BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open: first published as 10.1136/bmjopen-2024-095986 on 22 April 2025. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open

Healthcare needs, care use, and health status outcomes in adults with Bardet–Biedl syndrome: a cross-sectional study in Norway

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-095986
Article Type:	Original research
Date Submitted by the Author:	01-Nov-2024
Complete List of Authors:	Rustad, Cecilie Fremstad; Oslo University Hospital, Centre for Rare Disorders; University of Oslo, The Medical faculty Bragadottir, Ragnheidur; Oslo University Hospital, Department of Ophthalmology; University of Oslo, The Medical Faculty Nordgarden, Hilde; Lovisenberg Diakonale Hospital, National Resource Centre for Oral Health in Rare Disorders Miller, Jeanette Ullmann; Oslo University Hospital, Centre for Rare Disorders Weedon-Fekjær, Mina ; Oslo University Hospital, Centre for Rare Disorders Arfa, Shahrzad; Oslo University Hospital, Centre for Rare Disorders Åsten, Pamela ; Lovisenberg Diakonale Hospital, National Resource Centre for Oral Health in Rare Disorders Tveten, Kristian; Telemark Hospital, Department of Medical Genetics von der Lippe, Charlotte; Telemark Hospital, Department of Medical Genetics Sigurdardottir, Solrun; Oslo University Hospital, Centre for Rare Disorders
Keywords:	Quality of Life, Obesity, Disabled Persons, Health Services

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2024-095986 on 22 April 2025. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Healthcare needs, care use, and health status outcomes in adults with Bardet–Biedl syndrome: a cross-sectional study in Norway

Cecilie Fremstad Rustad[1,2], Ragnheidur Bragadottir[2,3], Hilde Nordgarden[4], Jeanette Ullmann Miller[1], Mina Susanne Weedon-Fekjær[1], Shahrzad Arfa[1], Pamela Marika Åsten[4], Kristian Tveten[5], Charlotte von der Lippe[5], Solrun Sigurdardottir[1]

[1] Centre for Rare Disorders, Oslo University Hospital, Oslo, Norway

[2] The Medical Faculty, University of Oslo, Oslo, Norway

[3] Department of Ophthalmology, Oslo University Hospital, Oslo, Norway

[4] National Resource Centre for Oral Health in Rare Disorders, Lovisenberg Diaconal Hospital, Oslo, Norway

[5] Department of Medical Genetics, Telemark Hospital Trust, Skien, Norway

Corresponding author:

Cecilie F. Rustad, MD, Centre for Rare Disorders, Oslo University Hospital, 4950 Nydalen, 0424 Oslo, Norway

Tel: +47 23 07 53 42

E-mail: cerus@ous-hf.no, cecilifr@uio.no

Word count: 4200, not including title page, abstract, keywords, references, figures and tables with titles and legends, acknowledgement, and statements on ethical approval, funding, competing interests, author contribution and availability of data.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

Abstract

Objectives: This study aimed to determine healthcare needs and care use (provision of healthcare) in adults with Bardet–Biedl syndrome (BBS) and the associations between care use and physical functioning, health status outcomes and distress.

Design: Cross-sectional study.

Setting: Outpatient hospital visits.

Participants: Thirty adults with BBS were included (50% female, aged 20-69 years) and assessed with the Needs and Provision Complexity Scale (NPCS), Short Physical Performance Battery (SPPB), EQ-5D-5L, and Hospital Anxiety and Depression Scale (HADS).

Results: The majority (80%) received disability benefits, 93% were obese, and all had retinal dystrophy. Unmet needs (needs–gets) were found within the domains of rehabilitation (83%), social and family support (65%), healthcare (50%), personal care (47%) and the environment (40%). Significant correlations were observed between care use (gets) and worse physical performance (τ = -.34, p = < 0.01), more problems with self-care (τ = .47, p < 0.01) and more problems with usual activities (τ = .41, p = 0.01). Compared with those in the general population, adults with BBS reported significantly more problems (EQ-5D-5L) with mobility, self-care, and usual activities (all p < 0.001).

Conclusions: Most adults with BBS have unmet physical, social and medical needs. Physical mobility and usual activities were correlated with the provision of healthcare. The complexity of BBS requires a multidisciplinary approach that focuses not only on the medical follow-up of the condition but also on healthcare needs for functional mobility and social care.

This study was registered at ClinicalTrials.gov, NCT05400278.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Keywords: rare disease; medical needs; quality of life; disability; obesity; blindness

STRENGTHS AND LIMITATIONS OF THIS STUDY

- A multidisciplinary research team, including different healthcare professionals working in hospitals and resource centres for rare conditions, performed the evaluations.
- Adults with Bardet–Biedl syndrome have unmet healthcare needs within rehabilitation and social and family support, which should be recognised.
- Raising awareness of unmet healthcare needs helps improve access to healthcare.
- Despite the low prevalence rate of Bardet–Biedl syndrome, the sample was largely representative of this condition in Norway.
- The small sample size limits the generalizability of the results and cannot be applied to children.
- Data were self-reported, which might result in participants underestimating their problems.

Introduction

Healthcare needs are an increasingly important issue in rare disease research. Frequent healthcare problems among people with rare diseases include a lack of appropriate access to diagnosis and a lack of treatment options (1, 2). Rare diseases, defined in Europe as conditions with a prevalence of less than 1:2000 people, affect approximately 300 million individuals worldwide (3-5). Many rare diseases are chronic, progressive, complex, and disabling, and the rarity of each of the ~7,000 rare diseases makes them difficult to diagnose (6). Studies have shown that health professionals and general practitioners lack knowledge about rare diseases and lack confidence in providing care, transitioning care and coordinating the care of people with rare diseases (7-9). Thus, individuals with rare diseases and their families unsurprisingly may face specific challenges when they seek information and support within health services. Delays in diagnosis and a lack of information about the diagnosis are shared challenges (10).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Furthermore, inequity in access to treatment and a lack of multidisciplinary care are health-related challenges that individuals with rare diseases may encounter (11-14).

One chronic, complex rare disease is the primary ciliopathy named Bardet–Biedl syndrome (BBS). This syndrome is characterized by retinal dystrophy, postaxial polydactyly, obesity, hypogonadism, renal abnormalities, and cognitive impairment (15, 16). The prevalence of BBS is estimated to be 1 in 160,000 in Northern European populations (17). The management of BBS poses challenges to health services because of the complexity of this condition, heterogeneity of the clinical phenotype, and limited treatment options (18). Treatment for BBS-related rod-cone dystrophy is not available (15), whereas the treatment options for obesity, diabetes and kidney failure are the same for people with BBS as for those in the general population. More recently, individuals with BBS who are obese might be eligible for treatment with the melanocortin 4 receptor agonist setmelanotide if the treatment is available in the country where they live and if they fulfil the criteria for treatment (19-21). Other management strategies are symptomatic, e.g., special education for cognitive impairment and training for visual loss (22). Because treatment options for BBS are limited, a personalized clinical approach is relevant to match individual needs (18). Therefore, diagnostics, prevention, treatment and follow-up are adapted to the biological condition of the individual. Multiple health needs have been identified in BBS, including vision-related needs (23), oral care needs (24), difficult airway management (25), type 2 diabetes mellitus needs (26), and problems accessing health services or treatments (27, 28). Unmet needs have been recognized regarding targeted treatments for hunger, hyperphagia and obesity (29). An unmet need can be defined as "difficulties receiving service in response to problems that significantly interfere with daily life" (30). Adults with BBS might, for example, experience a need for physical activities to achieve weight loss before kidney transplantation but do not meet understanding for their

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

obesity as one of the core features of BBS. The relationship between needs and health status in BBS needs to be better understood to address the unmet needs within the context of health status in order to improve healthcare. Despite the impact of BBS on the daily lives of individuals, to the best of our knowledge, no research has documented their unmet needs for healthcare or the support they need. This study aimed to determine healthcare needs and care use in adults with BBS in Norway and associations between care use and physical functioning, health status outcomes and distress.

