European Journal of Endocrinology, 2025, **193**, 685–703
https://doi.org/10.1093/ejendo/lvaf214
Advance access publication 28 October 2025
Original Research

Epidemiological and clinical data from the European Lipodystrophy Registry

Giovanni Ceccarini,[1,†‡] Camille Vatier,[2,†‡] Baris Akinci,[3,†] Ines Belalem,[2] Marjoleine Broekema,[4] Eva Csajbok,[5] Maria Rosaria D'Apice,[6] Alessandra Gambineri,[7] Kathrin Heldt,[8] Martin Heni,[9,10] Lotte Kleinendorst,[4,11] Kerstin Krause,[12] Giovanna Lattanzi,[13] Konstanze Miehle,[12] Lavinia Palladino,[1] Flavia Prodam,[14] Ferruccio Santini,[1] Ermelinda Santos Silva,[15,16] David B. Savage,[17,†] Paolo Sbraccia,[18] Thomas Scherer,[19] Ekaterina Sorkina,[20] Iztok Štotl,[21] Marie-Christine Vantyghem,[22,†] Corinne Vigouroux,[2] Elena Vorona,[23] David Araújo-Vilar,[24,†] Martin Wabitsch,[25,26,†] Gabriele Nagel,[27,†‡] and Julia von Schnurbein[25,*†‡]
ECLip Registry Consortium

[1]Obesity and Lipodystrophy Center, Endocrine Unit, University Hospital of Pisa, Via Paradisa, 2, Pisa 56124, Italy
[2]Sorbonne University, Inserm U938, AP-HP, Saint-Antoine University Hospital, National Reference Center for Rare Diseases of Insulin Secretion and Insulin Sensitivity (PRISIS), Departments of Endocrinology, Diabetology and Reproductive Endocrinology, and Molecular Biology and Genetics, 184, Rue du Faubourg Saint-Antoine, Paris 75012, France
[3]DEPARK, Dokuz Eylul University Health Campus, Department of Endocrinology and Metabolism & Izmir Biomedicine and Genome Center (IBG), Mithatpaşa Cad. 58/5, 35340 Balcova, Izmir, Turkey
[4]Department of Human Genetics, Amsterdam Reproduction & Development Research Institute, Amsterdam UMC, University of Amsterdam, Meibergdreef 9, Amsterdam 1105AZ, the Netherlands
[5]Department of Internal Medicine, Endocrinology-Diabetology Unit, University of Szeged, Szeged, Szolg. sor. 1, Hungary
[6]Medical Genetics Laboratory, Policlinico Tor Vergata, Viale Oxford, Rome 81 00133, Italy
[7]Division of Endocrinology and Diabetes Prevention and Care, Department of Medical and Surgical Sciences, ENDO ERN Center for Rare Endocrine Diseases, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Via Giuseppe Massarenti, 9, Bologna, BO 40138, Italy
[8]Stiftung Ostschweizer Kinderspital, Claudiusstrasse 6, 9000 St. Gallen, St. Gallen, Switzerland
[9]Division of Endocrinology and Diabetology, Department of Internal Medicine, Ulm University Medical Centre, Eythstrasse 24, Ulm 89075, Germany
[10]Department for Diagnostic Laboratory Medicine, Institute for Clinical Chemistry and Pathobiochemistry, University Hospital Tübingen, Oberer Wässere 8, Tübingen 72076, Germany
[11]Emma Center for Personalized Medicine, Meibergdreef 9, Amsterdam 1105 AZ, The Netherlands
[12]Medical Department III—Endocrinology, Nephrology, Rheumatology, Lipodystrophy Center Leipzig, University of Leipzig, Liebigstrasse 18, Leipzig 04103, Germany
[13]CNR Institute of Molecular Genetics "Luigi Luca Cavalli-Sforza", Unit of Bologna, c/o Istituto Ortopedico Rizzoli, via di Barbiano 1/10, Bologna 40136, Italy
[14]Department of Health Sciences, Unit of Endocrinology, Università del Piemonte Orientale, Via Solaroli 17, Novara 28100, Italy
[15]Pediatric Gastroenterology Unit, Department of Pediatrics, Centro Materno Infantil do Norte (CMIN), Centro Hospitalar Universitário de Santo António, Instituto de Ciências Biomédicas Abel Salazar (ICBAS), Universidade do Porto, Largo da Maternidade Júlio Dinis, 4050-651 Porto, Portugal
[16]UCIBIO—Applied Molecular Bioscienses Unit, Faculty of Pharmacy, Universidade do Porto, Rua de Jorge de Viterbo Ferreira, 228, 4050-313 Porto, Portugal
[17]University of Cambridge Metabolic Research Laboratories, IMS MRL, Box 289, Level 4 Addenbrooke's Hosp., Hills Rd., Cambridge CB2 0QQ, United Kingdom
[18]Internal Medicine Unit and Obesity Center, Department of Systems Medicine, University of Rome Tor Vergata, Via Cracovia, 50, Rome 00133, Italy
[19]Division of Endocrinology and Metabolism, Department of Medicine III, Medical University of Vienna, Waehringer Guertel 18-20, Vienna 1160, Austria
[20]Endocrinology Research Centre, Institute for Diabetes, 11 Dm. Ulianova, Moscow 117292, Russia
[21]Department of Endocrinology, Diabetes and Metabolic Diseases, University Medical Centre Ljubljana, Zaloška cesta 7, Ljubljana 1000, Slovenia
[22]CHU Lille, Department of Endocrinology and Metabolism, Inserm, Translational Research for Diabetes, UMR-1190, University of Lille, European Genomic Institute for Diabetes, Rue Polonovski, Lille 59000, France
[23]Medical Clinic B for Gastroenterology, Hepatology, Endocrinology and Clinical Infectiology, Division of Endocrinology, Diabetology and Nutritional Medicine, University Hospital Muenster, Albert-Schweitzer-Campus 1, Geb. A1, Muenster 89149, Germany
[24]Thyroid and Metabolic Diseases Unit, Centro de Investigación en Medicina Molecular y Enfermedades Crónicas (CIMUS)-IDIS, School of Medicine, Universidade de Santiago de Compostela, Rua de Ramón Baltar s/n, Santiago de Compostela 15782, Spain

Received: August 2, 2025. **Revised:** October 6, 2025. **Accepted:** October 8, 2025
© The Author(s) 2025. Published by Oxford University Press on behalf of European Society of Endocrinology.
This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (https://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

[25]Centre for Rare Endocrine Diseases, Division of Paediatric Endocrinology and Diabetes, Department of Paediatrics and Adolescent Medicine, ENDO-ERN Center for Rare Endocrine Diseases, Ulm University Medical Centre, Eythstraße 24, Ulm 89075, Germany
[26]Deutsches Zentrum für Kinder- und Jugendgesundheit, Ulm University Hospital, Eythstr. 24, 89075 Ulm, Germany
[27]Institute of Epidemiology and Medical Biometry, Ulm University, Helmholtzstrasse 22, Ulm 89081, Germany

*Corresponding author: Centre for Rare Endocrine Diseases, Division of Paediatric Endocrinology and Diabetes, Department of Paediatrics and Adolescent Medicine, Ulm University Medical Centre, Eythstrasse 24, Ulm 89075, Germany. Email: Julia.schnurbein@uniklinik-ulm.de

† ECLip Registry board member.
‡ Shared first/last authorship.

Abstract

Objective: Lipodystrophy syndromes comprise a group of rare diseases characterized by loss of adipose tissue without nutritional or catabolic causes. As the rarity of these conditions necessitates collaboration, the European Consortium of Lipodystrophies (ECLip) established an international, longitudinal registry for patients with all forms of lipodystrophy (excluding HIV-associated cases).

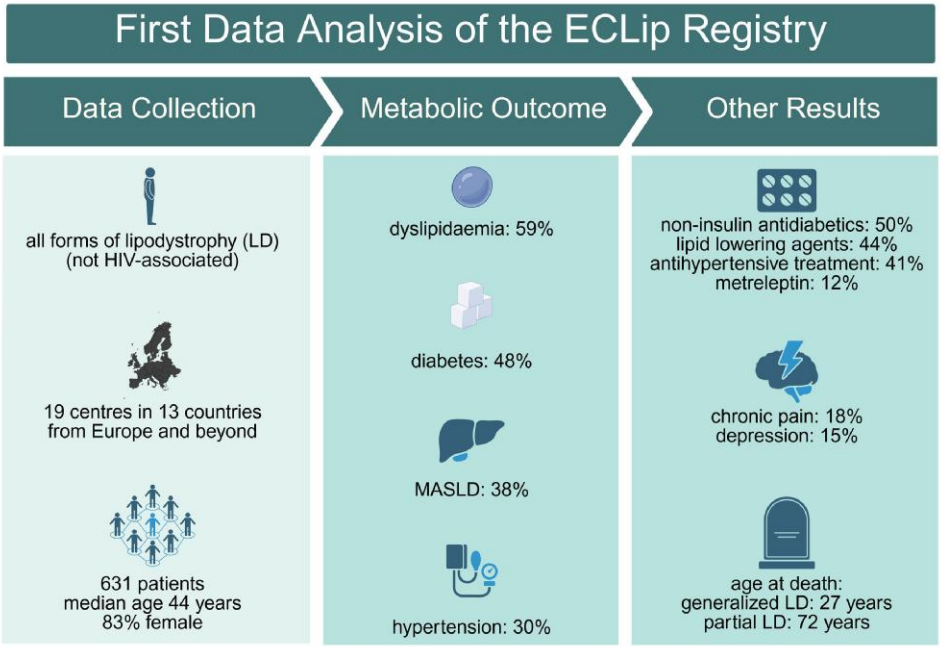
Methods: From December 2017 to November 2023, 19 centers from 13 countries recruited 631 patients into the ECLip Registry. Cross-sectional data were analyzed using descriptive statistics.

Results: Prospective data were available for 467 patients (82.7% female; 86.5% adults; median age 44.0 years). Familial partial lipodystrophy (FPLD) was the most common subtype (57.4%), especially FPLD2 (37.9%). However, in men, congenital generalized lipodystrophy was nearly as common as FPLD (33.3% vs. 35.8%). Symptoms at onset varied by subtype, with loss of adipose tissue being the most frequent. More than 70% of the patients suffered from metabolic complications, particularly dyslipidemia (59.0%) and diabetes (48.4%), but prevalence and severity varied between subtypes (prevalence of diabetes, eg, 76.9% in patients with acquired partial lipodystrophy vs. 8.7% in acquired localized lipodystrophy). Metreleptin, the only disease-specific treatment, was used by 11.6% of all patients. Thirty-four deaths were documented, primarily due to cardiovascular events and cancer. Patients with generalized forms of lipodystrophy died earlier compared to patients with partial forms (median age at death 27.0 vs. 72.0 years).

Conclusion: This study describes the largest cohort of patients with lipodystrophy reported to date. The dataset offers a comprehensive view of the epidemiology, clinical presentation, and associated comorbidities of lipodystrophy.

Keywords: lipodystrophy, registry, metabolic diseases, chronic complications, adipose tissue, leptin

Graphical Abstract



Significance

Lipodystrophy syndromes are ultra-rare disorders characterized by a lack of adipose tissue and development of an ample series of metabolic and non-metabolic complications leading to reduced life quality and expectancy. The European Lipodystrophy Registry (established in 2018) houses the largest global cohort of patients with lipodystrophy. In this first comprehensive data analysis of this cohort, we report a high prevalence (>70%) of metabolic comorbidities, analyzed in detail for each subgroup of lipodystrophy. Additionally, our findings underscore the significant burden of the disease (with more than 27% of all patients suffering from psychosocial problems), the causes of death (mainly cancer and major cardiovascular events), and treatment modalities. They also highlight the urgent need for improved diagnostic awareness and treatment options.

Introduction

Lipodystrophy syndromes (LDS) are a group of rare diseases characterized by selective and irreversible loss of adipose tissue, unrelated to malnutrition or catabolism.[1] Loss of adipose tissue can be complete (ie, generalized) or partial and is the result of impaired adipose tissue development (genetic cause) and/or inadequate tissue maintenance (acquired cause).

Detection of LDS is based on clinical history, physical examination, imaging, and biochemical tests.[2] The differential diagnoses include a range of disparate conditions, such as anorexia nervosa, constitutional leanness, malnutrition, uncontrolled diabetes mellitus, polycystic ovary syndrome (PCOS), Cushing's syndrome, hyperthyroidism, and acromegaly, among others.

LDS have been traditionally divided into 4 major categories.[3] However, today, 6 categories are recognized: congenital or familial forms (generalized, partial, systemic—including progeroid and autoinflammatory syndromes), and acquired forms (generalized, partial, localized).[1]

LDS, especially generalized and familial partial forms, are often associated with the development of severe metabolic complications such as insulin resistance, including diabetes, hypertriglyceridemia, and metabolic dysfunction-associated steatotic liver disease (MASLD) and steatohepatitis (MASH). Low leptin levels further disrupt hunger regulation, promoting hyperphagia and worsening metabolic dysfunction.

In partial forms of lipodystrophy (PLD), regional adipose tissue loss may be associated with the expansion of adipose depots in other areas of the body.

Furthermore, LDS may be associated with a range of other specific features, depending on the subtype.

The reported prevalence of LDS is 1.3-4.7 cases per million,[4] though the true prevalence is likely higher due to underdiagnosis.[5-7] A very recent estimate, based on the 2 largest lipodystrophy registries (LD-Lync and the European Consortium of Lipodystrophy (ECLip) Registry), calculated a prevalence for FPLD alone of 19.0-30.0 per million.[8]

The low prevalence and the high heterogeneity between subtypes hinder comprehensive characterization of genetic variants, natural history, complications, treatment outcomes, and prognosis, including mortality rate by individual centers. This challenge is widely acknowledged by experts around the world.[9] Thus, centers affiliated to the European Consortium of Lipodystrophies, an association of European expert centers in lipodystrophy (https://www.eclip-web.org/; date last accessed March, 7, 2025) decided in 2016 to create an international registry for patients affected by LDS, called the ECLip Registry, to meet the needs in characterization of various clinical phenotypes, to define the long-term natural history and assess treatment outcomes under real world conditions.[10]

The aim of this cross-sectional study is to describe the patient population of the ECLip Registry, explore the prevalence of the different disease subgroups, and characterize them according to demographic, clinical, and treatment patterns.

