)
7. Reduced exercise tolerance in children able to perform the test[#]

Fig. 12: From Clement et al, Eur Respir J 2016; 48: 1559–1563

Tab 1: Contrasts of Pulmonary exacerbations (until baseline) for confirmation of criterion validity of the chILD specific QoL Scale, PedsQL Psychological health summary score, Physical health summary score, Total score

Domain	Variable	PROXY						SELF					
		n	M	SD	T	p	d	n	M	SD	T	p	d
chILD specific QoL	Pulmonary exacerbation												
	No	39	70.91	24.44	2.09	.040*	.44	15	72.88	16.89	1.41	.166	.43
	Yes	54	58.99	28.98				23	62.12	29.89			
Psychosocial health summary score	No	61	76.12	16.79	3.41	.001**	.55	21	76.15	14.58	1.81	.076	.47
	Yes	84	64.42	24.58				32	65.70	27.19			
Physical health summary score	No	63	70.25	23.67	3.20	.002**	.52	21	66.82	25.22	1.84	.072	.52
	Yes	85	56.24	29.58				32	51.27	32.81			
Total Score	No	64	73.89	19.01	3.35	.001**	.56	21	73.79	15.97	1.98	.053	.52
	Yes	85	61.55	24.38				32	62.01	27.31			

Abbreviations: M = mean, SD = standard deviation, T = standard score of the Student's t-statistic, p = p value of the statistical significance test, d = effect size Cohen's d

Note: Total score = Psychosocial health summary score + Physical health summary score

*** < 0.001; ** < 0.01; * < 0.05

WP5 Treatments – determine variability and efficacy, deliver data to define specific pharmacologic treatments

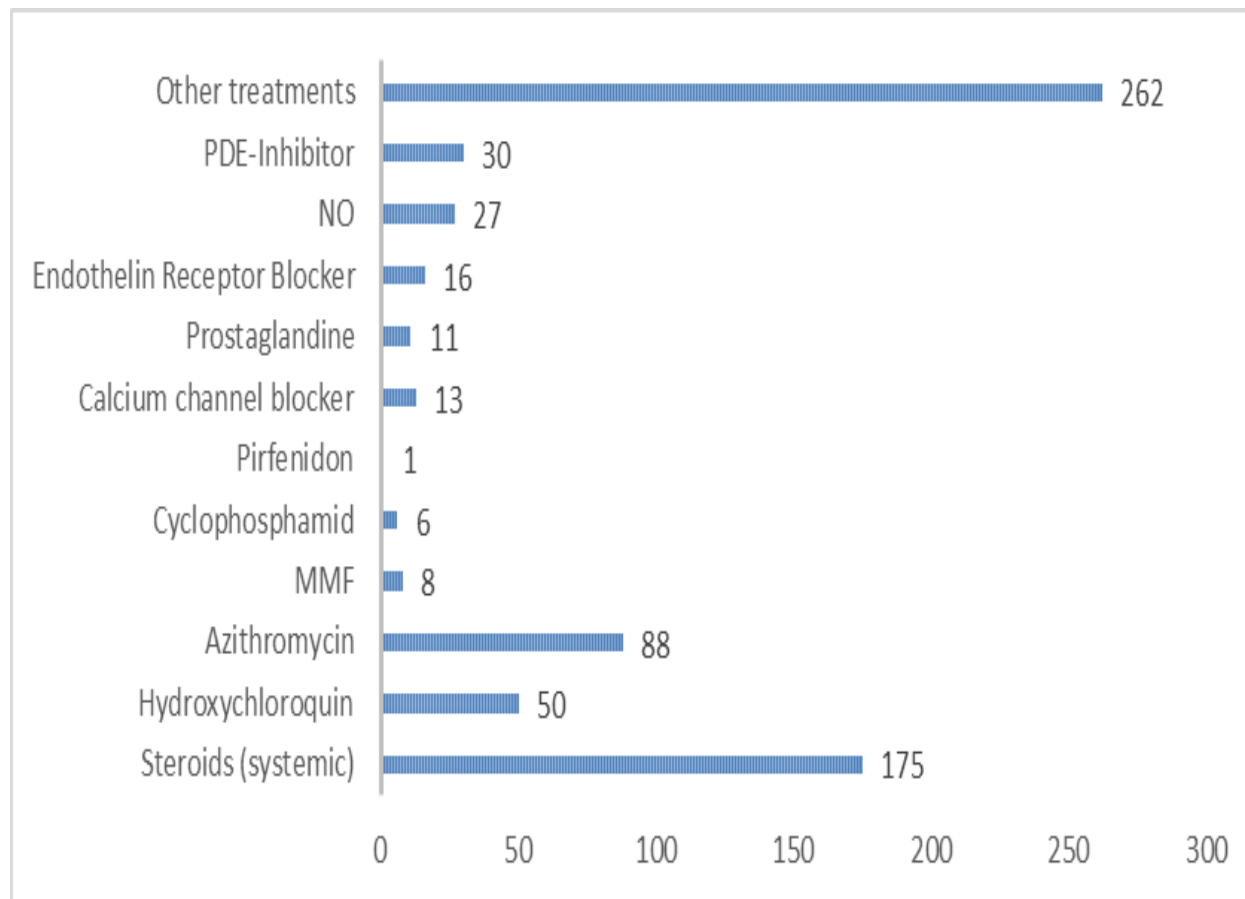


Figure 13: Analysis of different medications used in the whole cohort (n=366)