Methods

Participants

Eligible individuals were recruited through a register at the Centre for Rare Disorders, Oslo University Hospital, Norway, and by advertisement on the Norwegian BBS Organization's webpage. The inclusion criteria for adults with BBS were a clinical diagnosis and/or genetic confirmation of BBS and being 16 years of age or older. Forty-six individuals were invited to participate. One person died shortly after the invitations were sent out, and one was excluded because of not having BBS. Thirty individuals participated in this study, a response rate of 68% (30/44). When those who consented to participate (n=30) and nonparticipants (n=14) were compared, no differences in age (p=0.660) or sex (p=0.88) were identified. Informed consent was obtained from all participants prior to inclusion.

Study design and data collection

This study was designed as a cross-sectional study and was conducted at the level of specialized healthcare in Norway from January 2022 to March 2023. Data were collected at the Oslo University Hospital and Lovisenberg Diaconal Hospital, Oslo, Norway, but four participants were offered the option of a home visit because they were unable to travel. An eye examination

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

was performed by an ophthalmologist (author RB). Clinical examinations and interviews were conducted with a physician (author CFR or CvdL), including measuring height and weight and calculating body mass index (BMI = kg/m^2). The participants listened and replied to questionnaires read aloud by one of the clinicians, and a physical performance test was then undertaken. These questionnaires and measures are described below. The oral health examinations were performed by a dentist and a speech and language pathologist (authors HN and PMÅ) at the National Resource Centre for Oral Health in Rare Disorders, Lovisenberg Diaconal Hospital, Oslo, Norway. The general flow of the examinations included eye examinations, clinical examinations and interviews, questionnaires, physical performance tests, and, finally, oral health examinations. The four individuals who had home visits did not have an ophthalmology or oral exam.

Patient and public involvement statement

Two members of the Norwegian organization for BBS were closely involved in the planning of this study and were consulted to identify relevant research topics of interest to the organization. Both members were asked to test out the questionnaires.

Ethics

The study, registered at ClinicalTrials.gov, NCT05400278, was approved by the Norwegian Regional Committee for Medical Research Ethics in Southeast Norway (number 166639) and performed according to ethical guidelines (31).

Measurements

Demographics and clinical information

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Demographic information was based on self-reports from participants. Information was collected regarding education, employment, medical comorbidities and prior contact with health institutions (e.g., child and youth psychiatry, services within education and psychology, district psychiatry, child habilitation, and national service for special needs education). Education was defined as high school or less (13 years or less) or more than 13 years of education. Employment, including paid full-time, part-time, or self-employment, was classified as 'employed'. Any type of unpaid work, e.g., unemployed, support at the workplace, retirement, disability benefits, or home workers, was classified as 'unemployed'. In general, height and weight measurements were performed using a Seca 704 s (Seca GmbH & co. KG., Hamburg, Germany). Genetic analysis was offered to all participants, and genetic confirmation was found in all the participants analysed. Obesity was assessed by body mass index (BMI). BMI was calculated from the participants' height and body weight (BMI = kg/m^2). A BMI between 18.5 kg/m^2 and 25 kg/m^2 was considered normal weight, a BMI above 25 kg/m^2 but less than 30 kg/m^2 was considered overweight, and a BMI above 30 kg/m^2 was considered obese (32). Renal disease included prenatally described kidney abnormalities, kidney tumours, increased kidney blood parameters, any stage of kidney failure or having had a kidney transplant. High blood pressure included measured systolic blood pressure above 140 mmHg, diastolic pressure above 90 mmHg and/or treatment with blood pressure-reducing medication.

Needs for healthcare and social services

The Needs and Provision Complexity Scale (NPCS) (33) was used to evaluate the level of unmet needs for healthcare and social services. The NPCS was developed in the UK to identify healthcare and social support needs among individuals with neurological conditions (33). It has been translated and recently validated in Norway (34, 35) and used in several populations, including individuals with Huntington's disease (34, 36), traumatic brain injuries (37) and

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

myotonic dystrophy (38). The NPCS has not previously been used in adults with BBS. In this study, we used the Norwegian version 1.0. The NPCS has two parts: Part A (Needs) was completed by two clinicians (authors CFR and SS) to evaluate each participant's needs for health and social care, and Part B (Gets) was recorded by the clinician based on the information provided by the participants with BBS to evaluate care use (provision of healthcare). Each part includes 15 items with a total score ranging from 0–50, covering low/high levels of needs. Higher scores signify higher levels of needs. The percentage of participants needing the services (NPCS items) was converted to a binary variable (0 = no unmet need, 1 = unmet need) (33). The NPCS includes five subscales that represent two domains: health and personal care needs (healthcare, personal care, and rehabilitation) and social and support needs (social and family support, environment). The Norwegian version of the NPCS has excellent interrater reliability for the total scores of the NPCS-Needs and the NPCS-Gets, with values of 0.911 and 0.987, respectively (35).

Physical performance evaluation

The Short Physical Performance Battery (SPPB) is a group of measures that combines the results of a 4.0 metre walking test at a normal pace (walking test), five-times rising from a chair as fast as possible (sit-to-stand test) and a standing balance test in a two-legged stance (39). In this study, the SPPB was used to evaluate physical performance according to the standard guided procedure (39). Each test was scored from 0 to 4, and the total score ranged from 0 to 12. A higher SPPB score signifies better physical performance.

Self-reported health status

The EQ-5D-5L is a self-reported measure that is used to evaluate general health status. The EQ-5D-5L includes a visual analogue scale (EQ VAS) with scores ranging from 0 (the worst health

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

you can imagine) to 100 (the best health you can imagine). Permission to use the EQ-5D-5L was obtained from the EuroQoL Group, and the Norwegian version was used (40). The visual analogue scale was explained orally to each participant because of their reduced vision, and they were asked to rate their perceived health on the day of testing. The EQ-5D-5L consists of five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain has five levels ranging from 1 (no problems) to 5 (extreme problems/unable to). In this study, descriptive levels of each dimension were dichotomized to "no problems" (level one) or "any problems" (levels two to five) and compared to the Norwegian normative population (41). Furthermore, the EQ-5D-5L index values, ranging from 0 (dead) to 1 (full health), were calculated based on the UK value set used in Norway (41).

Self-reported psychological distress

The Hospital Anxiety and Depression Scale (HADS) was used to assess symptoms of anxiety and depression within the last seven days (42). The HADS includes an anxiety scale and a depression scale, each with seven items. Each item is scored on a 4-point scale, with the total scores for anxiety and depression ranging from 0 (best) to 21 (worst). A HADS score > 7 points was used to identify individuals with symptoms of anxiety or depression (43).

Statistical analysis

Descriptions of the participants and questionnaires are provided with descriptive statistics, including means, medians and percentages. Shapiro–Wilk tests were performed to assess continuous data for normality. The NPCS domains, the EQ-5D-5L index score and the HADS score were not normally distributed, and these data were summarized as medians and interquartile ranges (IQRs). The mean and standard deviation (±SD) were also given for the NPCS to allow comparisons with previous studies. The chi-square test was used for the

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

differences between categorical variables. Comparisons between normally distributed continuous variables were performed with Student's *t* test, whereas the Mann–Whitney U test was used for nonparametric variables. The Wilcoxon signed rank test for non-normally distributed variables was chosen to explore pairwise differences between the NPCS "Needs" and "Gets". Kendall's tau-b correlation coefficient (τ) was used to evaluate bivariate correlations between the NPCS subscales and other variables, with 1000 bootstrapped samples. All p values < 0.05 derived from two-sided tests were considered statistically significant. Because this study is observational with a small sample size, Bonferroni correction was not used, as it may overcorrect and increase the risk of type 2 error. Statistical tests were conducted in SPSS, version 29.0 (SPSS Statistics, IBM Corporation, Chicago, IL).