Methods

The ECLip Registry

The ECLip Registry is drafted as a multicentric, international, longitudinal, observational study. Expert centers from all over the world are invited to join the registry (contact: help-eclip-registry@uniklinik-ulm.de). All patients of all ages with any form of lipodystrophy presenting at a participating center are asked to participate in the ECLip Registry; the only exclusion criterion is HIV-associated lipodystrophy. Data in the registry are divided into (mostly) unchanging basic data (year of birth, sex, diagnosis, genetic, age at diagnosis, etc.), and dynamic clinical characteristics collected repeatedly at each new visit ("episode data": eg, anthropometry, laboratory values, comorbidities, clinical characteristics, and current medication). Physicians are encouraged to record annual follow-up visits. Data collection is based on standard of care examinations performed during the visit. Information on patient status (active, loss of follow-up, deceased) is collected regularly. In addition to this prospective data collection, entry of retrospective data from visits that occurred before the patient's participation in the registry is also encouraged.

The set-up of the registry and data entry were described in detail previously.[10] The registry is registered at ClinicalTrials.gov (ClinicalTrials.gov ID: NCT03553420) and is an affiliated registry to the European Registries for Rare Endocrine Conditions EuRRECa. The consortium is governed by a board elected from the ECLip Registry members and a representative of patient advocacy groups. The ECLip Registry began to enroll and follow up patients prospectively from December, 16, 2017 onwards.

Classification of subgroups of LD

The cases of lipodystrophy were coded according to online Mendelian Inheritance of Man (OMIM; https://www.omim.org/) and Orphanet (https://www.orpha.net/). For comparison, the disease subtypes were categorized into 10 different subgroups: congenital generalized lipodystrophy (CGL), FPLD1 (polygenic form of FPLD; defined by an increased ratio of either truncal fat percentage or skinfold thickness compared to lower extremity), FPLD2 (*LMNA*-related FPLD, also known as Dunnigan syndrome), and other forms of FPLD not including type 1 and 2 (oFPLD), acquired generalized lipodystrophy (AGL), acquired partial lipodystrophy (APL), acquired localized lipodystrophy (ALLD), progeroid syndrome associated with generalized lipodystrophy (PSGLD) and progeroid syndrome associated with partial lipodystrophy (PSPLD), and other forms of lipodystrophy (oLD) (for more information see Supplementary Methods and Table S1).

Ethics approval and consent to participate

All centers participating in the ECLip Registry obtained ethical approval from their respective medical ethics committees in their countries. All prospectively recruited patients (or their caregivers) gave informed consent. In addition, some ethical committee approval also allows retrospective anonymized inclusion of former patients who were either dead or lost-to-follow-up at the start of the registry in the respective center.[10]

Study sample and parameters, imaging

For the current analysis, all patients registered by November, 7, 2023, were included after plausibility checks and data harmonization procedures. Data plausibility checks were conducted centrally and included checks for completeness as well as checks for outliers. Centers were asked to complement missing data if possible or correct implausible data.

We defined 2 study cohorts:

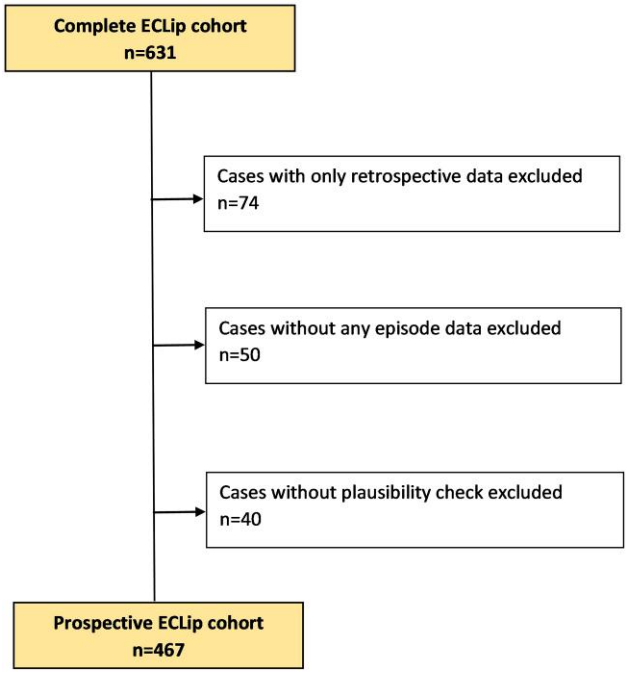


Figure 1. Flow chart. The figure shows the exclusion criteria for the prospective ECLip cohort.

1. all registered patients ("complete cohort"), including patients with only retrospectively collected data (see above) or basic data without episode data.
2. all prospectively registered patients ("prospective cohort"), which included only patients who had presented at least once to a center after the center had started participation in the ECLip Registry, and for whom episode data for at least one visit were available. Patients were excluded from the prospective cohort if only retrospective data were available for them, or no episode data at all, or if their center was not able to carry out data corrections identified to be necessary by the centralized plausibility check (Figure 1).

For the cross-sectional analysis of dynamic clinical characteristics, only the baseline visit was chosen. The baseline visit was defined as the main visit at the time of consent and was by definition only available for all patients in the prospective cohort. Therefore, data analysis of changeable parameters (such as anthropometry, laboratory values, and medication) was only performed in this cohort. In contrast, basic data such as diagnosis, age, and symptoms at diagnosis, and date and cause of death were analyzed in the complete cohort. The latter data were not strictly cross-sectional but reflected a snapshot of the recorded events at the time of the cross-sectional survey without systematic follow-up.

Based on the age at baseline, patients were classified as children/adolescents (<18 years) or adults (≥18 years).

In children, information on BMI was provided as BMI *z*-score based on World Health Organization (WHO) percentiles (https://www.who.int/toolkits/child-growth-standards/standards/body-mass-index-for-age-bmi-for-age).

Drug usage documented as Anatomical Therapeutic Chemical (ATC) codes (current valid version at the date of data entry) was subdivided into 11 different medication subgroups (Supplementary Methods).

Total body fat percentage was assessed using dual-energy X-ray absorptiometry (DEXA) and compared to measurements in healthy cohorts.[11]

Information on sex refers to the apparent biological sex identified and assigned at birth. In most patients, this is based on anatomic features without confirmation via chromosomal genotyping.

For further information on data acquisition, please refer to Supplementary Methods.

Statistical analyses

For the current study, the analyses focused on descriptive summary statistics, for which we used the statistical software package SAS release 9.4 (SAS Institute, Cary, NC, USA). For this first cross-sectional analysis, no group comparison was performed. Any differences between groups are therefore merely descriptive without testing for significance. Continuous data is presented as median and interquartile range (IQR). For categorical data, frequencies were calculated. If the percentage of patients is given, this always refers to the number of patients for whom information on the specific parameter (eg a specific comorbidity) was available.

Data and resource availability

The ECLip Registry encourages all researchers to use data from the ECLip Registry for scientific purposes. Interested researchers should submit an official application to the ECLip Registry Board (help-eclip-registry@uniklinik-ulm.de). Additional information about the ECLip Registry and access to data can be found at the registry's homepage (https://eclip-registry.com/; date last accessed July, 8, 2025).

Results

Number of patients and their characteristics

The complete cohort included 631 patients from 19 centers in 13 countries. For 74 patients, only retrospective data were available, 50 lacked any documentation of a visit (episode data), and plausibility checks were not possible in 40 patients, leaving 467 patients in the prospective cohort (Figure 1).

Both cohorts (complete and prospective) were mostly female (81.6% and 82.7%, respectively), adult-aged (85.9% and 86.5% adults; median age 45.0 years; IQR 32.0-57.0 and 44.0 years; IQR 30.0-57.0), and from Europe (84.6% and 81.8%, respectively; Table 1). Familial partial lipodystrophy (FPLD) was the most common subgroup (58.6% and 57.4%), with FPLD2 being the most common diagnosis (38.2% and 37.9%; Table 1 and Figure 2). In males, CGL was nearly as common as FPLD (33.3% vs. 35.8% in the prospective cohort, Figure 2). Only one male patient was diagnosed with FPLD1 (based on his high ratio of subscapular to calf skinfold thickness, low leptin levels, and severe metabolic phenotype; Figure 2). As expected, patient status differed by cohort, with more lost to follow-up and deceased cases in the complete cohort (23.7% vs. 16.2% and 5.5% vs. 3.7%, respectively; Table 1).

In the prospective cohort, the median BMI in adults was 24.8 kg/m² (IQR 21.9-29.0) and the median BMI z score in children was 0.00 (IQR −0.01 to 0.01). Median total body fat content was low-normal (around minus 1 SD) for male and female adults (22.3%, IQR 18.8%-25.0% and 28.9%, IQR 22.2-36.9, respectively) and male and female children

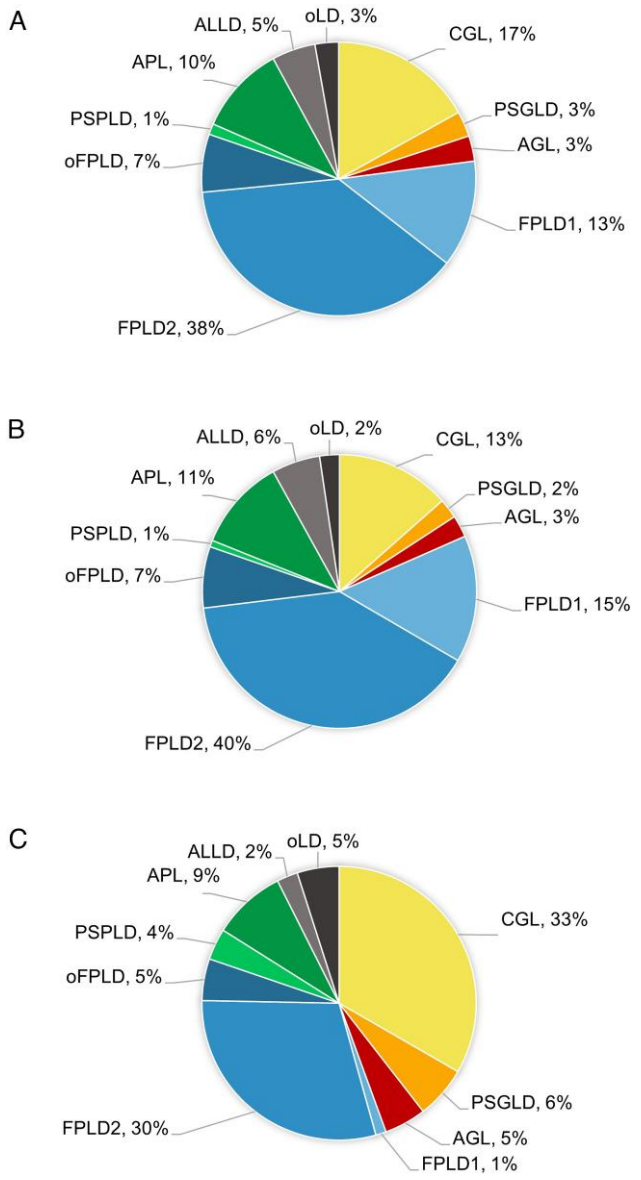


Figure 2. Distribution of lipodystrophy subtypes in the prospective ECLip cohort. The data show the percentage of patients living with the different lipodystrophy subtypes in the prospective ECLip cohort. (A) Shows the whole cohort ($n = 467$). (B) Shows only female patients ($n = 386$). (C) Shows only male patients ($n = 81$). AGL, acquired generalized lipodystrophy; ALLD, acquired localized lipodystrophy; APL, acquired partial lipodystrophy; CGL, congenital generalized lipodystrophy; FPLD, familial partial lipodystrophy; oLD, other forms of lipodystrophy; oFPLD, other forms of familial partial lipodystrophy not including type 1 and 2; PSGLD, progeroid syndrome associated with generalized lipodystrophy; PSPLD, progeroid syndrome associated with partial lipodystrophy.

(20.6%; IQR 17.3%-22.1% and 23.6%; IQR 18.5-30.9, respectively) according to their median age (Tables 1 and 2).[11]

Age at diagnosis and first symptoms

Age at diagnosis tended to be lower in patients with generalized forms of lipodystrophy (GLD, 13.0 years; IQR 3.0-32.0) compared to those with partial forms (PLD, 40.0 years; IQR 23.0-55.0) (Table 3, Figure 3). Except for patients with FPLD1, the most common first symptom was loss of adipose tissue (in 57.9% of all patients). In contrast, fatty tissue accumulation was the most frequent first symptom in FPLD1 and the second most frequent in FPLD2 and APL. Diabetes as first symptom of disease manifestation was also common, especially in patients with CGL, FPLD1, oFPLD, and oLD. Liver disease (including MASLD) as first symptom was common in patients with AGL (21.7%)

Laboratory values and metabolic status

Median leptin and adiponectin levels tended to be lower in patients with GLD compared to PLD (Table 4). Among patients without fibrate treatment, those with oFPLD had the highest median triglyceride levels (2.4 mmol/L, IQR 1.9-3.6), while in the fibrate-treated group, median triglyceride levels lay above the target value of 2.3 mmol/L[1] in all subtypes with available data. In patients not receiving glucose-lowering drugs, overall metabolic control was good (with a median glycated hemoglobin (HbA1c) below 7.0% [53 mmol/mol])[1] with the exception of patients with AGL (HbA1c 7.4% [57 mmol/mol]; IQR 5.9-8.4 [41-68]); however, HbA1c values in treated groups suggest a suboptimal control in patients with CGL, AGL, FPLD1 and APL (median HbA1c above 7.0% [53 mmol/mol] in each subtype[1]). In the untreated group, median fasting plasma glucose lay below the threshold for diabetes mellitus (7.0 mmol/L) in all patient groups with the exception of AGL. Median alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were mostly normal, except for patients with CGL and PSPLD (CGL median ALT 34.0 U/L, PSPLD median ALT 38.5 U/L, and median AST 36.0 U/L; Table 4).