Table 2: Definition of included disease categories

A1 - DPLD-Diffuse developmental disorders
A2 - DPLD-Growth abnormalities deficient alveolarisation
A3 - DPLD-Infant conditions of undefined etiology
A4 - DPLD-related to alveolar surfactant region
Ax - DPLD-unclear RDS in the mature neonate
Ay - DPLD-unclear RDS in the almost (30-36 wks) mature neonate
B1 - DPLD-related to systemic disease processes
B2 - DPLD-in the presumed immune intact host, related to exposures (infectious/non-infectious)
B3 - DPLD-in the immunocompromised host or transplanted
B4 - DPLD-related to lung vessels structural processes
B5 - DPLD-related to reactive lymphoid lesions
Bx - DPLD-unclear RDS in the NON-neonate
By - DPLD-unclear NON-neonate
Bz - DPLD
C1 - Localized, congenital gross structural abnormalities of the lungs
C2 - Localized, aquired gross structural abnormalities of the lungs
D - Airway disorders
E - Pleural disease
F - Lung infections

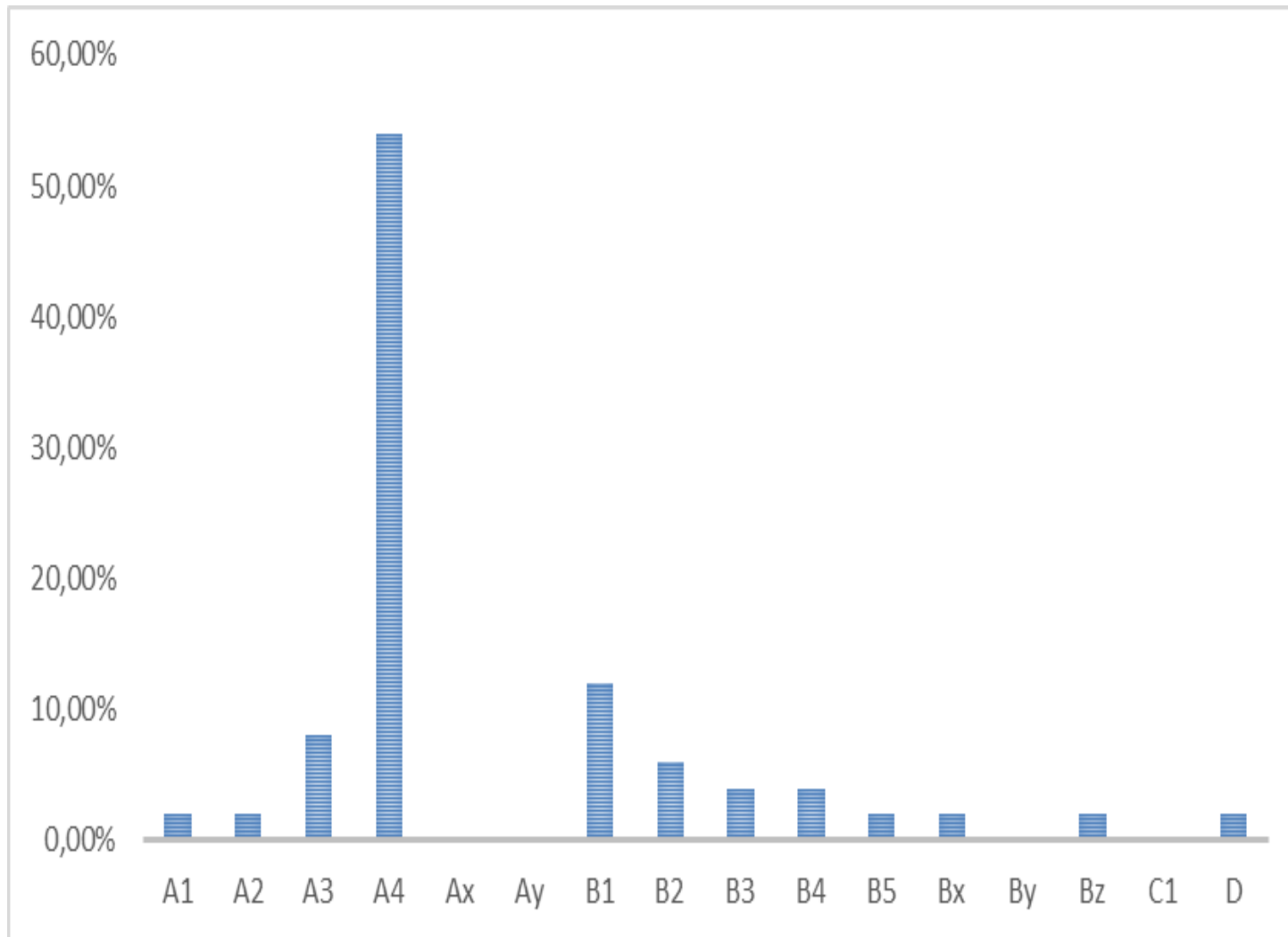


Figure 14: Amount of Hydroxychloroquine intake in different subcategories

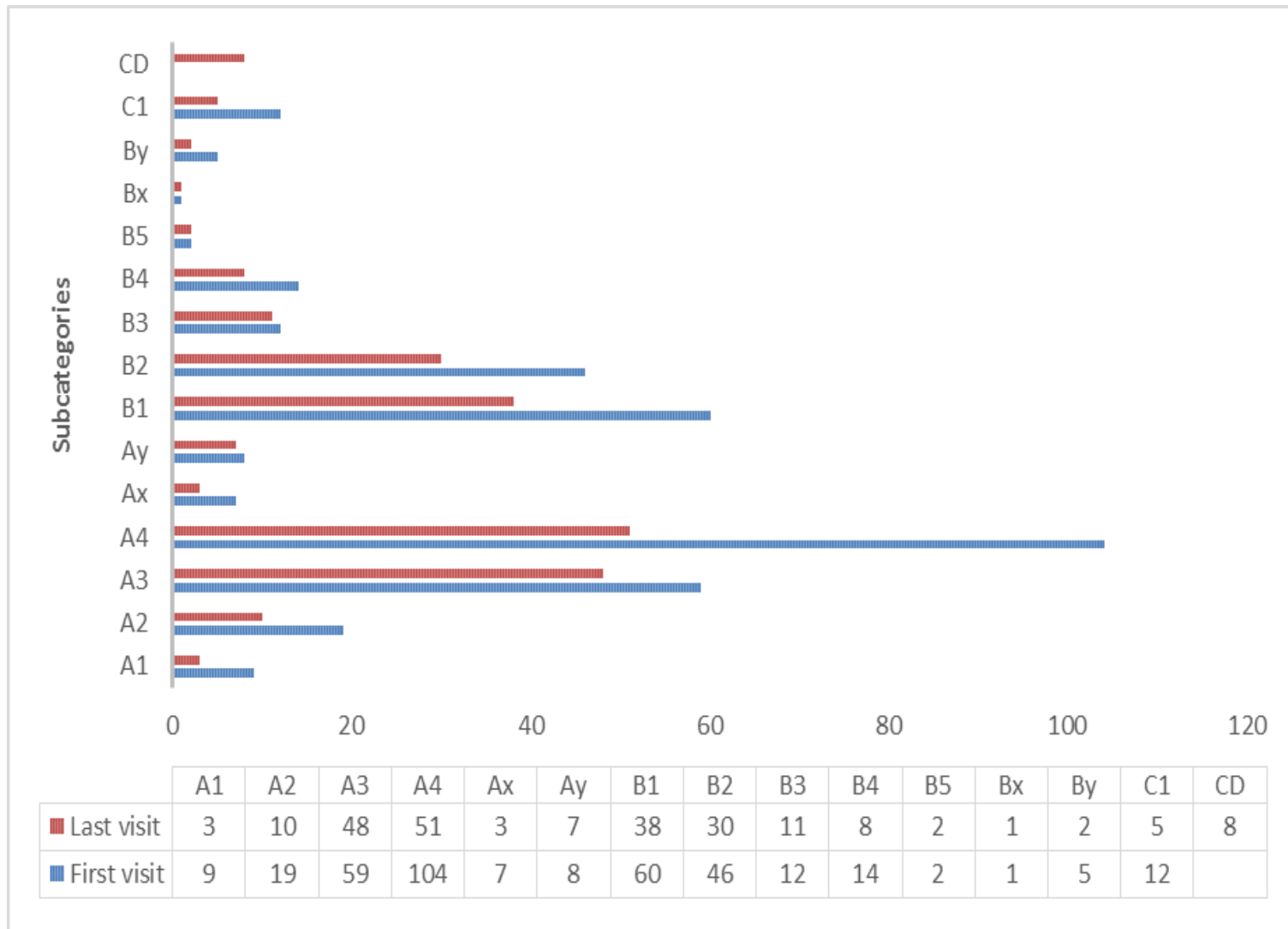


Figure 15: Distribution of different disease categories at baseline visit (n=366, blue) and at the last follow up visit (n=227, red)