Results

Study sample characteristics

Table 1 shows the characteristics of the 30 adult participants (mean age (± SD) 39.8 ± 13.6, age range 20–69 years, 50% females), presented separately for females and males. No sex differences were observed in any of the demographics. Overall, 17% of the participants were employed, either full- or part-time, one had retired, and the majority (80%) were receiving disability benefits. All participants had retinal dystrophy, and 93% were obese (BMI above 30 kg/m^2). Oral/dental abnormalities were more common in males than in females. Almost two-thirds had high blood pressure, 27% had renal disease, and 23% were diagnosed with type 2 diabetes. Four individuals had both renal disease and type 2 diabetes. The need for mental health services during childhood was reported by 20% of the participants, and 70 % had been followed by educational-psychological services in the school system. Moreover, 13% reported follow-ups with psychiatric services during adulthood.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Table 1. Demographics and characteristics of the study sample

	Females (*n* = 15)	**Males** (*n* = 15)	**Total** (*n* = 30)	***p***
Age at inclusion (mean, SD)	40.3 (13.1)	39.3 (14.7)	39.8 (13.6)	.835
Age diagnosed with BBS (median, IQR)	12 (18)	8.5 (13.8)	9 (13.5)	.827
Marital status single	13 (87 %)	13 (87 %)	26 (87 %)	-
Education (≤13 years)	13 (87 %)	14 (93 %)	27 (90 %)	.543
Employed (full time, part time)	3 (20 %)	2 (13 %)	5 (17 %)	NA
Disability benefits	11 (73 %)	13 (87 %)	24 (80 %)	.361
Body mass index	40.1 (9.9)	35.6 (12.1)	37.9 (11.1)	.272
Obesity	15 (100 %)	13 (87 %)	28 (93 %)	-
Retinal dystrophy*	15 (100 %)	15 (100 %)	30 (100 %)	-
Oral/dental abnormalities (n=26)	7 (58%)	13 (93%)	20 (77 %)	**.037**
Renal disease	3 (20 %)	5 (33 %)	8 (27 %)	NA
High blood pressure	11 (73%)	9 (60%)	20 (67 %)	.439
Diabetes	4 (27 %)	3 (20 %)	7 (23 %)	NA
Child mental health service	4 (27 %)	2 (13 %)	6 (20 %)	NA
Educational-psychological service	10 (67 %)	11 (73 %)	21 (70 %)	.690
Adult mental health clinic	2 (13 %)	2 (13 %)	4 (13 %)	NA

Note. Continuous variables are presented as mean (±SD) or median (IQR) and discrete variables as number (percentages).

NA = Chi-square analysis not performed ($n < 5$ in the cells).

*Four individuals who could not come for ophthalmology examinations self-reported that they have retinal dystrophy

Unmet needs

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

The data for the NPCS are summarized in Table 2 and presented separately for females and males. The mean overall score for the NPCS (Needs) was 17.9 (SD = 5.6), and for the NPCS (Gets), it was 12.4 (SD = 5.5). Mann–Whitney U test pairwise comparisons revealed no significant differences in clinician-rated scores (NPCS Needs) between females and males (all $p > 0.05$). With respect to self-rated scores (NPCS Gets), females had significantly higher scores in the Healthcare domain ($p = 0.050$) than males did. Thus, females received more medical healthcare than males.

Table 2. The mean and median scores of the Needs and Provision Complexity Scale by genders ($n = 30$)

	Females (n = 15)	**Males (n = 15)**	***p***
Clinical version (Part A)	Median (IQR) / M (SD)	Median (IQR) / M (SD)	
Total Needs score (score 0-50)	15.0 (8) / 16.9 (5.9)	20.0 (7) / 18.9 (5.2)	.382
Healthcare (score 0-6)	2.0 (1) / 2.7 (1.5)	2.0 (2) / 2.3 (1.4)	.432
Personal care (score 0-10)	3.0 (3) / 3.7 (2.3)	5.0 (3) / 4.4 (2.2)	.384
Rehabilitation (score 0-9)	5.0 (3) / 4.6 (2.1)	6.0 (4) / 5.1 (2.0)	.542
Social and family support (score 0-13)	1.0 (2) / 1.5 (1.6)	2.0 (3) /2.3 (1.6)	.122
Environment (score 0-12)	4.0 (4) / 4.5 (2.4)	5.0 (3) / 4.9 (2.0)	.644
Patient version (Part B)			
Total Gets score (score 0-50)	13.0 (5) / 12.6 (5.0)	11.0 (7) / 12.2 (6.1)	.532
Healthcare (score 0-6)	2.0 (2) / 2.4 (1.5)	1.0 (2) / 1.5 (1.6)	**.050***
Personal care (score 0-10)	3.0 (3) / 3.5 (2.4)	3.0 (3) / 2.8 (2.2)	.403
Rehabilitation (score 0-9)	3.0 (3) / 2.4 (2.0)	3.0 (3) / 2.6 (1.9)	.666
Social and family support (score 0-13)	0.0 (1) / 0.5 (0.8)	0.0 (2) / 1.3 (1.8)	.258
Environment (score 0-12)	3.0 (3) / 3.8 (2.2)	3.0 (3) / 4.0 (2.2)	.833

* $p = 0.05$ with the Mann-Whitney U-test.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

As shown in Table 3, clinicians (Needs) scored higher on all five domains compared to self-rated (Gets) scores. The Wilcoxon signed rank sum test confirmed the presence of significantly different pairwise comparisons between the measures of clinicians (NPCS Needs) compared with those of self-reports (NPCS Gets) (total: ($p < 0.001$); Healthcare: ($p = 0.002$); Personal care: ($p = 0.001$); Rehabilitation: ($p < 0.001$); Social and family support: ($p < 0.001$); and Environment; ($p = 0.002$); see Table 3). Most participants (97%) were found to have unmet needs. The majority had unmet needs for rehabilitation (83%), followed by unmet social and family support needs (63%), healthcare needs (50%), personal care needs (47%) and environmental needs (40%).

Table 3. Health service needs and gets according to the Needs and Provision Complexity Scale ($n = 30$)

	Needs	**Gets**	**Unmet Needs (Needs-Gets)**	**Frequency of Unmet Needs #**
	Median (IQR) / (range)	**Median (IQR) / (range)**	**Median (IQ) / (range)**	***n* (%)**
Total NPCS (score 0-50)	17.0 (8) / (8-27)	12.0 (6) / (3-27)**	4.0 (4.3)/ (0-16)	29/30 (97 %)
Healthcare (score 0-6)	2.0 (1) / (1-6)	2.0 (2) / (0-6)*	0.5 (1) / (-1-2)	15/30 (50 %)
Personal care (score 0-10)	5.0 (3) / (0-8)	3.0 (4) / (0-8)*	0.0 (2) / (-1-5)	14/30 (47 %)
Rehabilitation (score 0-9)	5.0 (3) / (0-8)	3.0 (2)/ (0-7)**	2.0 (2) / (0-8)	25/30 (83 %)
Social and family support (score 0-13)	1.5 (2) / (0-6)	0.0 (2)/ (0-6)**	1.0 (1.3) / (-1-4)	19/30 (63 %)
Environment (score 0-12)	4.5 (3)/ (0-9)	3.0 (3)/ (0-8)*	0.0 (1) (0-4)	12/30 (40 %)

Notes.