Comorbidities

In most patient groups, metabolic complications were the most common comorbidities, with the exception of patients with CGL or progeroid syndromes in whom abdominal problems, including MASLD (including MASH) and pancreatitis, were more common (Table 2, Figure 4). Patients with CGL frequently also suffered from hypertrophic cardiomyopathy (21%). In AGL, diabetes, conduction disorders, and fatigue were also prevalent. Ischemic cardiomyopathy was predominantly affecting patients with FPLD2, whereas conduction abnormalities were especially common in patients with CGL and with progeroid syndromes. Muscular weakness and pain were frequent in oLD and AGL (though small group sizes may bias these findings). For the latter, chronic pain was reported in more than 50% of patients. Depression was present in all groups, with oLD showing the highest rates.

Medication

Non-insulin glucose-lowering drugs were the most widely used medications (50.0%), followed by lipid-lowering agents (44.2%) and antihypertensive treatments (41.4%) (Table 5). Non-insulin glucose-lowering drugs were especially frequently prescribed in patients with FPLD1, oFPLD, and oLD. Patients with FPLD1, oFPLD, and AGL were also the main insulin users. Antihypertensive treatment/cardiovascular active drugs were most commonly used by patients living with FPLD1 and with AGL (60.4% and 50.0%). Lipid-lowering agents were mainly received by patients living with FPLD1 (62.5%) and FPLD2 (56.8%). Patients living with oLD were the ones receiving immunosuppressive therapy more often than other patient groups (16.7%). Antidepressive treatment was taken in

Table 1. Characterization of the ECLip registry cohorts.

	Complete ECLip cohort[a] ($n = 631$)		Prospective ECLip cohort[b] ($n = 467$)	
Sex, *n* (%)	631		467	
Female		515 (81.6)		386 (82.7)
Male		116 (18.4)		81 (17.3)
Age, years[c]	623		465	
Adults, *n* (%)		535 (85.9)		402 (86.5)
Median (Q1; Q3)		45.0 (32.0; 57.0)		44.0 (30.0; 57.0)
Children/adolescents, *n* (%)		88 (14.1)		63 (13.6)
Median (Q1; Q3)		11.0 (6.5; 14.0)		11.0 (6.0; 14.0)
BMI, kg/m^2 (median; Q1; Q3)			401	
Adults			343	24.8 (21.9; 29.0)
BMI *z*-score (median; Q1; Q3)				
Children/adolescents			58	0.00 (−0.01; 0.01)
Total fat, % (median; Q1; Q3)			167	
Adults			145	27.7 (21.9, 35.5)
Female			123	28.9 (22.2, 36.9)
Male			22	22.3 (18.8, 25.0)
Children/adolescents			22	21.6 (17.3; 30.9)
Female			13	23.6 (18.5, 30.9)
Male			9	20.6 (17.3, 22.1)
Country of origin, *n* (%)[d]	595		439	
Europe		502 (84.4)		359 (81.8)
Eastern Europe		41 (8.2)		5 (1.4)
Southern Europe		250 (49.8)		173 (48.2)
Western Europe		181 (36.1)		151 (42.1)
Undefined		30 (6.0)		30 (8.4)
Non-European countries		89 (15.0)		76 (17.3)
Mixed origin		4 (0.7)		4 (0.9)
Patient status, *n* (%)	621		457	
Active		366 (58.9)		366 (80.1)
Lost of follow-up		221 (35.6)		74 (16.2)
Deceased		34 (5.5)		17 (3.7)
Categories of LDS[e], *n* (%)	631		467	
CGL		**99 (15.7)**		**79 (16.9)**
CGL1		48 (48.5)		41 (51.9)
CGL2		18 (18.2)		14 (17.7)
CGL3		3 (3.0)		2 (2.5)
CGL4		8 (8.1)		7 (8.9)
PELD		4 (4.0)		0
CGL, undefined		18 (18.2)		15 (19.0)
PSGLD		**19 (3.0)**		**14 (3.0)**
Hutchinson–Gilford progeria syndrome		2 (10.5)		1 (7.1)
SHORT syndrome		3 (15.8)		3 (21.4)
Mandibuloacral dysplasia with type B lipodystrophy		1 (5.3)		0
MDPL syndrome		5 (26.3)		5 (35.7)
Atypical Werner syndrome		8 (42.1)		5 (35.7)
AGL		**27 (4.3)**		**14 (3.0)**
AGL, autoimmune		14 (51.9)		8 (57.2)
AGL, idiopathic		11 (40.7)		5 (35.7)
AGL, panniculitis		2 (7.4)		1 (7.1)
FPLD		**370 (58.6)**		**268 (57.4)**
FPLD1		84 (22.7)		59 (22.0)
FPLD2		241 (65.1)		177 (66.0)
FPLD3		20 (5.4)		13 (4.9)
FPLD4		18 (4.9)		16 (6.0)
FPLD, *AKT2* associated		1 (0.3)		0
FPLD, undefined		6 (1.6)		3 (1.1)
PSPLD		**9 (1.4)**		**6 (1.3)**
Mandibuloacral dysplasia with type A lipodystrophy		3 (33.3)		3 (50.0)
Werner syndrome		6 (66.7)		3 (50.0)
APL		**64 (10.1)**		**49 (10.5)**
Barraquer–Simons syndrome		40 (62.5)		28 (57.1)
APL associated with total body irradiation and hematopoietic stem cell transplant		7 (10.9)		6 (12.2)
APL, undefined		17 (26.6)		15 (30.6)
ALLD		**27 (4.3)**		**24 (5.1)**
OTULIN-associated autoinflammatory syndrome		1 (3.7)		1 (4.2)
Drug-induced localized lipodystrophy		8 (29.6)		7 (29.2)
Idiopathic localized lipodystrophy		17 (63.0)		15 (62.5)

(*continued*)

Table 1. Continued

	Complete ECLip cohort[a] ($n = 631$)	Prospective ECLip cohort[b] ($n = 467$)
Panniculitis-induced localized lipodystrophy	1 (3.7)	1 (4.2)
oLD	**16 (2.5)**	**13 (2.8)**
Proteasome-associated autoinflammatory syndrome 1	1 (6.3)	1 (7.7)
Donohue syndrome	1 (6.3)	1 (7.7)
Insulin receptor defect	4 (25.0)	4 (30.8)
Others, undefined	10 (62.5)	7 (53.8)

This table shows the basic characteristics of the 2 ECLip Registry cohorts.
[a]Complete cohort: all patients registered within the ECLip Registry at the November, 7, 2023.
[b]Prospective cohort: complete cohort without patients with only retrospectively collected data, basic data without episode data, or without plausibility check.
[c]Age at start of registry (2018) for patients without baseline-episode (patient who died before the start of the registry were excluded from this analysis).
[d]Countries of origin were defined following the United Nations classification for continents (https://unstats.un.org/unsd/methodology/m49/).
[e]Subtypes of LDS according to OMIM and ORPHA codes.
AGL, acquired generalized lipodystrophy; *AKT2*, AKT serine/threonine kinase; ALLD, acquired localized lipodystrophy; APL, acquired partial lipodystrophy; BMI, body mass index; CGL, congenital generalized lipodystrophy; FPLD, familial partial lipodystrophy; MDPL, mandibular hypoplasia, deafness, progeroid features and lipodystrophy syndrome; *n*, number of patients; oLD, other forms of lipodystrophy; oFPLD, other forms of familial partial lipodystrophy not including type 1 and 2; *OTULIN*, OTU deubiquitinase with linear linkage specificity; PELD, progressive encephalopathy with lipodystrophy; PSGLD, progeroid syndrome associated with generalized lipodystrophy; PSPLD, progeroid syndrome associated with partial lipodystrophy; SHORT syndrome, short stature, hyperextensibility of joints, ocular depression, Rieger anomaly and teething delay syndrome.

all patient groups apart from patients with progeroid syndrome, but was the most common in patients living with AGL (33.3%) and FPLD1 (20.8%). Patients living with FPLD1 were also most likely to take pain relief medication (16.7%).

Metreleptin, the only disease-specific treatment, was used in 11.6% of patients, most frequently in CGL and AGL, though still only 35.2% and 33.3%, respectively.

Causes of and age at death

There were 34 documented deaths, 17 in the prospective cohort. Major adverse cardiovascular events (MACE; including stroke) were the most common cause of death ($n = 7$), followed by cancer ($n = 6$) and infections ($n = 4$). All 4 patients (and only them) with progressive encephalopathy with lipodystrophy (PELD) died from epileptic status or encephalopathy. Additional pediatric deaths occurred in one child with undefined CGL, 2 with Hutchinson–Gilford progeria syndrome, and one with AGL (8 deaths under age 18). Even after excluding children, patients with GLD died younger than those with PLD (median age at death: 49.0 years, IQR 29.0-70.0 vs. 72.0 years, IQR 61.5-78.5). Including children, median age at death was 27.0 years (IQR 13.0-54.0) for GLD vs. 72.0 years (IQR 61.5-78.5) for PLD (Table 6).

Conclusion

We present the first cross-sectional analysis of the ECLip Registry. Prospective and detailed clinical data were available for 467 patients, representing the largest published cohort to date (previous largest: 292 patients from France[12]). This provides us with the unique possibility to describe a more accurate picture of single subgroups and compare the same parameters between subgroups. Due to the international multicentric approach, we minimize the effect of local accumulation of patients with a specific disease form, for example, due to founder variants or specific research interest of individual centers.

FPLD was the most common subgroup, with the majority of patients being female, which aligns with previous findings in other cohorts.[1,12-14] Similar to the above-mentioned French cohort,[12] our data show a 5-fold lower rate of diagnosed lipodystrophy in men (Figure 2). This may in part be due to reduced penetrance/expression of *LMNA* heterozygous variants in patients living with FPLD2, but is more likely to indicate underdiagnosis due to reduced socio-cosmetic pressure experienced by men,[8] and their tendency to present with less severe metabolic complications, or later in life.[15,16] Patients with GLD tended to be diagnosed earlier than those with PLD, and their mean age at diagnosis (13.0 years) was in accordance with an international study including patients from the US, Brazil, and Turkey (mean age at diagnosis 12.3 years[17]). Nevertheless, this is still a late time point for diagnosis, given that the majority of patients with GLD in our cohort had a congenital form, and at least in one cohort of patients with CGL, age at diagnosis was as low as 1 year.[18] However, most patients were diagnosed over 10 years ago, before the international consensus guidelines for lipodystrophy in 2016[1] raised awareness for these diseases. Together, the high age at diagnosis and underrepresentation of men indicate that lipodystrophy remains underrecognized. Raising awareness, particularly of atypical initial symptoms, is essential. Experts and registries like ECLip play a critical role in promoting earlier diagnosis and timely treatment.

While the first manifestation was loss of adipose tissue in the majority (57.9%) of all patients with GLD, surprisingly, for 5 patients with GLD, fat accumulation was reported as the first symptom. This might however reflect a fat distribution mismatch rather than true accumulation.

As expected, metabolic complications were a common factor among patients with FPLD, especially dyslipidemia (69.7%) and diabetes (57.6%). These results align with international data.[19,20] However, just as a former Spanish report[14] we found an unexpectedly lower prevalence of diabetes in patients living with GLD in our registry of "only" 40.4% compared to 62.5% in a Turkish cohort[21] and 58.0% (diabetes and or insulin resistance) in the above-mentioned international cohort,[17] even though patients with GLD in the ECLip Registry were on average not younger than patients in those 2 cohorts.

These data show that geographic aspects such as genetic background or diet might play an important role in the development of metabolic comorbidities in LDS and could partly explain the generally good metabolic control in our cohort.

Table 2. Patterns of comorbidities and body fat content by subtypes of lipodystrophy in the prospective ECLip cohort at baseline.