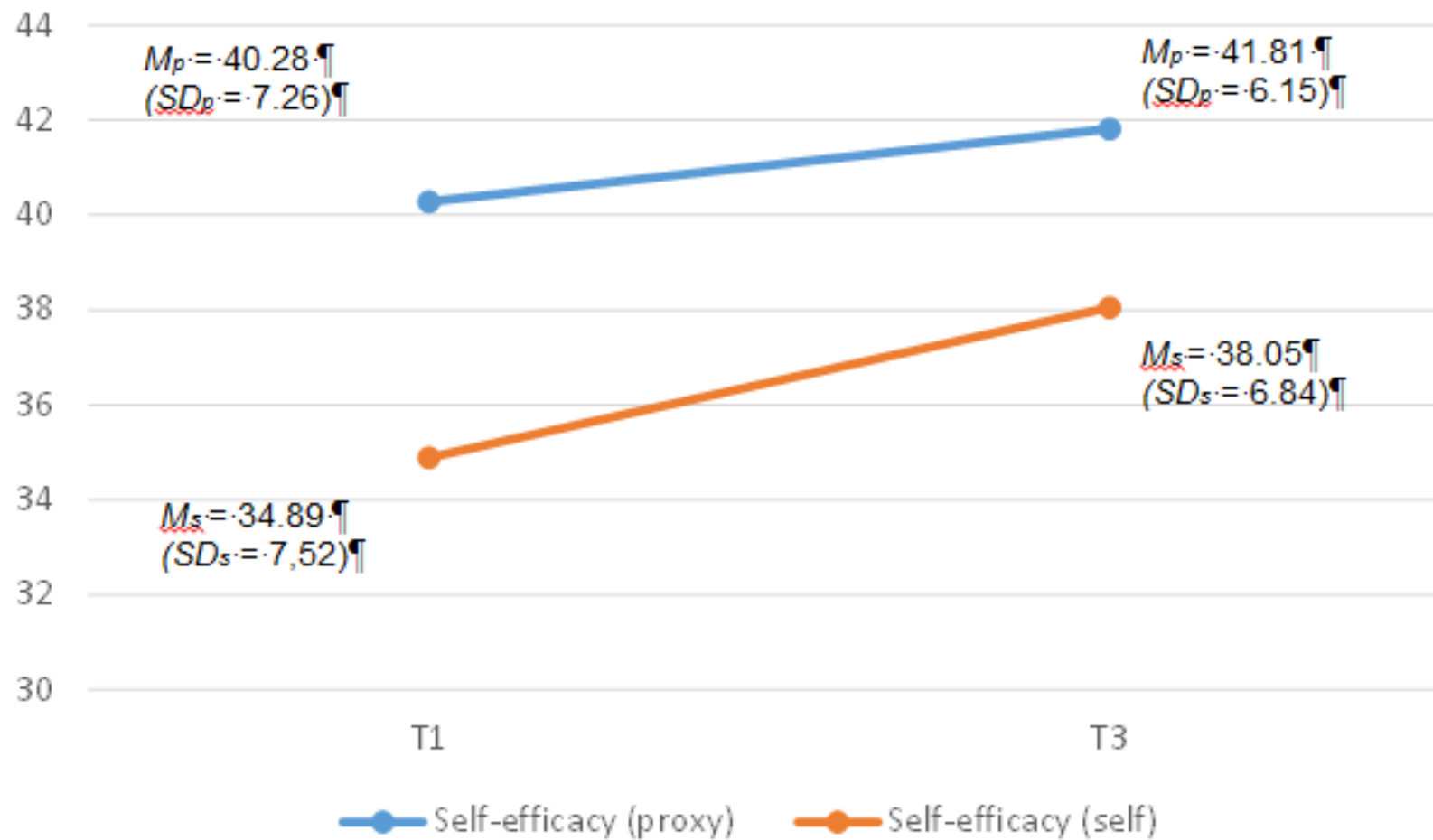


Figure 16: Pre- post comparison of the primary outcome self-efficacy

WP6

Randomized interventions with off-label treatments

Tab 3: Ethics committee and competent authorities' approvals for the clinical trials HCQ and Stop EAA

Ethics approvals		Competent authority approvals	
HCQ	Stop EAA	HCQ	Stop EAA
Germany		Germany (BfArM)	Germany (BfArM)
Munich (central site) and Hannover, Duisburg-Essen, Frankfurt, Leipzig, Gießen, Berlin	Munich (central site) and Hannover, Bochum, Duisburg-Essen, Frankfurt, Leipzig		
Bochum			
Tübingen			
Kiel-Luebeck			
Turkey	n.a.	n.a.	n.a.
Ankara			
UK	n.a.	UK (MHRA)	n.a.
Edinburgh			
London (3 sites)			
Nottingham			
Newcastle			
Southampton			
Liverpool			
Birmingham			

Tab 4: Scheduled insurance completion

Process of trial insurances	Start date	Finalized date
Germany for HCQ and EAA trial	01.11.2013	30.01.2015
Preparation of all ICF's in 4 other languages and request for insurance	01.06.2014	French not available
Turkey, police of HCQ trial received	01.11.2014	03.08.2015
Italy, police of HCQ trial received, version 2.0 requested according ethics request	01.11.2014	15.06.2015; changed version 2.0 26.04 2016
UK, police of HCQ trial received	01.11.2014	24.11.2015
France, police received	01.11.2014	no