Needs indicates that adults with BBS need this health service.

Gets indicate that adults receive this health service (provision).

Unmet needs are the difference between Needs and Gets.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Proportion of participants with a higher score on the NPCS Needs than the NPCS Gets.

* $p < 0.01$, ** $p < 0.001$ with the Wilcoxon signed rank test.

Figure 1 illustrates the proportions of unmet needs across all 15 items, using the binary variable described in the methods. Between 50% and 77% of the participants were found to have insufficient professional healthcare (e.g., medical care, social workers, physiotherapists, psychologists, occupational therapists, dieticians, and dentists).

---Insert Figure 1 here---

Physical performance, health status outcome and distress

The measures of general physical functioning, self-reported health status and distress (anxiety, depression) are presented in Table 4. None of the measures differed by sex. Two participants were unable to perform the SPPB because they were unable to stand without support and were therefore given a total score of zero. The EQ-5D-5L index value score was 0.83 (median, IQR = 0.27), and the EQ-5D VAS scale score was 63.8 (mean, SD=21.5).

Four individuals (13%) were identified as having potential anxiety (score > 7), and only one individual (3%) had potential depression (score > 7).

Table 4. Physical performance and self-reported psychological distress and health status by genders

	Females (*n* = 15)	**Males (*n* = 15)**	**Total (*n* = 30)**	***p***
SPPB Total (score 0-12) ǂ	7.0 (3.9)	6.4 (3.2)	6.7 (3.5)	.650
EQ-5D-5L VAS scale (score 0-100) ǂ	61.3 (24.3)	66.3 (18.7)	63.8 (21.5)	.528
EQ-5D-5L index score (score 0-1) #	0.80 (0.3)	0.89 (0.3)	0.83 (0.3)	.693
HADS total (score 0-42) #	2.0 (10)	4.0 (7)	2.0 (8)	.867

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

HADS Anxiety (score 0-21) #	2.0 (4)	2.0 (4)	2.0 (4)	.949
HADS Depression (score 0-21) #	0.0 (5)	1.0 (4)	0.5 (4)	.640

Notes.

‡ Scores presented as mean (±SD).

Scores presented as median (IQR)

P-values calculated with the Mann-Whitney U-test for medians or with the *t*-test for means.

Abbreviations: HADS = Hospital Anxiety and Depression Scale; SPPB = The Short Physical Performance Battery; VAS = Visual Analogue Scale.

Self-reported health status

Table 5 shows the results for the five domains of the EQ-5D-5L in adults with BBS and those in the general Norwegian population (41). Adults with BBS reported significantly more health problems in terms of mobility, self-care, and usual activities (all $p < 0.001$) than the general Norwegian population.

Table 5. Self-reported outcome measure (EQ-5D-5L) by adults with Bardet-Biedl syndrome (*n* = 30) compared with the general Norwegian population (*n* = 3120)

EQ-5D-5L domains	**Bardet-Biedl syndrome (n=30)**	**Normative data (n = 3120) #**	*p*
	Any problems, n (%)	**Any problems, n (%)**	
Mobility	16 (53 %)	562 (18.0 %)	< 0.001
Self-care	7 (23 %)	227 (7.3 %)	< 0.001
Usual activities	16 (53 %)	756 (24.2 %)	< 0.001
Pain / Discomfort	19 (63 %)	1937 (62.1 %)	.888
Anxiety / Depression	13 (43 %)	1104 (35.4 %)	.365

Notes.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Garratt, A. M., Hansen, T. M., Augestad, L. A., Rand, K., & Stavem, K. (2022). Norwegian population norms for the EQ-5D-5L: results from a general population survey. *Qual Life Res*, *31*(2), 517-526. Comparisons between our BBS population and the general Norwegian population were conducted using an online Chi square calculator.

Correlations between care use (NPCS Gets) and health status outcomes

The Healthcare subscale of the NPCS (Table 6) was correlated with having more problems with usual activities (τ = .41, p = 0.01). The Personal Care subscale was correlated with worse physical performance (τ = -.34, p = < 0.01) and having more problems with self-care (τ = .47, p < 0.01).

---Insert Table 6 here---

Discussion

This study focused on the healthcare needs of adults with BBS in Norway. In this nationally representative cross-sectional study, we found that a substantial proportion of adults with BBS who need supportive health services do not receive such services. Significant discrepancies were identified between needs (clinicians' ratings) and gets (participants' ratings), indicating that a majority of participants had unmet needs related to the domains of health and personal care as well as social and supportive care. This gap represents an opportunity to improve access to healthcare in this population with rare diseases. Additionally, needs for a specific health professional, particularly those related to medical treatment, therapy intensity and therapy disciplines, were unmet. This study builds on earlier studies of rare diseases, showing a need for supportive care in a broad range of domains and unmet needs in primary health care (2, 11, 44).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

In 2024, four European Reference Networks published a consensus statement and recommendations to address diagnosis, lifelong follow-up, symptomatic care and treatments for eye, neurological, and endocrinological diseases due to BBS (45). Prior research has also suggested that BBS care should be considered in the context of overall management, with comprehensive medical, genetic and mental healthcare (18) and multidisciplinary care (16). Many of the health issues presented in our study could be addressed in a multidisciplinary team setting by relevant professionals, e.g., physicians, physical therapists, social workers, ophthalmologists, dentists, registered dietitians and psychologists; however, none of the participants taking part in this study received such services. The rate of disability benefit was 80%, and all participants had retinal dystrophy, indicating severe low vision or blindness; moreover, 93% were obese, 27% had kidney disease, and 23% had diabetes. Dental abnormalities and high blood pressure were present in approximately two-thirds of the participants. These health problems represent broad types of healthcare needs and require multidisciplinary interventions in addition to pharmacological treatments (e.g., blood pressure, diabetes, obesity). Therefore, ensuring the delivery of healthcare and preventative measures to people diagnosed with BBS is important. Our findings only highlight a small group with a rare disease with unique needs arising from the primary features of BBS. However, they have the potential to provide insight not only into BBS but also into other complex rare diseases in terms of unmet physical, social and medical needs. Thus, aiming to improve access to the healthcare system is a major issue for those with rare conditions to achieve the best possible health outcomes, as presented in a scoping review on rare diseases (2).

In countries where the inhabitants live widely distributed, cost-related and health-related barriers may hinder some individuals with BBS from accessing healthcare. The Norwegian health system is provided based on need for treatment and funded through taxes. General practitioners provide primary care, which is the responsibility of municipalities, and they refer

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

patients to specialized healthcare when necessary (46). Generally, individuals with BBS require specialist care that is beyond the care offered by the general practioners. For individuals with poor access to health care services, the leverage of ambulatory teams could be explored. Resource centres for rare conditions might be addressed by professionals to participate in multidisciplinary teams, depending on the legislation in the country (47). Technological advances, including the mainstreaming of video consultations, might make this easier.

BBS lacks pathognomonic signs or symptoms at birth or later, which, combined with a lack of knowledge about BBS, might cause diagnostic delay (16, 48). The age at diagnosis was 9 years in the present study, and the majority of participants had been in contact with educational-psychological services during childhood. Furthermore, 20% of the participants had been referred to child and adolescent mental health services, indicating that children with BBS need treatment for their mental and/or behavioural problems. This finding highlights the importance of early disease intervention. Increased accessibility of genetic testing today may reduce the age at diagnosis compared with when our participants were diagnosed several decades ago.