	All patients $n = 417^a$	GLD[c] $n = 99^a$	CGL $n = 73^a$	PSGLD $n = 13^a$	AGL $n = 13^a$	PLD[d] $n = 282^a$	FPLD1 $n = 52^a$	FPLD2 $n = 150^a$	oFPLD $n = 29^a$	PSPLD $n = 6^a$	APL $n = 45^a$	ALLD $n = 23^a$	oLD $n = 13^a$
Age at baseline Median (Q1; Q3)	40 (25; 55)	26 (13; 40)	26 (13; 37)	28 (8; 42)	26 (15; 45)	45 (29; 57)	57 (44; 66)	44.5 (29; 56)	48 (38; 53)	28.5 (20; 37)	38 (20; 47)	45 (23; 57)	33 (25; 51)
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Metabolic comorbidities	296 (71.0)	59 (59.6)	42 (57.5)	6 (46.2)	11 (84.6)	217 (77.0)	47 (90.4)	118 (78.7)	25 (86.2)	1 (16.7)	26 (57.8)	11 (47.8)	9 (69.2)
– Dyslipidaemia	246 (59.0)	50 (50.5)	37 (50.7)	5 (38.5)	8 (61.5)	182 (64.5)	40 (76.9)	101 (67.3)	20 (69.0)	1 (16.7)	20 (44.4)	9 (39.1)	5 (38.5)
– Diabetes	202 (48.4)	40 (40.4)	26 (35.6)	4 (30.8)	10 (76.9)	152 (53.9)	39 (75.0)	73 (48.7)	21 (72.4)	1 (16.7)	18 (40.0)	2 (8.7)	8 (61.5)
– Diabetic complicationse	80 (19.2)	16 (16.2)	13 (17.8)	1 (7.7)	2 (15.4)	60 (21.3)	10 (19.2)	28 (18.7)	11 (37.9)	0	11 (24.4)	1 (4.4)	3 (23.1)
Abdominal comorbidities	247 (59.2)	62 (62.6)	47 (64.4)	8 (61.5)	7 (53.9)	173 (61.3)	35 (67.3)	92 (61.3)	19 (65.5)	3 (50.0)	24 (53.3)	3 (13.0)	9 (69.2)
– MASLD[f]	159 (38.1)	45 (45.5)	35 (48.0)	6 (46.2)	4 (30.8)	107 (37.9)	19 (36.5)	59 (39.3)	12 (41.4)	2 (33.3)	15 (33.3)	2 (8.7)	5 (38.5)
– MASH	50 (12.0)	14 (14.1)	10 (13.7)	1 (7.7)	3 (23.1)	33 (11.7)	9 (17.3)	15 (10.0)	2 (6.9)	1 (16.7)	6 (13.3)	0	3 (23.1)
– Cirrhosis	7 (1.7)	1 (1.0)	1 (1.4)	0	0	5 (1.8)	2 (3.9)	2 (1.3)	0	1 (16.7)	0	0	1 (7.7)
– Pancreatitis	22 (5.3)	7 (7.1)	6 (8.2)	0	1 (7.7)	15 (5.3)	2 (3.9)	10 (6.7)	1 (3.5)	0	2 (4.4)	0	0
– Umbilical hernia	23 (5.5)	13 (13.1)	10 (13.7)	1 (7.7)	2 (15.4)	10 (3.6)	2 (3.9)	6 (4.0)	0	0	2 (4.4)	0	0
Vascular comorbidities	132 (31.7)	25 (25.3)	16 (21.9)	6 (46.2)	3 (23.1)	100 (35.5)	25 (48.1)	52 (34.7)	14 (48.3)	0	9 (20.0)	3 (13.0)	4 (30.8)
– Peripheral arteriopathy	21 (5.0)	4 (4.0)	4 (5.5)	0	0	17 (6.0)	5 (9.6)	9 (6.0)	3 (10.3)	0	0	0	0
– High blood pressure	125 (30.0)	24 (24.2)	15 (20.6)	6 (46.2)	3 (23.1)	94 (33.3)	24 (46.2)	48 (32.0)	13 (44.8)	0	9 (20.0)	3 (13.0)	4 (30.8)
Cardiac comorbidities	97 (23.3)	36 (36.4)	26 (35.6)	6 (46.2)	4 (30.8)	58 (20.6)	13 (25.0)	31 (20.7)	5 (17.2)	2 (33.3)	7 (15.6)	1 (4.4)	2 (15.4)
– Ischemic cardiomyopathy	34 (8.2)	6 (6.1)	5 (6.9)	0	1 (7.7)	27 (9.6)	4 (7.7)	19 (12.7)	2 (6.9)	0	2 (4.4)	0	1 (7.7)
– Conduction abnormalities	37 (8.9)	13 (13.1)	10 (13.7)	2 (15.4)	1 (7.7)	22 (7.8)	3 (5.8)	13 (8.7)	3 (10.3)	1 (16.7)	2 (4.4)	1 (4.4)	1 (7.7)
– Valvulopathy	21 (5.0)	7 (7.1)	5 (6.9)	2 (15.4)	0	13 (4.6)	5 (9.6)	5 (3.3)	1 (3.5)	0	2 (4.4)	1 (4.4)	0
– Hypertrophic cardiomyopathy	29 (7.0)	19 (19.2)	15 (20.6)	2 (15.4)	2 (15.4)	9 (3.2)	2 (3.9)	4 (2.7)	1 (3.5)	1 (16.7)	1 (2.2)	0	1 (7.7)
– Dilated cardiomyopathy	4 (1.0)	1 (1.0)	1 (1.4)	0	0	2 (0.7)	1 (1.9)	0	0	0	1 (2.2)	0	1 (7.7)
Renal comorbidities	52 (12.5)	11 (11.1)	8 (11.0)	2 (15.4)	1 (7.7)	38 (13.5)	7 (13.5)	13 (8.7)	5 (17.2)	0	13 (28.9)	1 (4.4)	2 (15.4)
– Albuminuria	51 (12.2)	11 (11.1)	8 (11.0)	2 (15.4)	1 (7.7)	37 (13.1)	7 (13.5)	13 (8.7)	5 (17.2)	0	12 (26.7)	1 (4.4)	2 (15.4)
– Glomerulopathy	4 (1.0)	0	0	0	0	4 (1.4)	1 (1.9)	2 (1.3)	0	0	1 (2.2)	0	0
Neuromuscular comorbidities	88 (21.1)	24 (24.2)	18 (24.7)	2 (15.4)	4 (30.8)	59 (20.1)	8 (15.4)	37 (24.7)	5 (17.2)	1 (16.7)	8 (17.8)	1 (4.4)	4 (30.8)

(*continued*)

Table 2. Continued

	All patients $n = 417^a$	GLD[c] $n = 99^a$	CGL $n = 73^a$	PSGLD $n = 13^a$	AGL $n = 13^a$	PLD[d] $n = 282^a$	FPLD1 $n = 52^a$	FPLD2 $n = 150^a$	oFPLD $n = 29^a$	PSPLD $n = 6^a$	APL $n = 45^a$	ALLD $n = 23^a$	oLD $n = 13^a$
– Muscle weakness	30 (7.2)	10 (10.1)	8 (11.0)	0	2 (15.4)	16 (5.7)	4 (7.7)	8 (5.3)	3 (10.3)	1 (16.7)	0	1 (4.4)	3 (23.1)
– Muscular pain	62 (14.9)	9 (9.1)	5 (6.9)	1 (7.7)	3 (23.1)	49 (17.4)	8 (15.4)	32 (21.3)	2 (6.9)	1 (16.7)	6 (13.3)	1 (4.4)	3 (23.1)
– Speech delay	13 (3.1)	9 (9.1)	8 (11.0)	1 (7.7)	0	4 (1.4)	0	1 (0.7)	0	0	3 (6.7)	0	0
– Stroke	5 (1.2)	1 (1.0)	1 (1.4)	0	0	4 (1.4)	0	4 (2.7)	0	0	0	0	0
Psychological comorbidities	113 (27.1)	26 (26.3)	14 (19.2)	4 (30.8)	8 (61.5)	77 (27.3)	11 (21.2)	43 (28.7)	11 (37.9)	2 (33.3)	10 (22.2)	6 (26.1)	4 (30.8)
– Fatigue	43 (10.3)	11 (11.1)	5 (6.9)	2 (15.4)	4 (30.8)	29 (10.3)	4 (7.7)	13 (8.7)	7 (24.1)	2 (33.3)	3 (6.7)	2 (8.7)	1 (7.7)
– Chronic pain	73 (17.5)	18 (18.2)	8 (11.0)	3 (23.1)	7 (53.9)	47 (16.7)	4 (7.7)	32 (21.3)	5 (17.2)	0	6 (13.3)	5 (21.7)	3 (23.1)
– Depression	62 (14.9)	11 (11.1)	8 (11.0)	1 (7.7)	2 (15.4)	47 (16.7)	9 (17.3)	24 (16.0)	4 (13.8)	1 (16.7)	9 (20.0)	1 (4.4)	3 (23.1)
Reproductive comorbidities[g]	88 (21.1)	16 (16.2)	11 (15.1)	1 (7.7)	4 (30.8)	70 (24.8)	3 (5.8)	52 (34.7)	9 (31.0)	0	6 (13.3)	0	2 (15.4)
– PCOS	46 (11.0)	9 (9.1)	5 (6.9)	0	4 (30.8)	37 (13.1)	2 (3.9)	27 (18.0)	5 (17.2)	0	3 (6.7)	0	0
– Hirsutism	64 (15.4)	11 (11.1)	9 (12.3)	1 (7.7)	1 (7.7)	51 (18.1)	2 (3.9)	37 (24.7)	7 (24.1)	0	5 (11.1)	0	2 (15.4)

DEXA analysis	All patients $n = 167^b$ Median (Q1; Q3)	GLD[c] $n = 30^b$ Median (Q1; Q3)	CGL $n = 18^b$ Median (Q1; Q3)	PSGLD $n = 10^b$ Median (Q1; Q3)	AGL $n = 2^b$ Median (Q1; Q3)	PLD[d] $n = 121^b$ Median (Q1; Q3)	FPLD1 $n = 24^b$ Median (Q1; Q3)	FPLD2 $n = 59^b$ Median (Q1; Q3)	oFPLD $n = 13^b$ Median (Q1; Q3)	PSPLD $n = 3^b$ Median (Q1; Q3)	APL $n = 22^b$ Median (Q1; Q3)	ALLD $n = 10^a$ Median (Q1; Q3)	oLD $n = 6^a$ Median (Q1; Q3)
– Total body fat content (%), $n = 167$	27.0 (21.1; 35.4)	18.4 (10.3; 21.8)	15.0 (9.2; 25.0)	20.6 (18.5; 21.8)	16.4 (15.7; 17.0)	27.8 (22.2; 35.8)	37.8 (33.8; 40.5)	24.3 (22.0; 28.9)	21.8 (20.6; 23.7)	41.0 (30.3; 47.7)	31.7 (25.3; 36.4)	35.1 (31.8; 37.2)	38.5 (23.9; 46.7)
– Upper extremity fat content (%), $n = 122$	27.7 (21.2; 38.5)	17.6 (11.0; 31.1)	12.7 (10.1; 28.7)	26.2 (18.6; 40.1)	17.6 ($n = 1$)	27.7 (22.4; 38.5)	40.3 (37.8; 44.4)	24.0 (20.8; 31.3)	26.4 (22.2; 33.6)	27.7 ($n = 1$)	28.4 (22.2; 38.5)	41.4 (32.6; 45.4)	38.5 (26.4; 53.3)
– Lower extremity fat content (%), $n = 121$	22.9 (17.4; 29.9)	17.9 (12.0; 23.6)	14.8 (11.3; 22.4)	22.6 (17.5; 27.9)	19.2 ($n = 1$)	22.6 (17.7; 28.5)	28.2 (25.7; 30.0)	19.4 (15.7; 22.8)	22.4 (17.7; 24.5)	36.6 (n = 1)	30.2 (22.9; 44.8)	35.4 (34.3; 40.2)	29.9 (29.8; 43.7)
– Trunk fat content (%), $n = 123$	29.5 (22.0; 38.6)	15.0 (6.7; 26.7)	10.4 (6.6; 26.7)	18.7 (15.8; 26.4)	10.9 ($n = 1$)	31.8 (24.9; 40.4)	46.9 (43.0; 49.7)	29.2 (24.3; 32.8)	22.7 (19.6; 44.2)	28.1 ($n = 1$)	32.5 (21.2; 35.5)	35.8 (23.6; 40.2)	37.6 (20.0; 43.8)

Body fat content and comorbidity patterns are analyzed according to the different lipodystrophy subtypes.
AGL, acquired generalized lipodystrophy; ALLD, acquired localized lipodystrophy; APL, acquired partial lipodystrophy; CGL, congenital generalized lipodystrophy; FPLD1, familial partial lipodystrophy type 1; FPLD2, familial partial lipodystrophy type 2; GLD, generalized forms of lipodystrophy; MASLD, metabolic dysfunction associated steatotic liver disease; MASH, metabolic dysfunction associated steatohepatitis; *n*, number of patients; oLD, other forms of lipodystrophy; oFPLD, other forms of familial partial lipodystrophy not including type 1 and 2; PCOS, polycystic ovary syndrome; PLD, partial forms of lipodystrophy; PSGLD, progeroid syndrome associated with generalized lipodystrophy; PSPLD, progeroid syndrome associated with partial lipodystrophy.
[a]Number of patients of this subgroup for whom any question of the here mentioned comorbidities has been answered.
[b]Number of patients of this subgroup for whom any measurement of the here mentioned DEXA analysis has been answered.
[c]GLD includes: CGLD, PSGLD, AGLD.
[d]PLD includes: FPLD1, FPLD2, oFPLD, PSPLD, APLD.
[e]Diabetic complications comprise nephropathy, retinopathy, neuropathy, and macroangiopathy.
[f]MASLD here shown without MASH.
[g]Reproductive symptoms and comorbidities are listed for women only.

Table 3. Age at diagnosis and symptoms of first manifestation in the complete ECLip cohort.

Type of lipodystrophy	*n*[a]	Age at diagnosis	Symptoms of first manifestation						
		Median (Q1; Q3)	Lipoatrophy *n* (%[b])	Accumulation of fat *n* (%[b])	Muscular hypertrophy *n* (%[b])	Diabetes *n* (%[b])	Liver disease *n* (%[b])	Hirsutism *n* (%[b])	Infertility *n* (%[b])
GLD	133	13.0 (3.0; 32.0)	84 (63.2)	5 (3.8)	26 (19.6)	31 (23.3)	20 (15.0)	4 (3.0)	2 (1.5)
CGL	92	13.5 (1.0; 30.0)	55 (59.8)	1 (1.1)	24 (26.1)	27 (29.4)	14 (15.2)	4 (4.4)	1 (1.1)
PSGLD	18	14.5 (9.0; 39.0)	13 (72.2)	3 (16.7)	0	0	1 (5.6)	0	0
AGL	23	8.0 (4.0; 34.0)	16 (69.6)	1 (4.4)	2 (8.7)	4 (17.4)	5 (21.7)	0	1 (4.4)
PLD	367	40.0 (23.0; 55.0)	200 (54.5)	115 (31.3)	68 (18.5)	86 (23.4)	21 (5.7)	22 (6.0)	11 (3.0)
FPLD1	68	53.0 (39.5; 64.5)	23 (33.8)	30 (44.1)	7 (10.3)	22 (32.4)	5 (7.4)	2 (2.9)	3 (4.4)
FPLD2	197	38.0 (23.0; 53.0)	116 (58.9)	61 (31.0)	51 (25.9)	41 (20.8)	9 (4.6)	14 (7.1)	5 (2.5)
oFPLD	35	47.0 (33.0; 55.0)	15 (42.9)	11 (31.4)	8 (22.9)	13 (37.1)	3 (8.6)	4 (11.4)	3 (8.6)
PSPLD	9	27.0 (20.0; 36.0)	7 (77.8)	1 (11.1)	0	2 (22.2)	1 (11.1)	0	0
APL	58	25.0 (11.0; 45.0)	39 (67.2)	12 (20.7)	2 (3.5)	8 (13.8)	3 (5.2)	2 (3.5)	0
ALLD	25	44.0 (30.0; 55.0)	21 (84.0)	1 (4.0)	0	6 (24.0)	0	0	0
oLD	10	31.0 (18.0; 71.0)	5 (50.0)	4 (40.0)	0	5 (50.0)	1 (10.0)	1 (10.0)	0

This table shows age at diagnosis and reported symptoms of first manifestation of patients with LDs in the complete ECLip cohort categorized by disease subgroups.
AGL, acquired generalized lipodystrophy; ALLD, acquired localized lipodystrophy; APL, acquired partial lipodystrophy; CGL, congenital generalized lipodystrophy; FPLD1, familial partial lipodystrophy type 1; FPLD2, familial partial lipodystrophy type 2; GLD, generalized forms of lipodystrophy; *n*, number of patients; oLD, other forms of lipodystrophy; oFPLD, other forms of familial partial lipodystrophy not including type 1 and 2; PLD, partial forms of lipodystrophy; PSGLD, progeroid syndrome associated with generalized lipodystrophy; PSPLD, progeroid syndrome associated with partial lipodystrophy.
[a]Number of patients for whom any question of any of the here mentioned symptoms of first manifestation and age of diagnosis has been answered.
[b]Percentage of patients in this subgroup in whom this symptom was one of the first manifestations. Multiple answers were possible for symptom of first manifestation; therefore, percentage in each line might add up to more than 100%.