Tab 5: Contracts prepared and status of processing for HCQ- and EAA trial

Central contracts		
	tasks	Completely signed
EAA trial contract Annex I: Grant Agreement Annex II: Responsibility Split	Data collection (electronically case record forms)	Sponsor (LMU) and Marburg - EAA
	Clinical Monitoring	Sponsor (LMU) and IZKS Mainz
		Sponsor (LMU) and IZKS Mainz: Addendum I for SUSAR's
	Clinical study medication	Sponsor (LMU) and pharmacy Mainz
HCQ trial contract Annex I: Grant Agreement Annex II: Responsibility Split	Data collection (electronically case record forms)	Sponsor (LMU) and Marburg
	Clinical Monitoring	Sponsor (LMU) and IZKS Mainz
		Sponsor (LMU) and IZKS Mainz: Addendum I for SUSAR's
	Clinical study medication	Sponsor (LMU) and pharmacy Munich

Tab 6: Contracts with German sites and national coordinators for HCQ- and EAA trial

Contracts with sites in Germany (EAA and HCQ trial)	initiated	signed
Contracted: Munich, Hannover, Essen, Frankfurt, Leipzig, Gießen, Bochum, Tübingen, Lübeck/Kiel	02.12.2013	04.11.2016
In Progress: Berlin, Heidelberg,	02.12.2013	ongoing
Contract national coordinator	01.10.2013	
Turkey	01.10.2013	Not done, ongoing competent authority process
Italy	01.10.2013	15.10.2014
France (dependent on Paris site)	01.10.2013	Will not participate
UK	01.10.2013	10.05.2016

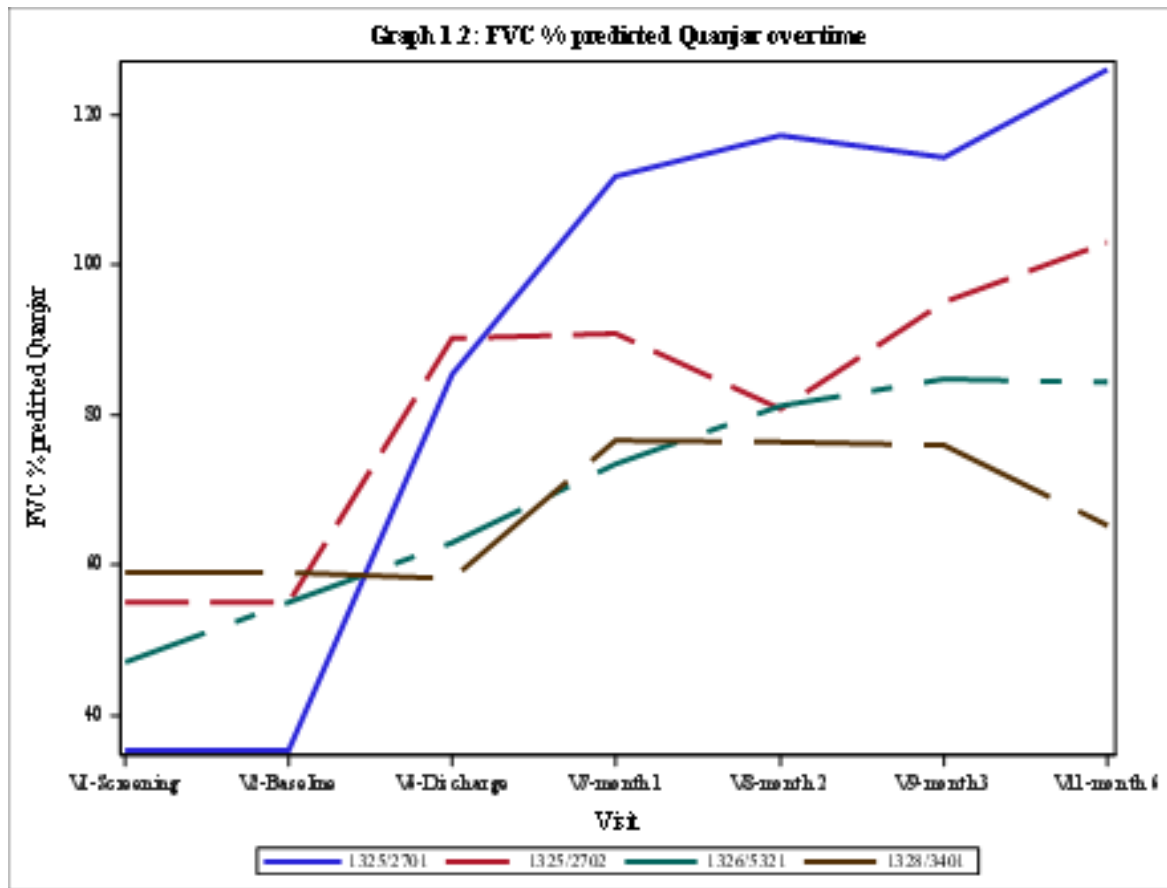


Fig. 17 FVC as primary outcome in the exogen allergic alveolitis trial (Stop-EAA),