We analysed a range of health outcomes and needs for healthcare for each sex and only found that males tended to have more dental problems than females. However, this result should be interpreted with caution, because 26 participants had dental assessments. Clinicians did not differ in how they rated the healthcare needs (NPCS) for females and males. However, the self-ratings of medical healthcare suggested that females received more medical healthcare than males, which may suggest that females with BBS tended to actively manage their health better than males with BBS. In rare diseases, females have a greater risk of diagnostic delays after entering the health system (49). In the general population, sex disparities are also reported in primary care and specialized care, with females being diagnosed later than males (50, 51). Other studies have shown that limitations in healthcare access, healthcare coverage and primary care affect females (52, 53). Gender inequality in healthcare access is scarcely

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

reported in rare diseases, and more research is needed to identify whether our results are reproducible. Further analysis is needed to identify the cause of this discrepancy.

The NPCS instrument used in our study was designed for evaluating neurological conditions. BBS is a primary ciliopathy and not primarily a neurological condition, although some individuals with BBS might have neurological symptoms and disease. The present findings based on the NPCS were compared with those of another study on neurological disability (33), which revealed clinicians reported higher total scores on needs for the BBS group. In addition, adults with BBS reported higher scores in the social care and support domain (care gets). The total scores for needs and gets within healthcare and social support in the BBS group were also higher than those for Huntington disease in Stages I and II but lower than those for Huntington disease in Stages III and V (34).

Higher scores on medical healthcare and personal care services (care gets) in the present study were only correlated with greater difficulty with physical balance (SPPB), self-care and usual activities among adults with BBS. Self-reported problems with mobility and usual activities (EQ-5D-5L) were found in just over half of the participants; these problems were reported statistically more often than those reported by the general Norwegian population (41).

Only 17% of adults with BBS were employed, which is notably lower than the rate reported in people with various eye diseases (44%) in Norway (54) and lower than the work participation in rare diseases (55%) reported in a recent scoping review (55). The complexity of BBS makes it difficult to pinpoint the exact reasons for unemployment. Our findings may be limited because the analyses were exploratory and based on a small sample, and further research is needed to evaluate this in more detail. Complex conditions such as BBS with reduced vision, possible cognitive challenges and obesity pose difficulties to the working environment, which needs to be addressed to improve work participation.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

The strengths of this study are the high response rate (68%), which did not differ by sex. Also, this sample of responders appears to be largely representative (age and sex) of adults with BBS in the country (Norway). Evaluations were performed by a multidisciplinary research team, including different healthcare professionals working in hospitals and resource centres for rare conditions in Norway. This study could subsequently contribute to increasing awareness of BBS among professionals working in primary care but also in mental health and specialist health services, where treatments may be administered. No previous study has focused on describing healthcare needs and the provision of and access to healthcare in BBS. Based on present findings, substantial physical and social healthcare needs are currently not addressed and this study can serve as a starting point for future research on BBS or other rare diseases.

The small sample size may be considered a limitation because it significantly reduces the statistical power. The data were self-reported, which might have resulted in participants underestimating their problems because of a lack of self-awareness or having cognitive difficulties understanding the questions. Because individuals under 16 years of age were excluded, the study has limited generalizability to children. In addition, adults with BBS who did not participate in this study might have other healthcare needs. The cross-sectional design limits the assessments of longitudinal changes and causal associations between healthcare use (gets) and health outcomes.

Conclusions

Adults with BBS were found to have unmet physical, social and medical needs, which may contribute to health concerns. Physical mobility and usual activities were correlated with access to health services, with half of the participants having difficulties in both. Given the complexity and heterogeneity of BBS, effective management requires a multidisciplinary approach that

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

focuses not only on medical follow-up but also on functional mobility and social care to provide optimal personalized care for all individuals with BBS.

Acknowledgement

The research team is deeply grateful to all the individuals with Bardet-Biedl syndrome for their time and investment in taking part in this study. We would like to thank the two representatives of the Norwegian Organization for Bardet-Biedl syndrome for their involvement: Richard Ødegaard and Lill Susann Lerudsmoen.

Funding

This study was supported by grants from Raagholtstiftelsen in Norway (to Solrun Sigurdardottir).

Author contributions

All the authors meet the criteria for authorship stated in the requirements for manuscript submitted to BMJ Open and all four ICJME criteria. In particular, the authors' contributions to the manuscript were as follows: conceptualization and methodology: all the authors. Formal data analyses and writing of the original draft: CFR, SS. Supervision: SS, CvdL, RB. Review of the manuscript and editing and validation of the final text: all the authors.

Availability of data and materials

Norwegian ethical and legal restrictions prevent the authors from uploading or sharing data with public repositories. Individuals with Bardet–Biedl syndrome in Norway belong to a relatively small group, and very little personal data are needed to indirectly identify individual study participants.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Ethics approval and consent to participate

The Norwegian Regional Committee for Medical Research Ethics in Southeast Norway (number 166639) and the Data Protection officer at Oslo University Hospital (number 20/21045) approved the study. Written informed consent was obtained from all the included individuals.

Figure title

Figure 1. Percentage of unmet and met needs of the 15 items of the Needs and Provision Complexity Scale.

Table title

Table 6. Correlation analysis between NPCS (Gets), HADS, SPPB and EQ-5D-5L and demographics in the total sample (*n* = 30)

References

1. Austin CP, Cutillo CM, Lau LPL, et al. Future of Rare Diseases Research 2017-2027: An IRDiRC Perspective. Clin Transl Sci. 2018;11(1):21-7.
2. Long JC, Best S, Nic Giolla Easpaig B, et al. Needs of people with rare diseases that can be supported by electronic resources: a scoping review. BMJ Open. 2022;12(9):e060394.
3. Haendel M, Vasilevsky N, Unni D, et al. How many rare diseases are there? Nat Rev Drug Discov. 2020;19(2):77-8.
4. Union E. Regulation (EC) N 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medical products. 2000.
5. Ferreira CR. The burden of rare diseases. Am J Med Genet A. 2019;179(6):885-92.
6. Chung CCY, Hong Kong Genome P, Chu ATW, et al. Rare disease emerging as a global public health priority. Front Public Health. 2022;10:1028545.
7. Evans WR, Rafi I. Rare diseases in general practice: recognising the zebras among the horses. Br J Gen Pract. 2016;66(652):550-1.
8. Vandeborne L, van Overbeeke E, Dooms M, et al. Information needs of physicians regarding the diagnosis of rare diseases: a questionnaire-based study in Belgium. Orphanet J Rare Dis. 2019;14(1):99.
9. Fredwall S, Allum Y, AlSayed M, et al. Optimising care and follow-up of adults with achondroplasia. Orphanet J Rare Dis. 2022;17(1):318.
10. Groft SC, Posada M, Taruscio D. Progress, challenges and global approaches to rare diseases. Acta Paediatr. 2021;110(10):2711-6.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