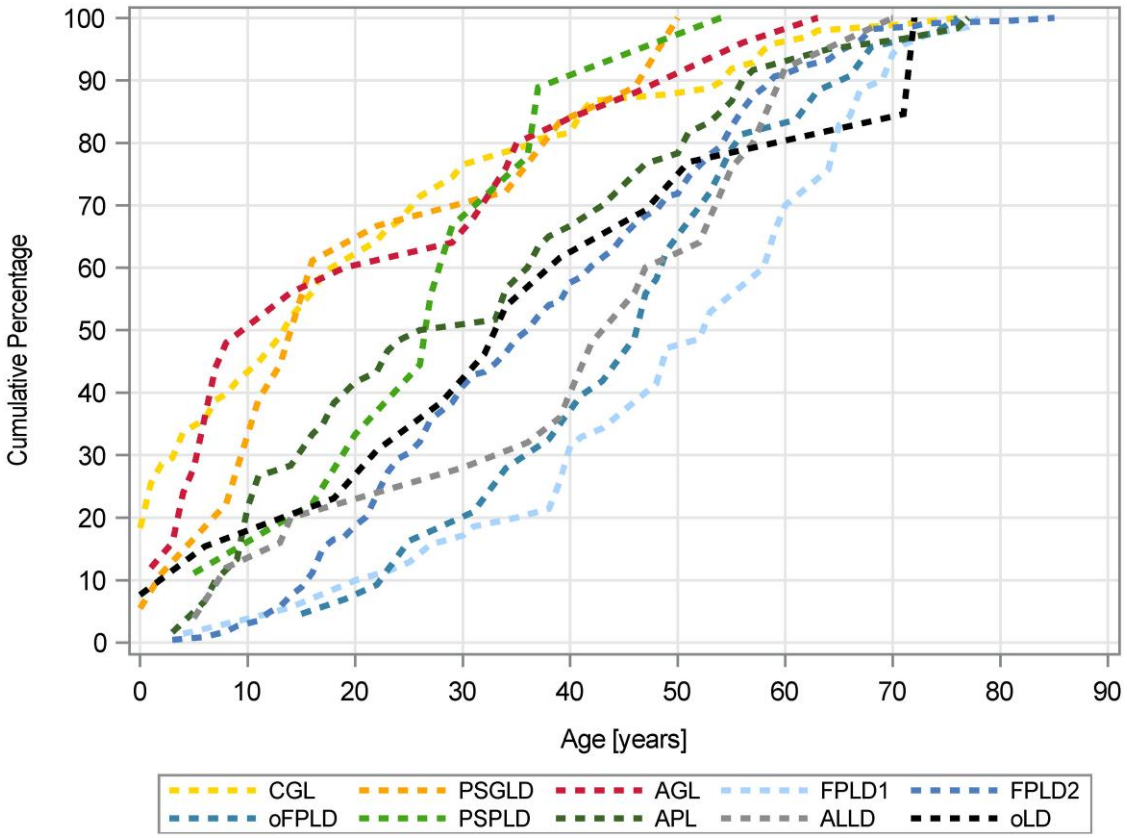


Figure 3. Age at diagnosis in the different lipodystrophy subtypes. The data represent age at diagnosis in all patients in the complete ECLip cohort, differentiated by subtypes. The data are shown as cumulative percentage. AGL, acquired generalized lipodystrophy; ALLD, acquired localized lipodystrophy; APL, acquired partial lipodystrophy; CGL, congenital generalized lipodystrophy; FPLD, Familial partial lipodystrophy; oLD, other forms of lipodystrophy; oFPLD, other forms of familial partial lipodystrophy not including type 1 and 2; PSGLD, progeroid syndrome associated with generalized lipodystrophy; PSPLD, Progeroid syndrome associated with partial lipodystrophy.

Table 4. Selected laboratory parameters in the prospective ECLip cohort at baseline.

	CGL $n = 76^a$ Median (Q1; Q3)	PSGLD $n = 13^a$ Median (Q1; Q3)	AGL $n = 12^a$ Median (Q1; Q3)	FPLD1 $n = 56^a$ Median (Q1; Q3)	FPLD2 $n = 151^a$ Median (Q1; Q3)	oFPLD $n = 30^a$ Median (Q1; Q3)	PSPLD $n = 6^a$ Median (Q1; Q3)	APL $n = 46^a$ Median (Q1; Q3)	ALLD $n = 24^a$ Median (Q1; Q3)	oLD $n = 13^a$ Median (Q1; Q3)
Fasting plasma glucose (mmol/L) $n = 370^b$	5.9 (4.8; 8.3)	4.5 (4.1; 5.0)	5.2 (4.9; 9.2)	6.8 (5.7; 8.9)	5.6 (4.8; 7.9)	6.3 (5.1; 8.1)	4.8 (4.4; 6.2)	5.6 (4.8; 7.4)	4.5 (4.4; 6.4)	5.7 (4.4; 12.4)
Fasting glucose (mmol/L) (treated[c]) $n = 168^b$	7.2 (5.9; 9.7)	—	5.2 (5.1; 6.1)	7.8 (6.0; 9.1)	6.6 (4.8; 8.2)	6.7 (4.7; 8.6)	—	7.4 (6.6; 9.2)	7.2 (6.4; 11.6)	5.1 (4.3; 11.5)
Fasting glucose (mmol/L) (untreated[c]) $n = 202^b$	5.3 (4.6; 6.9)	4.6 (4.3; 4.9)	7.1 (4.8; 10.0)	6.4 (5.5; 7.6)	5.2 (4.8; 6.4)	5.4 (5.4; 7.6)	—	5.2 (4.4; 10.6)	4.4 (4.2; 4.5)	—
Fasting insulin (pmol/L) [d] $n = 225^b$	114.0 (75.0; 250.8)	47.0 (35.1; 117.5)	—	81.1 (53.1; 118.8)	102.5 (69.5; 216.3)	112.7 (75.0; 155.2)	—	56.4 (40.2; 113.4)	24.2 (19.9; 42.8)	129.0 (99.6; 198.1)
Fasting insulin (pmol/L) (treated[e]) $n = 64^a$	323.7 (63.0; 529.5)	—	—	74.2 (53.1; 85.4)	139.8 (72.0; 200.0)	—	—	105.6 (43.8; 156.0)	—	—
Fasting insulin (pmol/L) (untreated[e]) $n = 161^b$	104.4 (76.3; 165.0)	46.7 (29.6; 70.0)	—	114.5 (60.9; 174.2)	97.2 (67.8; 222.6)	142.7 (76.2; 211.2)	–	54.1 (37.9; 112.5)	25.5 (19.6; 46.2)	–
HbA1c (%) $n = 404^b$	6.2 (5.2; 7.9)	5.5 (5.1; 5.9)	7.4 (5.5; 8.4)	7.2 (6.3; 8.3)	6.2 (5.4; 7.8)	6.9 (6.0; 7.8)	5.6 (5.1; 5.8)	6.1 (5.4; 7.3)	5.5 (5.2; 6.5)	5.7 (5.4; 7.1)
HbA1c (%) (treated[c]) $n = 181^b$	7.3 (6.2; 7.7)	—	7.3 (5.5; 7.5)	7.3 (6.5; 8.3)	6.9 (5.9; 8.0)	7.0 (6.3; 8.2)	—	7.2 (6.6; 8.1)	6.8 (6.3; 7.5)	5.7 (5.5; 7.1)
HbA1c (%) (untreated[c]) $n = 223^b$	5.8 (5.1; 8.8)	5.3 (5.0; 5.8)	7.4 (5.9; 8.4)	6.4 (5.9; 8.5)	5.7 (5.3; 7.0)	6.5 (5.3; 7.8)	5.7 (5.3; 6.8)	5.4 (5.1; 5.7)	5.3 (5.2; 5.5)	6.1 (5.4; 7.2)
HbA1c (mmol/mol) $n = 404^b$	44 (33; 63)	37 (32; 41)	56 (37; 68)	56 (45; 67)	44 (36; 62)	52 (42; 62)	38 (32; 40)	43 (36; 56)	37 (33; 48)	39 (36; 54)
HbA1c (mmol/mol) (treated[c]) $n = 181^b$	56 (44; 61)	—	56 (37; 58)	56 (48; 67)	52 (41; 64)	53 (45; 66)	—	55 (49; 65)	51 (45; 58)	39 (37; 54)
HbA1c (mmol/mol) (untreated[c]) $n = 223^b$	40 (32; 73)	34 (31; 40)	57 (41; 68)	46 (41; 69)	39 (34; 53)	48 (34; 62)	39 (34; 51)	36 (32; 39)	34 (33; 37)	43 (36; 55)
Fasting triglycerides (mmol/L) $n = 402^b$	2.2 (1.4; 5.1)	1.2 (0.8; 2.0)	2.2 (0.9; 5.5)	2.0 (1.6; 3.4)	2.3 (1.6; 3.5)	2.5 (2.0; 3.6)	0.9 (0.7; 1.6)	1.4 (0.9; 2.6)	0.9 (0.6; 1.2)	1.5 (0.9; 2,2)
Fasting triglycerides (mmol/L) (treated[f]) $n = 46^b$	2.8 (1.8; 3.9)	—	—	3.2 (1.8; 6.1)	2.6 (1.7; 5.3)	—	—	—	—	—
Fasting triglycerides (mmol/L) (untreated[f]) $n = 356^b$	2.2 (1.3; 5.0)	1.1 (0.8; 1.9)	2.0 (0.8; 3.0)	2.0 (1.5; 3.1)	2.3 (1.6; 3.4)	2.4 (1.9; 3.6)	0.9 (0.7; 1.6)	1.4 (0.9; 2.4)	0.9 (0.6; 1.2)	1.5 (0.9; 2.2)
Total cholesterol (mmol/L) $n = 394^b$	4.0 (3.4; 5.0)	4.1 (4.0; 4.8)	4.5 (3.7; 5.7)	4.7 (3.9; 5.5)	4.8 (3.9; 5.6)	4.8 (3.3; 5.7)	4.0 (3.8; 4.1)	4.2 (3.8; 5.4)	4.9 (4.2; 5.7)	4.4 (3.5; 5.5)
LDL (mmol/L) $n = 383^b$	2.1 (1.6; 2.8)	2.4 (2.2; 2.8)	2.4 (1.8; 3.4)	2.7 (1.9; 3.6)	2.9 (2.1; 3.5)	2.3 (1.4; 2.8)	2.5 (2.3; 2.9)	2.3 (1.7; 3.3)	3.1 (2.8; 3.7)	2.5 (1.5; 3.2)
HDL (mmol/L) $n = 392^b$	0.8 (0.7; 1.0)	1.2 (1.0; 1.8)	0.9 (0.7; 1.3)	1.1 (0.9; 1.4)	1.0 (0.8; 1.2)	0.9 (0.7; 1.0)	1.0 (0.8; 1.3)	1.1 (0.9; 1.4)	1.8 (1.5; 2.1)	1.3 (1.2; 1.9)

(*continued*)