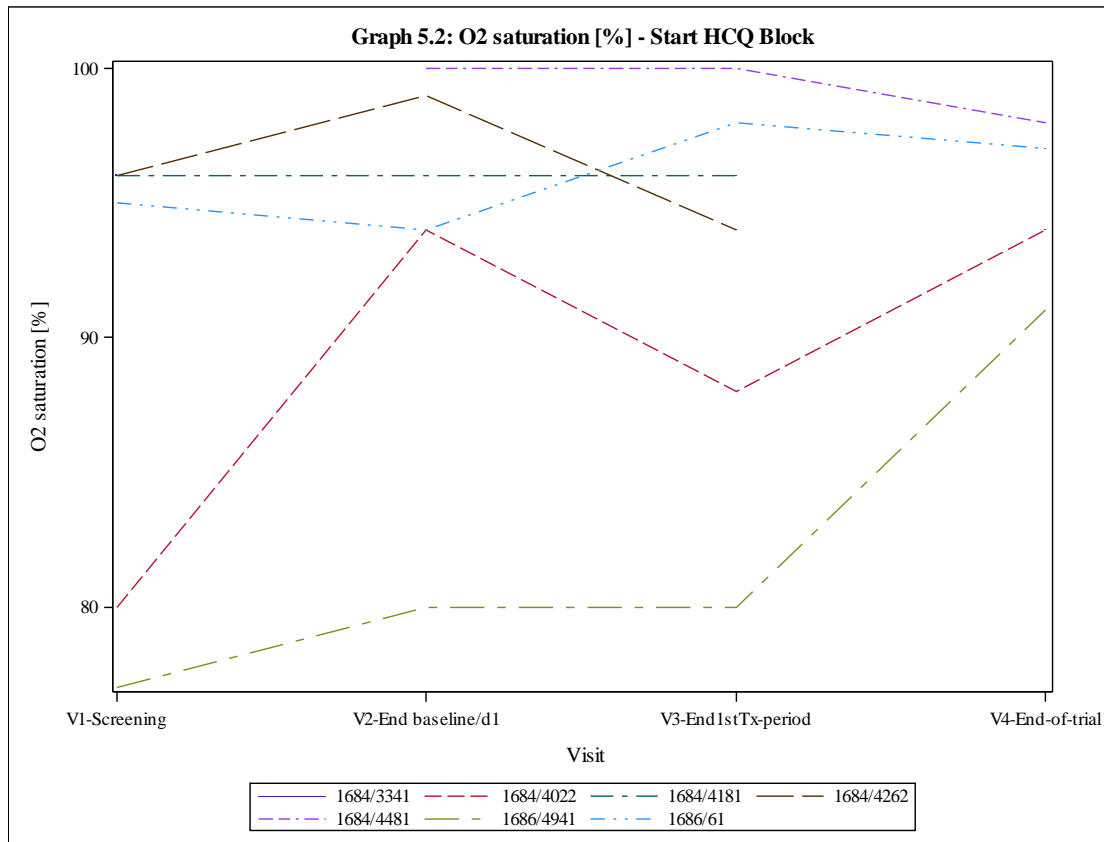


Fig. 18: O2-saturation as primary outcome in the hydroxychloroquine START trial (START-HCQ).