11. Depping MK, Uhlenbusch N, von Kodolitsch Y, et al. Supportive care needs of patients with rare chronic diseases: multi-method, cross-sectional study. Orphanet J Rare Dis. 2021;16(1):44.
12. Zelihic D, Hjardemaal FR, Lippe CV. Caring for a child with Bardet-Biedl syndrome: A qualitative study of the parental experiences of daily coping and support. Eur J Med Genet. 2020;63(4):103856.
13. Pelentsov LJ, Fielder AL, Laws TA, et al. The supportive care needs of parents with a child with a rare disease: results of an online survey. BMC Fam Pract. 2016;17:88.
14. Benito-Lozano J, Arias-Merino G, Gomez-Martinez M, et al. Diagnostic Process in Rare Diseases: Determinants Associated with Diagnostic Delay. Int J Environ Res Public Health. 2022;19(11).
15. Chandra B, Tung ML, Hsu Y, et al. Retinal ciliopathies through the lens of Bardet-Biedl Syndrome: Past, present and future. Prog Retin Eye Res. 2022;89:101035.
16. Forsythe E, Kenny J, Bacchelli C, et al. Managing Bardet-Biedl Syndrome-Now and in the Future. Front Pediatr. 2018;6:23.
17. Forsythe E, Beales PL. Bardet-Biedl syndrome. Eur J Hum Genet. 2013;21(1):8-13.
18. Kenny J, Forsythe E, Beales P, et al. Toward personalized medicine in Bardet-Biedl syndrome. Per Med. 2017;14(5):447-56.
19. Meyer JR, Krentz AD, Berg RL, et al. Kidney failure in Bardet–Biedl syndrome. Clin Genet. 2022;101(4):429-41.
20. Tomlinson JW. Bardet-Biedl syndrome: A focus on genetics, mechanisms and metabolic dysfunction. Diabetes Obes Metab. 2024.
21. Forsythe E, Haws RM, Argente J, et al. Quality of life improvements following one year of setmelanotide in children and adult patients with Bardet-Biedl syndrome: phase 3 trial results. Orphanet J Rare Dis. 2023;18(1):12.
22. Melluso A, Secondulfo F, Capolongo G, et al. Bardet-Biedl Syndrome: Current Perspectives and Clinical Outlook. Ther Clin Risk Manag. 2023;19:115-32.
23. Denniston AK, Beales PL, Tomlins PJ, et al. Evaluation of visual function and needs in adult patients with bardet-biedl syndrome. Retina. 2014;34(11):2282-9.
24. Panny A, Glurich I, Haws RM, et al. Oral and Craniofacial Anomalies of Bardet-Biedl Syndrome: Dental Management in the Context of a Rare Disease. J Dent Res. 2017;96(12):1361-9.
25. Smith BB, Barbara DW, Hyder JA, et al. Anesthetic considerations for patients with Bardet-Biedl syndrome: a case series and review of the literature. Paediatr Anaesth. 2016;26(4):429-37.
26. Pomeroy J, Krentz AD, Richardson JG, et al. Bardet-Biedl syndrome: Weight patterns and genetics in a rare obesity syndrome. Pediatr Obes. 2021;16(2):e12703.
27. Mujahid S, Hunt KF, Cheah YS, et al. The Endocrine and Metabolic Characteristics of a Large Bardet-Biedl Syndrome Clinic Population. J Clin Endocrinol Metab. 2018;103(5):1834-41.
28. Keifer E, Berg RL, Richardson JG, et al. Early development and adaptive functioning in children with Bardet-Biedl syndrome. Am J Med Genet A. 2024;194(1):31-8.
29. Forsythe E, Mallya UG, Yang M, et al. Burden of hyperphagia and obesity in Bardet-Biedl syndrome: a multicountry survey. Orphanet J Rare Dis. 2023;18(1):182.
30. McColl MA, Shortt S, Gignac M, et al. Disentangling the effects of disability and age on health service utilisation. Disabil Rehabil. 2011;33(13-14):1253-61.
31. World Medical A. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191-4.
32. Force USPST. Screening for obesity in adults: recommendations and rationale. Ann Intern Med. 2003;139(11):930-2.
33. Turner-Stokes L, McCrone P, Jackson DM, et al. The Needs and Provision Complexity Scale: a multicentre prospective cohort analysis of met and unmet needs and their cost implications for patients with complex neurological disability. BMJ Open. 2013;3(2).
34. van Walsem MR, Howe EI, Iversen K, et al. Unmet needs for healthcare and social support services in patients with Huntington's disease: a cross-sectional population-based study. Orphanet J Rare Dis. 2015;10:124.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

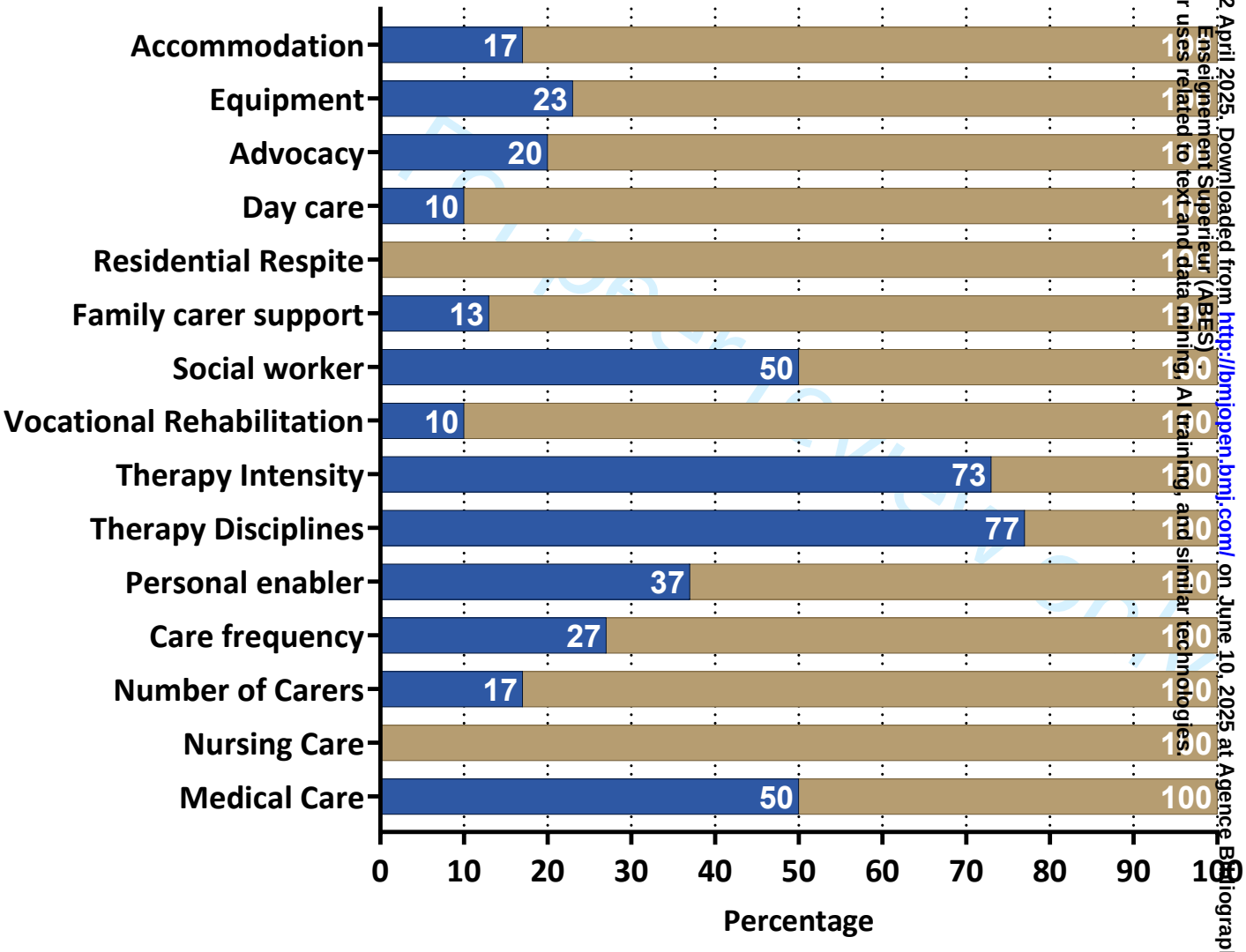
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