Table 4. Continued

	CGL $n = 76^a$ Median (Q1; Q3)	PSGLD $n = 13^a$ Median (Q1; Q3)	AGL $n = 12^a$ Median (Q1; Q3)	FPLD1 $n = 56^a$ Median (Q1; Q3)	FPLD2 $n = 151^a$ Median (Q1; Q3)	oFPLD $n = 30^a$ Median (Q1; Q3)	PSPLD $n = 6^a$ Median (Q1; Q3)	APL $n = 46^a$ Median (Q1; Q3)	ALLD $n = 24^a$ Median (Q1; Q3)	oLD $n = 13^a$ Median (Q1; Q3)
Leptin (μg/L)[g] $n = 258^b$	0.6 (0.4; 2.5)	3.0 (0.8; 7.1)	—	23.6 (15.0; 34.4)	6.2 (3.0; 11.2)	5.2 (2.5; 7.7)	—	8.8 (2.8; 23.6)	10.1 (4.8; 13.8)	13.5 (8.1; 23.8)
Adiponectin (μg/mL) $n = 141^b$	0.6 (0.3; 1.4)	1.8 (1.1; 6.1)	—	2.9 (2.0; 5.7)	4.2 (2.5; 8.0)	3.0 (1.5; 3.6)	—	5.6 (1.8; 7.9)	10.4 (7.5; 12.2)	—
ALT (U/L) $n = 402^b$	34.0 (22.0; 47.0)	23.0 (17.0; 61.0)	24.0 (20.0; 237.0)	28.0 (18.0; 40.0)	29.0 (19.0; 46.2)	31.0 (16.6; 44.5)	38.5 (33.0; 67.0)	23.0 (16.5; 32.5)	15.0 (13.0; 19.0)	20.0 (16.0; 34.2)
AST (U/L) $n = 387^b$	29.0 (20.0; 42.0)	24.0 (19.0; 34.0)	28.6 (21.0; 88.0)	23.4 (18.0; 36.0)	26.0 (18.0; 36.0)	26.0 (19.0; 32.0)	36.0 (23.0; 40.0)	22.0 (17.4; 31.0)	20.5 (17.0; 23.5)	21.0 (18.0; 31.0)
yGT (U/L) $n = 382^b$	32.0 (22.0; 59.0)	23.5 (13.0; 49.0)	48.0 (20.0; 137.0)	30.0 (22.0; 55.0)	32.0 (20.0; 48.5)	35.0 (22.0; 52.0)	—	23.0 (15.0; 36.0)	13.0 (10.0; 18.0)	18.5 (14.0; 25.0)
Bilirubin (μmol/L) $n = 168^b$	6.8 (6.8; 8.6)	8.6 (6.8; 8.6)	8.6 (3.4; 17.1)	5.1 (3.4; 6.8)	8.6 (5.1; 13.7)	12.0 (8.6; 17.1)	—	8.6 (5.1; 13.7)	10.3 (6.8; 25.7)	6.8 (3.4; 8.6)
Serum creatinine (μmol/L) $n = 380^b$	62.0 (44.3; 79.7)	35.4 (26.6; 53.1)	53.1 (44.3; 79.7)	70.8 (62.0; 115.0)	70.8 (53.1; 97.4)	70.8 (62.0; 637.2)	44.3 (44.3; 53.1)	62.0 (53.1; 79.7)	62.0 (44.3; 70.8)	62.0 (53.1; 309.8)
Estimated GFR (mL/min/1.73 m) $n = 316^b$	104.0 (65.0; 136.0)	126.3 (106.5; 210.8)	127.5 (62.0; 150.5)	90.0 (72.0; 102.0)	93.0 (82.0; 111.0)	95.0 (89.0; 125.0)	130.0 (120.0; 133.0)	112.0 (84.0; 137.1)	98.9 (89.0; 117.0)	109.0 (98.0; 128.0)
Serum urea (mmol/L) $n = 225^b$	4.1 (2.5; 6.5)	—	5.3 (3.6; 9.0)	4.4 (1.0; 5.2)	4.7 (3.6; 6.0)	5.7 (4.1; 6.7)	4.7 (3.4; 7.7)	3.5 (2.8; 4.2)	—	4.5 (4.2; 4.8)
hsCRP (mg/L) $n = 205^b$	3.0 (0.2; 4.0)	0.5 (0.2; 1.3)	3.0 (1.5; 3.5)	1.3 (0.5; 4.1)	3.0 (1.2; 4.0)	4.0 (3.0; 4.0)	—	1.5 (0.4; 5.0)	0.1 (0; 0.2)	4.0 (3.0; 4.9)
CK (U/L)[h] $n = 197^b$	122.0 (81.0; 259.0)	98.0 (48.0; 147.0)	—	95.0 (63.0; 138.0)	125.5 (82.0; 199.2)	109.5 (78.0; 130.0)	—	108.0 (68.0; 116.0)	109.0 (79.0; 134.0)	—
Albumin (g/L) $n = 219^b$	42.0 (4.4; 46.6)	47.0 (5.0; 49.0)	4.7 (2.9; 48.9)	42.5 (4.4; 45.0)	42.3 (4.5; 47.0)	38.6 (4.5; 45.0)	4.8 (4.5; 44.0)	44.0 (17.4; 47.5)	24.9 (0.5; 46.0)	40.3 (4.8; 41.0)
Calcium (mmol/L) $n = 302^b$	2.4 (2.3; 2.5)	2.5 (2.3; 2.6)	2.4 (2.4; 2.5)	2.4 (2.3; 2.5)	2.4 (2.4; 2.5)	2.4 (2.3; 2.5)	2.5 (2.4; 2.5)	2.4 (2.4; 2.5)	2.4 (2.4; 2.4)	2.4 (2.3; 2.4)
PTH (pmol/L) $n = 166^b$	3.1 (2.2; 3.9)	2.8 (2.3; 3.6)	—	3.1 (2.1; 3.9)	3.0 (1.9; 3.9)	3.6 (3.6; 4.9)	5.4 (4.0; 7.4)	2.2 (1.8; 3.3)	2.5 (2.1; 3.7)	3.8 (3.3; 4.6)
25 OH Vit D (nmol/L) $n = 221^b$	38.0 (22.5; 67.5)	66.3 (54.8; 71.8)	27.5 (0; 52.5)	46.5 (21.8; 78.3)	47.5 (32.5; 71)	32.5 (0.8; 77.5)	—	61.3 (43.0; 81.8)	80.0 (53.5; 124.5)	65.0 (30.0; 75.0)
C3 complement (g/L) $n = 131^b$	1.1 (0.9; 1.2)	1.2 (1.1; 1.3)	—	1.4 (1.3; 1.6)	1.3 (1.0; 1.5)	—	—	1.2 (0.5; 1.4)	1.0 (0.9; 1.2)	—
Hb (g/dL) $n = 355^b$	13.3 (12.3; 14.1)	13.3 (12.7; 13.9)	13.8 (11.7; 15.4)	13.1 (12.5; 14.0)	13.5 (12.7; 14.8)	13.6 (12.5; 14.6)	13.0 (12.0; 14.0)	13.5 (12.3; 14.0)	13.2 (12.2; 13.7)	13.8 (12.8; 14.9)
WBC (giga/L) $n = 348^b$	6.6 (5.4; 8.1)	5.7 (5.1; 7.9)	7.8 (5.8; 8.5)	7.0 (6.0; 8.3)	7.4 (6.2; 8.9)	6.4 (5.8; 8.1)	6.5 (5.9; 9.0)	6.5 (5.0; 8.2)	5.5 (4.9; 7.4)	7.0 (6.2; 7.9)
Platelets (giga/L) $n = 346^b$	216.0 (177.0; 282.0)	272.0 (244.0; 296.0)	255.0 (199.0; 497.0)	294.0 (228.0; 344.0)	264.0 (227.0; 317.0)	251.5 (203.0; 291.0)	242.0 (228.0; 294.0)	264.0 (218.5; 306.5)	295.0 (217.0; 319.0)	233.0 (228.0; 258.0)

(*continued*)

Table 4. Continued

	CGL $n = 76^a$ Median (Q1; Q3)	PSGLD $n = 13^a$ Median (Q1; Q3)	AGL $n = 12^a$ Median (Q1; Q3)	FPLD1 $n = 56^a$ Median (Q1; Q3)	FPLD2 $n = 151^a$ Median (Q1; Q3)	oFPLD $n = 30^a$ Median (Q1; Q3)	PSPLD $n = 6^a$ Median (Q1; Q3)	APL $n = 46^a$ Median (Q1; Q3)	ALLD $n = 24^a$ Median (Q1; Q3)	oLD $n = 13^a$ Median (Q1; Q3)
TSH (mU/L) $n = 306^b$	2.0 (1.4; 3.3)	1.8 (1.3; 2.2)	1.5 (1.1; 1.9)	1.7 (1.1; 2.4)	1.8 (1.1; 2.4)	1.4 (0.9; 2.1)	2.1 (0.9; 4.2)	1.7 (1.2; 2.8)	1.7 (1.2; 2.9)	1.9 (1.2; 2.4)

The table shows the distribution of selected laboratory parameters according to the different lipodystrophy subgroups in median and interquartile ranges. Only laboratory values with data from more than 3 patients available are displayed.
AGL, acquired generalized lipodystrophy; ALLD, acquired localized lipodystrophy; ALT, alanine aminotrasferase; APL, acquired partial lipodystrophy; AST, aspartate aminotransferase; CGL, congenital generalized lipodystrophy; CK, creatine kinase; FPLD1, familial partial lipodystrophy type 1; FPLD2, familial partial lipodystrophy type 2; GLD, generalized forms of lipodystrophy; Hb, hemoglobin; HbA1c, hemoglobin A1c; HDL, high-density lipoproteins; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoproteins; *n*, number of patients; oFPLD, other forms of familial partial lipodystrophy not including type 1 and 2; PLD, partial forms of lipodystrophy; PSGLD, progeroid syndrome associated with generalized lipodystrophy; PSPLD, progeroid syndrome associated with partial lipodystrophy; PTH, parathyroid hormone; TSH, thyroid stimulating hormone; WBC, white blood cells; γGT, gamma-glutamyl transferase.
[a]Number of patients in this subgroup with any laboratory data available.
[b]Total number of patients for whom this specific laboratory value was available.
[c]Treatment referring to insulin or non-insulin glucose-lowering drugs.
[d]In patients not insulin treated.
[e]Treatment referring to non-insulin glucose-lowering drugs (patients treated with insulin were completely excluded from this analysis).
[f]Treatment referring to fibrates.
[g]In patients not leptin treated.
[h]Without children and adolescents.

Though patients with FPLD2 did not show increased cardiometabolic risk factors compared to the other subgroups, they showed the highest prevalence of ischemic cardiomyopathy. This premature and severe atherosclerosis has been proposed to arise from developmental alterations due to mesodermal and endothelial differentiation defects.[22] Overall, however, patients with PLD tended to display less cardiac comorbidities (20.6%) compared to patients with GLD (36.4%). Patients with GLD showed a particularly high rate of cardiomyopathy (dilated and hypertrophic) of 20.2% which lay, for example, above the prevalence rate in the Turkish cohort (13.9%).[21] However, in a National Institute of Health (NIH) study[23] formally studying cardiac phenotype in patients with GLD, an even higher rate of increased left ventricular mass/hypertrophic cardiomyopathy of 55% was found, indicating that cardiomyopathy might be an underdiagnosed comorbidity.

The most commonly used drugs in the registry were non-insulin glucose-lowering drugs (50.0%), lipid-lowering agents (44.2%), antihypertensive treatment/cardiovascular drugs (41.4%), and insulin (29.3%), reflecting the importance of managing metabolic complications. Metreleptin, the only LD specific medication, was used only by 29.1% of GLD patients and 7.3% of PLD patients at baseline, despite approval from the European Medicines Agency (EMA) for most of these patients, possibly due to the acceptable metabolic control achieved in many patients in our cohort even without metreleptin treatment or maybe due to health insurance or local regulatory limitations. Furthermore, the visit analyzed in this data set presented the first visit to a specialized center for many patients thus they might have been started on metreleptin shortly after this visit.

Despite the fact that we see a fairly good metabolic control in our cohort, this did not translate into a median higher age at death. The mean age at death in patients with GLD (49.0 years after excluding the children) and PLD (72.0 years) was remarkably similar to those reported (51 and 67 years, respectively) by the large international, multicenter study.[17] This indicates that we might also have a similar rate of death compared to other cohorts. Future analyses are required to understand why this might be the case, and how we can improve care to increase life expectancy of our patients.

Psychosocial repercussions also presented a huge burden of disease in patients with LD in our cohort with comparable prevalence rates between patients with PLD and GLD (27.3 vs. 26.3%). While the prevalence of chronic pain was comparable between our registry (17.5%) and other studies (19.4% QuaLip study,[24] 25% in an Italian cohort[25]), the rates of reported depression varied widely between these cohorts (6.8% QuaLip study,[24] 14.9% ECLip Registry, 37.5% in the Italian cohort[25]). So we see that while it is possible to achieve acceptable metabolic control in patients living with lipodystrophy, we should not underestimate the psycho-social burden of the disease. For the future, we urgently need lipodystrophy-specific patient-reported outcome measures to systematically assess quality of life, pain, and psychological disorders accompanying LDS.

Strengths of our study include standardized and prospective data collection, continuous data monitoring, and diagnosis updates. Limitations include varied clinical assessments by different physicians and lack of treatment recommendations for all subgroups. However, cooperation within the ECLip Registry fostered alignment in treatment approaches.

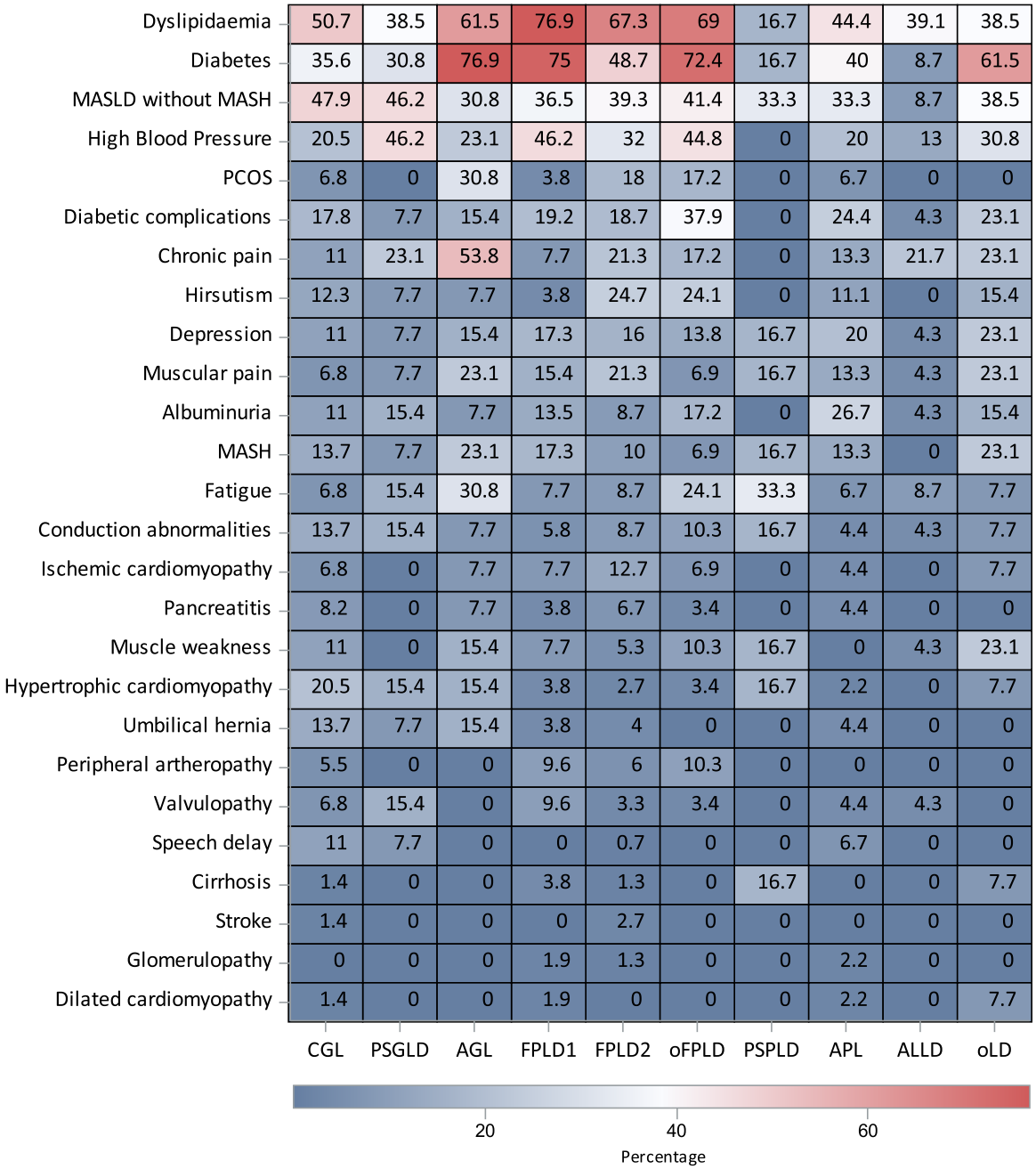


Figure 4. Prevalence of comorbidities according to subgroup. The figure shows the prevalence of selected comorbidities at baseline for the patients in the prospective ECLip cohort differentiated by lipodystrophy subtype. AGL, acquired generalized lipodystrophy; ALLD, acquired localized lipodystrophy; APL, acquired partial lipodystrophy; CGL, congenital generalized lipodystrophy; FPLD, familial partial lipodystrophy; MAFLD, metabolic dysfunction associated liver disease; MASH, metabolic dysfunction associated steatotic hepatitis; oLD, other forms of lipodystrophy; oFPLD, other forms of familial partial lipodystrophy not including type 1 and 2; PSGLD, progeroid syndrome associated with generalized lipodystrophy; PSPLD, progeroid syndrome associated with partial lipodystrophy.