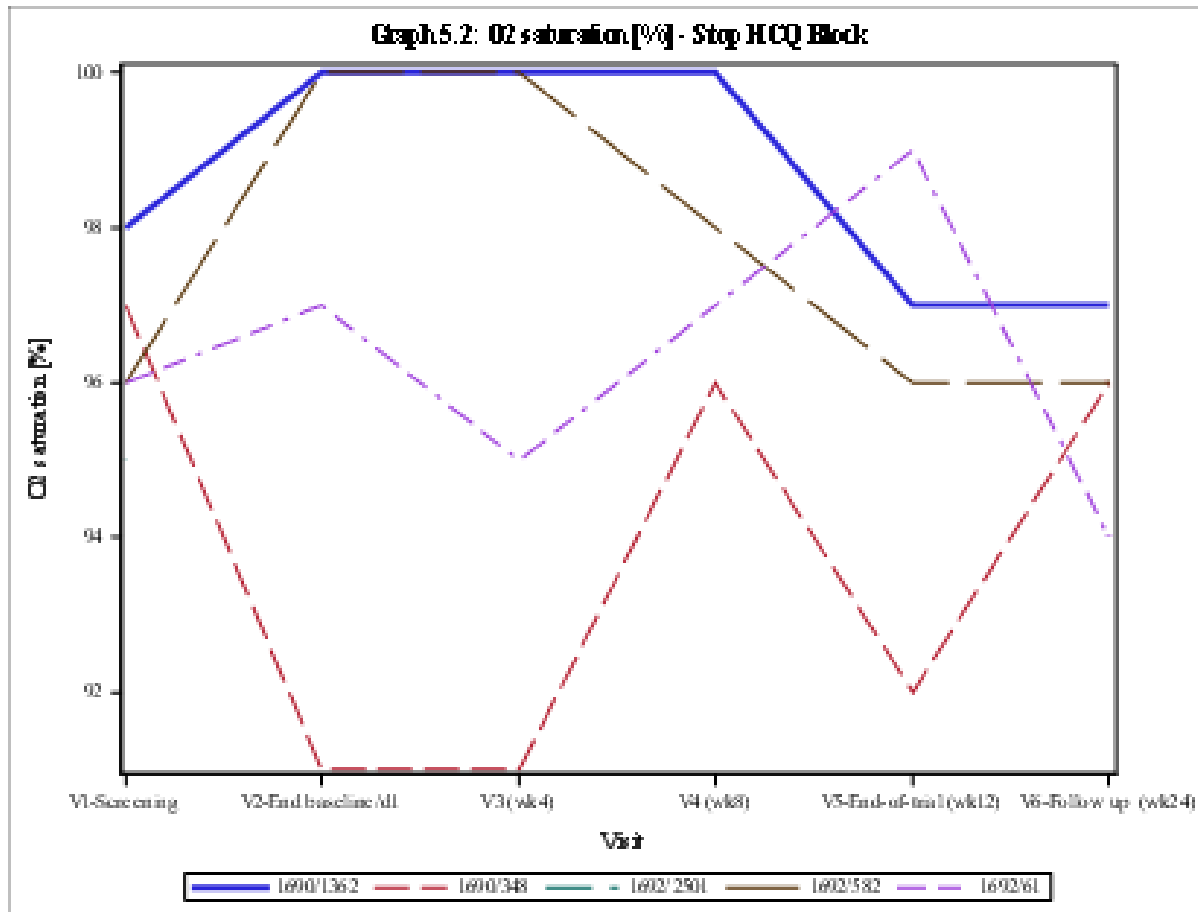


Fig. 19: O2-saturation as primary outcome in the hydroxychloroquine STOP trial (STOP-HCQ).