35. Forslund MV, Borgen IMH, Karic T, et al. Validity of the Norwegian Version of the Needs and Provision Complexity Scale (NPCS) in Patients with Traumatic Brain Injury and Atraumatic Subarachnoid Hemorrhage. J Clin Med. 2024;13(3).
36. van Walsem MR, Howe EI, Ruud GA, et al. Health-related quality of life and unmet healthcare needs in Huntington's disease. Health Qual Life Outcomes. 2017;15(1):6.
37. Laurie K, Foster MM, Borg DN, et al. Perceived service adequacy and unmet need after discharge from brain injury rehabilitation. Disabil Rehabil. 2023;45(20):3252-61.
38. Holmoy AKT, Johannessen CH, Hope S, et al. Uncovering health and social care needs among myotonic dystrophy patients: Utility of the Needs and Provisions Complexity Scale. Acta Neurol Scand. 2019;139(6):526-32.
39. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci. 2000;55(4):M221-31.
40. Nord E. EuroQol: health-related quality of life measurement. Valuations of health states by the general public in Norway. Health Policy. 1991;18(1):25-36.
41. Garratt AM, Hansen TM, Augestad LA, et al. Norwegian population norms for the EQ-5D-5L: results from a general population survey. Qual Life Res. 2022;31(2):517-26.
42. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res. 2002;52(2):69-77.
43. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361-70.
44. Bogart K, Hemmesch A, Barnes E, et al. Healthcare access, satisfaction, and health-related quality of life among children and adults with rare diseases. Orphanet J Rare Dis. 2022;17(1):196.
45. Dollfus H, Lilien MR, Maffei P, et al. Bardet-Biedl syndrome improved diagnosis criteria and management: Inter European Reference Networks consensus statement and recommendations. Eur J Hum Genet. 2024.
46. Saunes IS, Karanikolos M, Sagan A. Norway: Health System Review. Health Syst Transit. 2020;22(1):1-163.
47. Willmen T, Willmen L, Pankow A, et al. Rare diseases: why is a rapid referral to an expert center so important? BMC Health Serv Res. 2023;23(1):904.
48. Berezovsky A, Rocha DM, Sacai PY, et al. Visual acuity and retinal function in patients with Bardet-Biedl syndrome. Clinics (Sao Paulo). 2012;67(2):145-9.
49. Faye F, Crocione C, Anido de Pena R, et al. Time to diagnosis and determinants of diagnostic delays of people living with a rare disease: results of a Rare Barometer retrospective patient survey. Eur J Hum Genet. 2024.
50. Westergaard D, Moseley P, Sorup FKH, et al. Population-wide analysis of differences in disease progression patterns in men and women. Nat Commun. 2019;10(1):666.
51. Alcalde-Rubio L, Hernandez-Aguado I, Parker LA, et al. Gender disparities in clinical practice: are there any solutions? Scoping review of interventions to overcome or reduce gender bias in clinical practice. Int J Equity Health. 2020;19(1):166.
52. Ribeiro PS, Jacobsen KH, Mathers CD, et al. Priorities for women's health from the Global Burden of Disease study. Int J Gynaecol Obstet. 2008;102(1):82-90.
53. Daher M, Al Rifai M, Kherallah RY, et al. Gender disparities in difficulty accessing healthcare and cost-related medication non-adherence: The CDC behavioral risk factor surveillance system (BRFSS) survey. Prev Med. 2021;153:106779.
54. Brunes A, Heir T. Visual impairment and employment in Norway. BMC Public Health. 2022;22(1):648.
55. Velvin G, Dammann B, Haagensen T, et al. Work participation in adults with rare genetic diseases - a scoping review. BMC Public Health. 2023;23(1):910.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Figure 1.



bmjopen-2024-095986 on 22 April 2025. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES). Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Table 6. Correlation analysis between NPCS (Gets), HADS, SPPB and EQ-5D-5L and demographics in the total sample (N = 30)

	Healthcare		Personal care		Rehabilitation		Social/family support		Environment	
	τ	*p*	τ	*p*	τ	*p*	τ	*p*	τ	*p*
Age	.27	.060	.10	.458	.15	.295	.01	.967	-.21	.135
Kidney disease (0=no, 1=yes)	.27	.106	-.10	.554	-.16	.341	.17	.338	-.24	.133
High blood pressure (0=no, 1=yes)	.27	.113	.21	.190	.04	.801	.14	.424	.171	.293
BMI	.09	.543	.15	.279	-.21	.136	.13	.370	.18	.184
HADS Anxiety	-.20	.170	.10	.473	.16	.278	.03	.852	-.11	.425
HADS Depression	-.21	.178	.14	.342	.04	.794	.05	.760	-.14	.338
SPPB Total score	-.20	.159	-.34	**.014***	-.086	.548	.24	.870	-.05	.742
EQ-5D-5L Mobility	.28	.08	.07	.649	-.12	.461	.026	.876	-.14	.379
EQ-5D-5L Self-care	.14	.395	.47	**.003****	.14	.389	.21	.224	.22	.158
EQ-5D-5L Usual activity	.41	**.010***	.21	.169	.02	.903	.121	.465	-.17	276
EQ-5D-5L Pain / Discomfort	.21	.179	-.03	.834	-.28	.076	.01	.931	-.11	.488
EQ-5D-5L Anxiety / Depression	-.08	.605	.25	.105	.08	.601	.09	.599	-.10	.500

Notes.

Abbreviations: NPCS = Needs and Provision Complexity Scale; HADS = Hospital Anxiety and Depression Scale; SPPB = Short Physical Performance Battery.

Correlation calculated with Kendall's tau beta correlation coefficient (τ). Bootstrapping with 1000-samples.

* $p < 0.05$; ** $p < 0.01$

For peer review only

bmjopen-2024-095486 on 22 April 2025. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

BMJ Open

Healthcare needs, care use, and health status outcomes in adults with Bardet–Biedl syndrome: a cross-sectional study in Norway

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-095986.R1
Article Type:	Original research
Date Submitted by the Author:	17-Feb-2025
Complete List of Authors:	Rustad, Cecilie Fremstad; Oslo University Hospital, Centre for Rare Disorders; University of Oslo, The Medical faculty Bragadottir, Ragnheidur; Oslo University Hospital, Department of Ophthalmology; University of Oslo, The Medical Faculty Nordgarden, Hilde; Lovisenberg Diakonale Hospital, National Resource Centre for Oral Health in Rare Disorders Miller, Jeanette Ullmann; Oslo University Hospital, Centre for Rare Disorders Weedon-Fekjær, Mina ; Oslo University Hospital, Centre for Rare Disorders Arfa, Shahrzad; Oslo University Hospital, Centre for Rare Disorders Åsten, Pamela ; Lovisenberg Diakonale Hospital, National Resource Centre for Oral Health in Rare Disorders Tveten, Kristian; Telemark Hospital, Department of Medical Genetics von der Lippe, Charlotte; Telemark Hospital, Department of Medical Genetics Sigurdardottir, Solrun; Oslo University Hospital, Centre for Rare Disorders
Primary Subject Heading:	Patient-centred medicine
Secondary Subject Heading:	Genetics and genomics, Diabetes and endocrinology, General practice / Family practice, Health services research, Medical management
Keywords:	Quality of Life, Obesity, Disabled Persons, Health Services

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2024-095986 on 22 April 2025. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Healthcare needs, care use, and health status outcomes in adults with Bardet–Biedl syndrome: a cross-sectional study in Norway

Cecilie Fremstad Rustad[1,2], Ragnheidur Bragadottir[2,3], Hilde Nordgarden[4], Jeanette Ullmann Miller[1], Mina Susanne Weedon-Fekjær[1], Shahrzad Arfa[1], Pamela Marika Åsten[4], Kristian Tveten[5], Charlotte von der Lippe[5], Solrun Sigurdardottir[1]