Conclusion

The ECLip Registry provides a comprehensive dataset on patients living with LD, highlighting the importance of geographic and genetic factors in metabolic comorbidities as well as emphasizing the need for improved diagnosis and awareness. Despite achieving good metabolic control in many patients, the psychosocial burden of LD remains significant. To reduce mortality and improve quality of life for patients with LDS, future research must focus on early diagnosis, increasing access to adequate therapies, and addressing the psychological challenges. Additionally, the ECLip Registry's extensive dataset offers a unique resource for future research and the refinement of clinical guidelines aimed at improving patient outcomes.

Table 5. Medication in the prospective ECLip cohort at baseline.

	All patients $n = 362^a$ n (%)	GLD[b] $n = 79^a$ n (%)	CGL $n = 54^a$ n (%)	PSGLD $n = 13^a$ n (%)	AGL $n = 12^a$ n (%)	PLD[c] $n = 247^a$ n (%)	FPLD1 $n = 48^a$ n (%)	FPLD2 $n = 125^a$ n (%)	oFPLD $n = 25^a$ n (%)	PSPLD $n = 6$ n (%)	APL $n = 43^a$ n (%)	ALLD $n = 24^a$ n (%)	oLD $n = 12^a$ n (%)
Metreleptin	42 (11.6)	23 (29.1)	19 (35.2)	0	4 (33.3)	18 (7.3)	0	12 (9.6)	2 (8.0)	0	4 (9.3)	0	1 (8.3)
Insulin	106 (29.3)	16 (20.3)	11 (20.4)	0	5 (41.7)	78 (31.6)	24 (50.0)	33 (26.4)	10 (40.0)	0	11 (25.6)	8 (33.3)	4 (33.3)
Non-insulin glucose low. drugs	181 (50.0)	29 (36.7)	20 (37.0)	3 (23.1)	6 (50.0)	142 (57.5)	34 (70.8)	71 (56.8)	17 (68.0)	3 (50.0)	17 (39.5)	2 (8.3)	8 (66.7)
Lipid-lowering agents	160 (44.2)	27 (34.2)	17 (31.5)	5 (38.5)	5 (41.7)	127 (51.4)	30 (62.5)	71 (56.8)	13 (52.0)	1 (16.7)	12 (27.9)	2 (8.3)	4 (33.3)
Antihyper-tensive treatment	150 (41.4)	34 (43.0)	24 (44.4)	4 (30.8)	6 (50.0)	108 (43.7)	29 (60.4)	55 (44.0)	11 (44.0)	0	13 (30.2)	4 (16.7)	4 (33.3)
Immunosup-pressive therapy	11 (3.0)	1 (1.3)	0	0	1 (8.3)	7 (2.8)	3 (6.3)	2 (1.6)	0	0	2 (4.7)	1 (4.2)	2 (16.7)
Anticoagulation treatment	44 (12.2)	9 (11.4)	7 (13.0)	0	2 (16.7)	33 (13.4)	5 (10.4)	23 (18.4)	1 (4.0)	0	4 (9.3)	1 (4.2)	1 (8.3)
Cardiac treatment	9 (2.5)	5 (6.3)	4 (7.4)	1 (7.7)	0	4 (1.6)	1 (2.1)	3 (2.4)	0	0	0	0	0
Pain medication	21 (5.8)	4 (5.1)	4 (7.4)	0	0	17 (6.9)	8 (16.7)	6 (4.8)	0	0	3 (7.0)	0	0
Antidepressive therapy	46 (12.7)	11 (13.9)	7 (13.0)	0	4 (33.3)	31 (12.6)	10 (20.8)	15 (12.0)	3 (12.0)	0	3 (7.0)	2 (8.3)	2 (16.7)
Bisphos-phonates	5 (1.4)	0	0	0	0	2 (0.8)	1 (2.1)	0	0	0	1 (2.3)	2 (8.3)	1 (8.3)

The medication used at baseline in the prospective ECLip cohort is shown according to lipodystrophy subgroup. The drugs were categorized into subgroups according to the ATC nomenclature; the detailed classification of the medication subgroups can be found in the supplement.
AGL, acquired generalized lipodystrophy; ALLD, acquired localized lipodystrophy; APL, acquired partial lipodystrophy; CGL, congenital generalized lipodystrophy; FPLD1, familial partial lipodystrophy type 1; FPLD2, familial partial lipodystrophy type 2; GLD, generalized forms of lipodystrophy; low, lowering *n*, number of patients; oLD, other forms of lipodystrophy; oFPLD, other forms of familial partial lipodystrophy not including type 1 and 2; PLD, partial forms of lipodystrophy; PSGLD, progeroid syndrome associated with generalized lipodystrophy; PSPLD, progeroid syndrome associated with partial lipodystrophy.
[a]Number of patients with data for medication available.
[b]GLD includes: CGL, PSGLD, AGL.
[c]PLD includes: FPLD1, FPLD2, oFPLD, PSPLD, APL.

Table 6. Cause and age of death in the complete ECLip cohort.

Categories of causes of death	Cause of death in detail	Type of LD	Sex	Age at death
MACE	Myocardial infarction	CGL1	F	54
	Stroke	CGL1	F	61
	Myocardial infarction	CGL1	F	62
	Myocardial infarction	CGL1	M	66
	Myocardial infarction	Hutchinson–Gilford progeria syndrome	F	16
	Myocardial infarction	FPLD 2	M	61
	Stroke	FPLD 2	F	62
Cancer	Metastatic angiosarcoma	CGL1	F	29
	Cerebral lymphoma	Atypical Werner syndrome	M	21
	Pelvic cancer	MDPL syndrome	F	56
	Gastric cancer	FPLD 2	M	65
	Colon cancer	FPLD 2	F	90
	Multimetastatic adenocarcinoma of the lung	APL, undefined	F	78
Infections	Aspiration pneumonia	CGL undefined	M	5
	Sepsis	AGL autoimmune	F	15
	Respiratory sepsis	AGL autoimmune	M	24
	COVID 19 pneumonia	FPLD 1	F	71
Heart failure	Heart disease	CGL undefined	F	25
	Heart failure	FPLD 2	F	75
	Severe heart failure	oFPLD	M	79
	Heart failure during recovery from a surgical operation	Mandibuloacral dysplasia, type A	M	54
Epilepsy/encephalopathy	Status epilepticus	PELD	F	8
	Status epilepticus	PELD	F	10
	Status epilepticus	PELD	F	13
	Encephalopathy	PELD	M	11
Bleeding	Cerebral haemorrhage due to traumatic brain injury	Hutchinson–Gilford progeria syndrome	M	8
	aortic dissection	AGL autoimmune	F	70
Multiorgan failure	Multiorgan failure	CGL2	F	35
Cirrhosis	Decompensated liver cirrhosis	CGL3	F	47
Overdose	Unknown—supposedly gastrointestinal bleeding as a result of opioid overdose	CGL4	F	40
Unknown	unknown	CGL undefined	M	51
	unknown	FPLD 2	M	56
	unknown	FPLD 2	F	86
	unknown	FPLD 3	F	73

Data on cause and age of death for the complete ECLip cohort is shown in detail.
AGL, acquired generalized lipodystrophy; APL, acquired partial lipodystrophy; CGLD, congenital generalized lipodystrophy; CGLD, congenital generalized lipodystrophy; FPLD1, familial partial lipodystrophy; MDPL syndrome, mandibular hypoplasia, deafness, progeroid features and lipodystrophy syndrome; oFPLD, other forms of familial partial lipodystrophy not including type 1 and 2; PELD, progressive encephalopathy with lipodystrophy.

Acknowledgments

Personal thanks. We thank all the patients who agreed to participate in the ECLip Registry, as well as the clinical teams across the participating centers, for their dedicated work in managing data entry and support of the patients.Gertrud Feike (documentation officer, University of Ulm) provided outstanding support in data processing, and Kim Ulrich (documentation officer, University of Ulm) provided valuable help in data structuring. Support in data entry was provided by Silvia Magno (Pisa). ECLip Registry Consortium: This article has been authored by the ECLip Registry Consortium, which includes, for the current publication, all above-listed authors and in addition Carolina Cerchetti, Laura Rotolo, Roza Sabia, Gisa Ufer, Marianna Beghini, Hippolyte Dupuis, Elaine Withers, Anna Stears, Héléna Mosbah, Sophie Lamothe, Bruno Donadille, Sonja Janmaat, Martina Romanisio, Silvia Magno, Donatella Gilio, and Giuseppe Novelli, who all contributed significantly to data collection and approved the final version of the article. The Obesity and Lipodystrophy Center at the University Hospital of Pisa, the National Reference Center for Rare Diseases of Insulin Secretion and Insulin Sensitivity (PRISIS), Department of Endocrinology, Diabetology and Reproductive Endocrinology, Paris, the Division of Endocrinology and Diabetes Prevention and Care, Department of Medical and Surgical Sciences, IRCCS Azienda Ospedaliero-Universitaria di Bologna, and the Centre for Rare Endocrine Diseases, Division of Paediatric Endocrinology and Diabetes, Department of Paediatrics and Adolescent Medicine, Ulm University Medical Centre, Ulm, and the Division of Endocrinology and Diabetology, Department of Internal Medicine, Ulm University Medical Centre, Ulm, are part of the European Reference Network for Rare Endocrine Conditions (EndoERN Project ID No. 739527). The Obesity and Lipodystrophy Center at the University Hospital of Pisa is also part of the European Reference Network for Rare Hereditary Metabolic Disorders (MetabERN-Project ID No. 739543).

Supplementary material

Supplementary material is available at *European Journal of Endocrinology* online.

Funding

The set-up and data entry of the ECLip Registry is funded by the participating institutions.

G.C. was supported for this research by the Italian Ministry of University and Research Grants PRIN 2020NCKXBR, entitled "Suscettibilita alle malattie infettive nell'obesita: una valutazione endocrina, traslazionale e sociologica (SIDERALE)'.

The institution of M.R.D'A and Gi.N. is supported by the Italian Ministry of University and Research PRIN MUR project ADIPOAGE prot. 20223WFJJ3.

D.B.S. is supported by the Wellcome Trust (WT 219417) and The National Institute for Health Research (NIHR) Cambridge Biomedical Research Centre and NIHR Rare Disease Translational Research Collaboration.

D.A.-V. is supported by the Instituto de Salud Carlos III-PI22/00514 and Xunta de Galicia Axudas Consolidación-ED431C 2024/11.

M.C.V. is supported by Lille University Hospital.

F.P received the following grants: Grant PRIN (SIDERALE project; 2020NCKXBR_004), Cariplo Foundation (prot. 2021–4652), NODES projects M4C2 1.5 of PNRR (grant agreement no. ECS00000036) from the MUR, Grant PRIN (WESTERNAGE project; P2022Z4EB5_002), Grant PRIN (MISS.GO project).

Amryt Pharma/Chiesi Farmaceutici is providing the financial support to the ECLip Registry necessary for their post-authorization study MEASuRE, which is embedded in the ECLip Registry. The structural improvements necessary for this embedment also benefit the rest of the ECLip Registry.

None of the above named institutions has any influence on registry structure or data acquisition, processing, or analysis and were not involved in the writing of the report nor in the decision to submit the paper for publication.