4.1.4 Potential impact and the main dissemination activities and exploitation of results

Dissemination and Exploitation

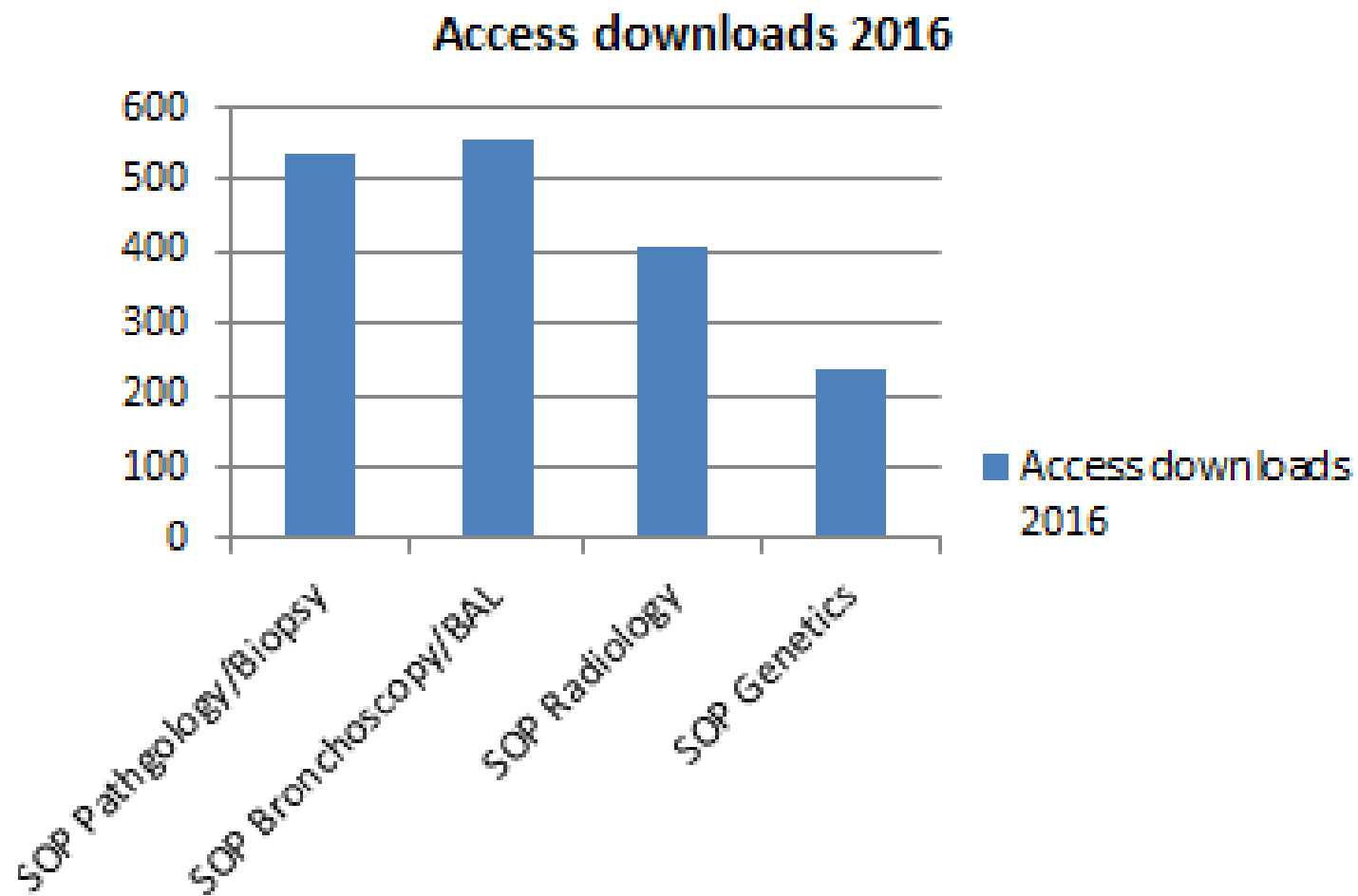


Fig. 20: Access numbers for SOPs

Access downloads 2016

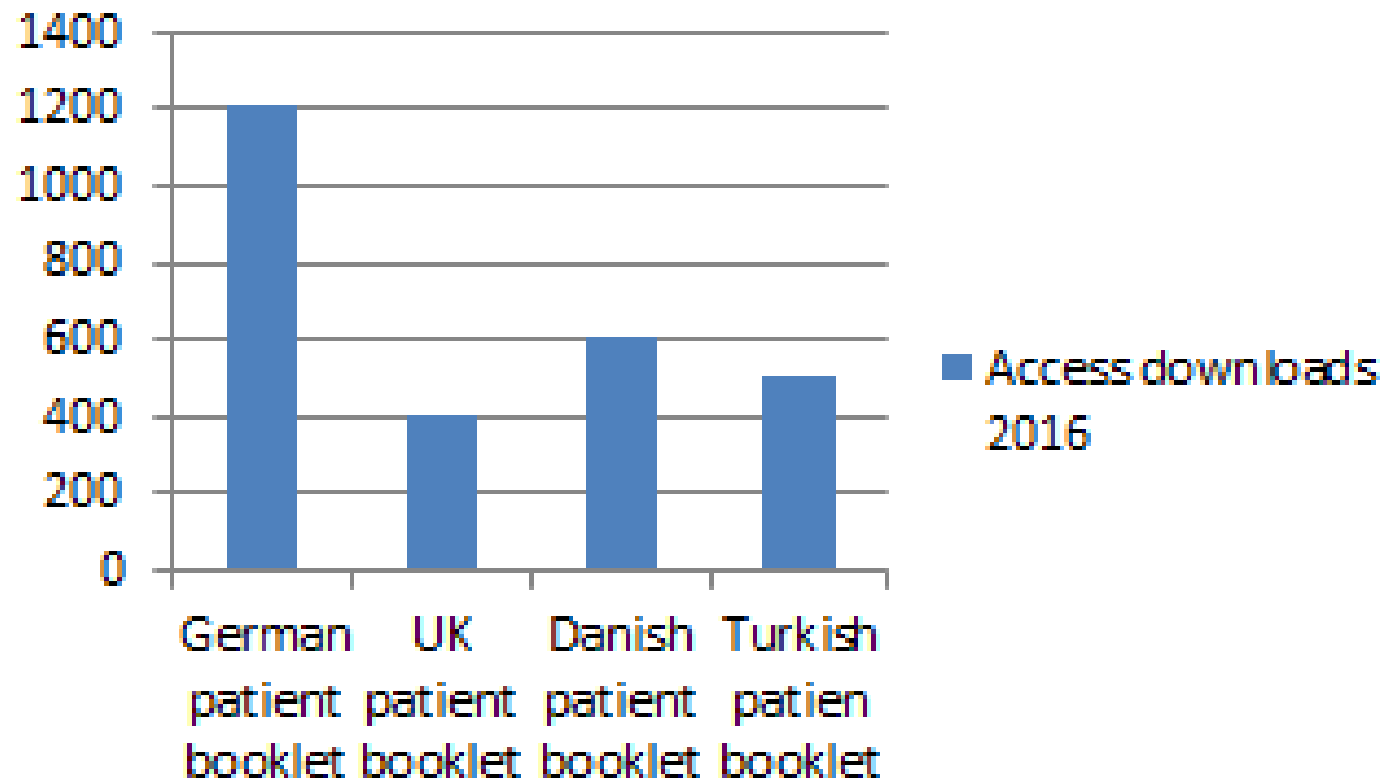


Fig. 21: Access numbers for patient booklets

4.1.6 Project logo, diagrams or photographs illustrating and promoting the work of the project (including videos, etc...), as well as the list of all beneficiaries with the corresponding contact names can be submitted without any restriction



Fig. 22: Logo chILD EU project



European Management Platform for **Childhood** Interstitial **Lung Diseases**

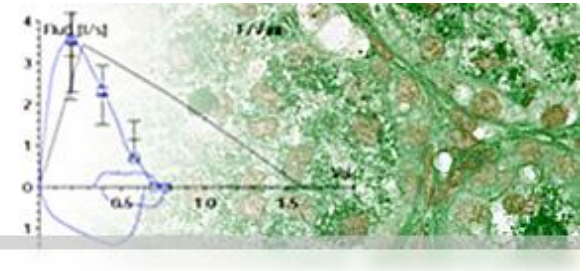


Fig. 23: Head chILD EU project website www.childeu.net

Tab. 7: Beneficiary list chILD EU project

COORDINATOR Organisation - LUDWIG-MAXIMILIANS-UNIVERSITAET MUENCHEN

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