Authors' contributions

GIOVANNI CECCARINI (Conceptualization [equal], Formal analysis [equal], Investigation [equal], Methodology [equal], Project administration [equal], Writing—original draft [lead], Writing—review & editing [lead]), Camille Vatier (Conceptualization [equal], Formal analysis [equal], Investigation [equal], Methodology [equal], Project administration [equal], Writing—original draft [lead], Writing—review & editing [lead]), Baris Akinci (Investigation [equal], Project administration [equal], Writing—review & editing [equal]), Ines Belalem (Investigation [equal], Writing—review & editing [equal]), Marjoleine Broekema (Investigation [equal], Writing—review & editing [equal]), Eva Csajbok (Investigation [equal], Writing—review & editing [equal]), Maria Rosaria D'apice (Investigation [equal], Writing—review & editing [equal]), Alessandra Gambineri (Investigation [equal], Writing—review & editing [equal]), Kathrin Heldt (Investigation [equal], Writing—review & editing [equal]), Martin Heni (Investigation [equal], Writing—review & editing [equal]), Lotte Kleinendorst (Investigation [equal], Writing—review & editing [equal]), Kerstin Krause (Investigation [equal], Writing—review & editing [equal]), Giovanna Lattanzi (Investigation [equal], Writing—review & editing [equal]), Konstanze Miehle (Investigation [equal], Writing—review & editing [equal]), Lavinia Palladino (Investigation [equal], Writing—review & editing [equal]), Flavia Prodam (Investigation [equal], Writing—review & editing [equal]), Ferruccio Santini (Investigation [equal], Writing—review & editing [equal]), Ermelinda Santos Silva (Investigation [equal], Writing—review & editing [equal]), DB Savage (Investigation [equal], Project administration [equal], Writing—review & editing [equal]), Paolo Sbraccia (Investigation [equal], Writing—review & editing [equal]), Thomas Scherer (Investigation [equal], Writing—review & editing [equal]), Ekaterina Sorkina (Investigation [equal], Project administration [equal], Writing—review & editing [equal]), Iztok Štotl (Investigation [equal], Writing—review & editing [equal]), Marie-Christine VANTYGHEM (Investigation [equal], Project administration [equal], Writing—review & editing [equal]), Corinne Vigouroux (Investigation [equal], Writing—review & editing [equal]), Elena Vorona (Investigation [equal], Writing—review & editing [equal]), David Araújo-Vilar (Investigation [equal], Project administration [equal], Writing—review & editing [equal]), Martin Wabitsch (Investigation [equal], Project administration [equal], Writing—review & editing [equal]),

Gabriele Nagel (Conceptualization [equal], Data curation [equal], Formal analysis [lead], Methodology [equal], Validation [lead], Visualization [equal], Writing—original draft [equal], Writing—review & editing [equal]), Julia von Schnurbein (Conceptualization [equal], Data curation [equal], Formal analysis [equal], Investigation [equal], Methodology [equal], Project administration [lead], Validation [equal], Visualization [equal], Writing—original draft [lead], Writing—review & editing [lead]), and the ECLip Registry Consortium (Investigation [supporting], Writing—review & editing [supporting])

Conflict of interest; B.A. received consulting fees from Amryt/Chiesi, Regeneron, Alnylam, ThirdRock Ventures; payments or honoraria for lectures, presentations, speaker bureaus, manuscript writing, or educational events from AstraZeneca, Novo Nordisk, Boehringer Ingelheim, Sanofi, Amryt/Chiesi, Bilim Pharmaceuticals, Servier; support for attending meetings and/or travel from Amryt/Chiesi, participated on Data Safety Monitoring Board or Advisory Board for Amryt/Chiesi, ThirdRock Ventures, Servier, NovoNordisk, Boehringer Ingelheim.

G.C. received a research grant (PRIN 2020NCKXBR) by the Italian Ministry of University and Research, and payment of a research fellowship to one of the contributors (Dr Silvia Magno), furthermore, payments or honoraria for lectures, presentations, speaker bureaus, manuscript writing, or educational events from Amryt/Chiesi, Rhythm, Novo Nordisk.

J.v.S. received payments for lectures, and presentations and support for attending meetings and/or travel from Amryt/Chiesi and Rhythm Pharmaceuticals. For Rhythm Pharmaceuticals, she participated on advisory boards.

D.B.S. is supported by the Wellcome Trust (WT 219417) and the National Institute for Health Research (NIHR) Cambridge Biomedical Research Centre and NIHR Rare Disease Translational Research Collaboration and declares no further COI.

M.H. reports lecture fees from Amryt/Chiesi, AstraZeneca, Bayer, Boehringer Ingelheim, Lilly, Novartis, Novo Nordisk, and Sanofi. He also served on advisory boards for Amryt/Chiesi, Boehringer Ingelheim, and Sanofi, and travel reimbursement from Amryt/Chiesi.

D.A.-V. has received speaker honoraria and consulting fees from Amryt/Chiesi and Regeneron. He received fees for expert testimonies from Amryt/Chiesi and participates on a Data Safety Monitoring Board or Advisory Board for Regeneron and MEASuRE Steering Committee for Amryt/Chiesi. He received support for attending meetings and/or travel from Amryt/Chiesi. He is supported from the Instituto de Salud Carlos III-PI22/00514 and Xunta de Galicia Axudas Consolidación-ED431C 2024/11.

F.S. served as a consultant, board member, steering committee member, and/or speaker to Amryt/Chiesi, Novo Nordisk, Boehringer Ingelheim, Lilly, Pfizer, Bruno Farmaceutici, and BioItalia.

K.M. received consultation or advisory fees for board memberships from Amryt/Chiesi and payments or honoraria for lectures, presentations, speaker bureaus, manuscript writing, or educational events from Chiesi/Amryt. She also received support for attending meetings and/or travel from Amryt/Chiesi.

F.P. received payments or honoraria for lectures, presentations, speaker bureaus, manuscript writing, or educational events from Amryt/Chiesi, Novo Nordisk, Menarini, Sanofi, and participated on a Data Safety Monitoring Board or Advisory Board for Amryt/Chiesi, Novo Nordisk, and Novartis. She received equipment, materials, drugs, medical writing, gifts, or other services from Therascience (for her University). Her institution received the following grants: Grant PRIN (SIDERALE project; 2020NCKXBR_004), Cariplo Foundation (prot. 2021-4652), NODES projects M4C2 1.5 of PNRR (grant agreement no. ECS00000036) from the MUR, Grant PRIN (WESTERNAGE project; P2022Z4EB5_002), Grant PRIN (MISS.GO project).

M.W. received grants or contracts from Merck Healthcare, Rhythm Pharmaceuticals, Amryt/Chiesi, Novo Nordisk Pharma; consulting fees from Novo Nordisk Pharma, Amryt/Chiesi, Rhythm Pharmaceuticals, and payments or honoraria for lectures, presentations, speaker bureaus, manuscript writing, or educational events from Merck Healthcare, Rhythm Pharmaceuticals, Amryt/Chiesi, Novo Nordisk Pharma, InfectoPharm. He received support for attending meetings and/or travel from InfectoPharm, Merck Healthcare, Novo Nordisk Pharma, and participated on a Data Safety Monitoring Board or Advisory Board for Novo Nordisk Pharma, Amryt/Chiesi, Rhythm Pharmaceuticals.

M.W. is also funded by Deutsches Zentrum für Kinder- und Jugendmedizin, Ulm University Hospital, Eythstr. 24, 89075 Ulm, Germany.

P.S. received payment of honoraria and consulting fees from Amryt/Chiesi, Novo Nordisk, Eli Lilly, Pfizer, Boehringer Ingelheim, and Roche as a member of advisory boards.

E.S.S. participated on a Data Safety Monitoring Board or Advisory Board for Chiesi.

Ca.Va. received lecture fees from Amryt/Chiesi, Sanofi, Lilly, Novo Nordisk, AstraZeneca, MSD and received support for attending meetings from Sanofi.

Co.Vi. has served as speaker and received support for attending meetings from Amryt/Chiesi and Sanofi.

T.S. has received honoraria for lectures, travel support for attending scientific meetings, and consulting fees from Amryt/Chiesi.

G.L.'s institution is supported by the Italian Ministry of University and Research PRIN MUR project ADIPOAGE prot. 20223WFJJ3, AIPROSAB, and AIDMED.

M.C.V. received honoraria for lectures from Sanofi and Ascendis and was supported for attending scientific meetings/travel by Amryt/Chiesi and Sanofi.

R.S. has received support for attending scientific meetings/travel from Amryt/Chiesi.

K.H. has received grants from the "Vereinigung für Kinderorthopädie" and has received support for attending meetings/travel from Merck and Sanofi. She participates on Data Monitoring/Advisory Boards for "Screening for Diabetes in Switzerland," sponsored by Sanofi and "Hypophosphatasia," sponsored by Alexion.

A.G. serves on the Editorial Board for the European Journal of Endocrinology.

I.B., M.B., E.C., L.K., L.P., E.S., I.S., E.V., K.K., and G.N. declare they have no conflict of interest.

References

1. Brown RJ, Araujo-Vilar D, Cheung PT, *et al.* The diagnosis and management of lipodystrophy syndromes: a multi-society practice

guideline. *J Clin Endocrinol Metab*. 2016;101(12):4500-4511. https://doi.org/10.1210/jc.2016-2466
2. Foss-Freitas MC, Akinci B, Luo Y, Stratton A, Oral EA-O. Diagnostic strategies and clinical management of lipodystrophy. *Expert Rev Endocrinol Metab*. 2020;15(2):95-114. https://doi.org/10.1080/17446651.2020.1735360
3. Garg A. Acquired and inherited lipodystrophies. *N Engl J Med*. 2004;350(12):1220-1234. https://doi.org/10.1056/NEJMra025261
4. Chiquette E, Oral E, Garg A, Araujo-Vilar D, Dhankhar P. Estimating the prevalence of generalized and partial lipodystrophy: findings and challenges. *Diabetes Metab Syndr Obes*. 2017;10:375-383. https://doi.org/10.2147/DMSO.S130810
5. Dutour A, Roll P, Gaborit B, *et al*. High prevalence of laminopathies among patients with metabolic syndrome. *Hum Mol Genet*. 2011;20(19):3779-3786. https://doi.org/10.1093/hmg/ddr294
6. Gonzaga-Jauregui C, Ge W, Staples J, *et al*. Clinical and molecular prevalence of lipodystrophy in an unascertained large clinical care cohort. *Diabetes*. 2020;69(2):249-258. https://doi.org/10.2337/db19-0447
7. Kwapich M, Lacroix D, Espiard S, *et al*. Cardiometabolic assessment of lamin A/C gene mutation carriers: a phenotype-genotype correlation. *Diabetes Metab*. 2019;45(4):382-389. https://doi.org/10.1016/j.diabet.2018.09.006
8. Akinci B, von Schnurbein J, Araujo-Vilar D, Wabitsch M, Oral EA. Lipodystrophy prevalence, "lipodystrophy-like phenotypes," and diagnostic challenges. *Diabetes*. 2024;73(7):1039-1042. https://doi.org/10.2337/dbi24-0018
9. Polyzos SA, Mantzoros CS. Lipodystrophy: time for a global registry and randomized clinical trials to assess efficacy, safety and cost-effectiveness of established and novel medications. *Metabolism*. 2017;72:A4-a10. https://doi.org/10.1016/j.metabol.2017.06.003
10. von Schnurbein J, Adams C, Akinci B, *et al*. European lipodystrophy registry: background and structure. *Orphanet J Rare Dis*. 2020;15(1):17. https://doi.org/10.1186/s13023-020-1295-y
11. Kelly TL, Wilson KE, Heymsfield SB. Dual energy X-ray absorptiometry body composition reference values from NHANES. *PLoS One*. 2009;4(9):e7038. https://doi.org/10.1371/journal.pone.0007038
12. Donadille B, Janmaat S, Mosbah H, *et al*. Diagnostic and referral pathways in patients with rare lipodystrophy and insulin-resistance syndromes: key milestones assessed from a national reference center. *Orphanet J Rare Dis*. 2024;19(1):177. https://doi.org/10.1186/s13023-024-03173-2
13. Akinci B, Onay H, Demir T, *et al*. Clinical presentations, metabolic abnormalities and end-organ complications in patients with familial partial lipodystrophy. *Metabolism*. 2017;72:109-119. https://doi.org/10.1016/j.metabol.2017.04.010
14. Fernández-Pombo A, Sánchez-Iglesias S, Castro-Pais AI, *et al*. Natural history and comorbidities of generalised and partial lipodystrophy syndromes in Spain. *Front Endocrinol (Lausanne)*. 2023;14:1250203. https://doi.org/10.3389/fendo.2023.1250203
15. Fernández-Pombo A, Yildirim Simsir I, Sánchez-Iglesias S, *et al*. A cohort analysis of familial partial lipodystrophy from two Mediterranean countries. *Diabetes Obes Metab*. 2024;26(11):4875-4886. https://doi.org/10.1111/dom.15882
16. Garg A. Gender differences in the prevalence of metabolic complications in familial partial lipodystrophy (Dunnigan variety). *J Clin Endocrinol Metab*. 2000;85(5):1776-1782. https://doi.org/10.1210/jcem.85.5.6605
17. Akinci B, Oral EA, Neidert A, *et al*. Comorbidities and survival in patients with lipodystrophy: an international chart review study. *J Clin Endocrinol Metab*. 2019;104(11):5120-5135. https://doi.org/10.1210/jc.2018-02730
18. Al Yaarubi S, Alsagheir A, Al Shidhani A, *et al*. Analysis of disease characteristics of a large patient cohort with congenital generalized lipodystrophy from the Middle East and North Africa. *Orphanet J Rare Dis*. 2024;19(1):118. https://doi.org/10.1186/s13023-024-03084-2
19. Vasandani C, Li X, Sekizkardes H, Brown RJ, Garg A. Phenotypic differences among familial partial lipodystrophy due to LMNA or PPARG variants. *J Endocr Soc*. 2022;6(12):bvac155. https://doi.org/10.1210/jendso/bvac155
20. Guidorizzi NR, Valerio CM, Viola LF, *et al*. Comprehensive analysis of morbidity and mortality patterns in familial partial lipodystrophy patients: insights from a population study. *Front Endocrinol (Lausanne)*. 2024;15:1359211. https://doi.org/10.3389/fendo.2024.1359211
21. Yildirim Simsir I, Tuysuz B, Ozbek MN, *et al*. Clinical features of generalized lipodystrophy in Turkey: a cohort analysis. *Diabetes Obes Metab*. 2023;25(7):1950-1963. https://doi.org/10.1111/dom.15061
22. Mosbah H, Vatier C, Boccara F, *et al*. Cardiovascular complications of lipodystrophic syndromes—focus on laminopathies. *Ann Endocrinol (Paris)*. 2021;82(3-4):146-148. https://doi.org/10.1016/j.ando.2020.03.002
23. Lupsa BC, Sachdev V, Lungu AO, Rosing DR, Gorden P. Cardiomyopathy in congenital and acquired generalized lipodystrophy: a clinical assessment. *Medicine (Baltimore)*. 2010;89(4):245-250. https://doi.org/10.1097/MD.0b013e3181e9442f
24. Demir T, Simsir IY, Tuncel OK, *et al*. Impact of lipodystrophy on health-related quality of life: the QuaLip study. *Orphanet J Rare Dis*. 2024;19(1):10. https://doi.org/10.1186/s13023-023-03004-w
25. Calabrò PF, Ceccarini G, Calderone A, *et al*. Psychopathological and psychiatric evaluation of patients affected by lipodystrophy. *Eat Weight Disord*. 2020;25(4):991-998. https://doi.org/10.1007/s40519-019-00716-6