[1] Centre for Rare Disorders, Oslo University Hospital, Oslo, Norway

[2] The Medical Faculty, University of Oslo, Oslo, Norway

[3] Department of Ophthalmology, Oslo University Hospital, Oslo, Norway

[4] National Resource Centre for Oral Health in Rare Disorders, Lovisenberg Diaconal Hospital, Oslo, Norway

[5] Department of Medical Genetics, Telemark Hospital Trust, Skien, Norway

Corresponding author:

Cecilie F. Rustad, MD, Centre for Rare Disorders, Oslo University Hospital, 4950 Nydalen, 0424 Oslo, Norway

Tel: +47 23 07 53 42

E-mail: cerus@ous-hf.no, cecilifr@uio.no

Word count: 4215, not including title page, abstract, keywords, references, figures and tables with titles and legends, acknowledgement, and statements on ethical approval, funding, competing interests, author contribution and availability of data.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

Abstract

Objectives: This study aimed to determine healthcare needs and care use (provision of healthcare) in adults with Bardet–Biedl syndrome (BBS) and the associations between care use and physical functioning, health status outcomes and distress.

Design: Cross-sectional study.

Setting: Outpatient hospital visits.

Participants: Thirty adults with BBS were included (50% female, aged 20-69 years) and assessed with the Needs and Provision Complexity Scale (NPCS), Short Physical Performance Battery (SPPB), EQ-5D-5L, and Hospital Anxiety and Depression Scale (HADS).

Results: The majority (80%) received disability benefits, 93% were overweight or obese, and all had retinal dystrophy. Unmet needs (needs–gets) were found within the domains of rehabilitation (83%), social and family support (65%), healthcare (50%), personal care (47%) and the environment (40%). Significant correlations were observed between care use (gets) and worse physical performance (τ = -.34, p = < 0.01), more problems with self-care (τ = .47, p < 0.01) and more problems with usual activities (τ = .41, p = 0.01). Compared with those in the general population, adults with BBS reported significantly more problems (EQ-5D-5L) with mobility, self-care, and usual activities (all p < 0.001).

Conclusions: Most adults with BBS have unmet physical, social and medical needs, with the majority having unmet rehabilitation needs that require special attention. Physical mobility and usual activities were correlated with the provision of healthcare. The complexity of BBS requires a multidisciplinary approach that focuses not only on the medical follow-up of the condition but also on healthcare needs for functional mobility and social care.

This study was registered at ClinicalTrials.gov, NCT05400278.

Keywords: rare disease; medical needs; quality of life; disability; obesity; blindness

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

STRENGTHS AND LIMITATIONS OF THIS STUDY

- A multidisciplinary research team, including different healthcare professionals working in hospitals and resource centres for rare conditions, performed the evaluations.
-Generic, validated outcome measures were used to estimate and interpret physical and mental health in the BBS population
- The small sample size limits the generalizability of the results and cannot be applied to children.
- Data were self-reported, which might result in participants underestimating their problems.

Introduction

Healthcare needs are an increasingly important issue in rare disease research. Frequent healthcare problems among people with rare diseases include a lack of appropriate access to diagnosis and a lack of treatment options [1, 2]. Rare diseases, defined in Europe as conditions with a prevalence of less than 1:2000 people, affect approximately 300 million individuals worldwide [3-5]. Many rare diseases are chronic, progressive, complex, and disabling, and the rarity of each of the ~7,000 rare diseases makes them difficult to diagnose [6]. Studies have shown that health professionals and general practitioners lack knowledge about rare diseases and lack confidence in providing care, transitioning care and coordinating the care of people with rare diseases [7-9]. Thus, individuals with rare diseases and their families unsurprisingly may face specific challenges when they seek information and support within health services. Delays in diagnosis and a lack of information about the diagnosis are shared challenges [10]. Furthermore, inequity in access to treatment and a lack of multidisciplinary care are health-related challenges that individuals with rare diseases may encounter [11-14].

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

One chronic, complex rare disease is the primary ciliopathy named Bardet–Biedl syndrome (BBS). This syndrome is characterized by retinal dystrophy, postaxial polydactyly, obesity, hypogonadism, renal abnormalities, and cognitive impairment [15, 16]. The prevalence of BBS is estimated to be 1 in 160,000 in Northern European populations [17]. The management of BBS poses challenges to health services because of the complexity of this condition, heterogeneity of the clinical phenotype, and limited treatment options [18]. Treatment for BBS-related rod-cone dystrophy is not available [15], whereas the treatment options for obesity, diabetes and kidney failure are the same for people with BBS as for those in the general population. More recently, individuals with BBS who are obese might be eligible for treatment with the melanocortin 4 receptor agonist setmelanotide if the treatment is available in the country where they live and if they fulfil the criteria for treatment [19-21]. Other management strategies are symptomatic, e.g., special education for cognitive impairment and training for visual loss [22]. Because treatment options for BBS are limited, a personalized clinical approach is relevant to match individual needs [18]. Therefore, diagnostics, prevention, treatment and follow-up are adapted to the biological condition of the individual. Multiple health needs have been identified in BBS, including vision-related needs [23], oral care needs [24], difficult airway management [25], type 2 diabetes mellitus needs [26], and problems accessing health services or treatments [27, 28]. Unmet needs have been recognized regarding targeted treatments for hunger, hyperphagia and obesity [29]. An unmet need can be defined as "difficulties receiving service in response to problems that significantly interfere with daily life" [30]. Adults with BBS might, for example, experience a need for physical activities to achieve weight loss before kidney transplantation but do not meet understanding for their obesity as one of the core features of BBS. The relationship between needs and health status in BBS needs to be better understood to address the unmet needs within the context of health status in order to improve healthcare. Despite the impact of BBS on the daily lives of individuals, to

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

the best of our knowledge, no research has documented their unmet needs for healthcare or the support they need. This study aimed to determine healthcare needs and care use in adults with BBS in Norway and associations between care use and physical functioning, health status outcomes and distress.

Methods

Participants

This study was performed to offer inclusion of all adults with BBS in Norway. Eligible individuals were recruited through a register at the Centre for Rare Disorders, Oslo University Hospital, Norway, and by advertisement on the Norwegian BBS Organization's webpage. The inclusion criteria were: (1) a clinical and/or genetic diagnosis of BBS; (2) ≥ 16 years of age; (3) residence in Norway; and (4) adequate knowledge of Norwegian for communication and understanding the questionnaires. The exclusion criterion was not having BBS. A clinical diagnosis meant fulfilling clinical criteria for Bardet-Biedl syndrome as outlined in Forsythe and Beales [17]. Informed consent was to be obtained from all participants prior to inclusion. Norway had a population of around 5.5 million individuals in 2022. The national resource centre for BBS had 46 adults registered and the Norwegian BBS Organization had approximately 50 members. Based on this information, half the number of adults with BBS was estimated to participate, that is 25 individuals.

Study design and data collection

This study was designed as a cross-sectional study and was conducted at the level of specialized healthcare in Norway from January 2022 to March 2023. Data were collected at the Oslo University Hospital and Lovisenberg Diaconal Hospital, Oslo, Norway. An eye examination was performed by an ophthalmologist (author RB). Clinical examinations and interviews were

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

conducted with a physician (author CFR or CvdL), including measuring height and weight and calculating body mass index (BMI = kg/m^2). The questionnaires were read aloud by one of the clinicians and answered orally, and a physical performance test was undertaken. These questionnaires and measures are described below. The oral health examinations were performed by a dentist and a speech and language pathologist (authors HN and PMÅ) at the National Resource Centre for Oral Health in Rare Disorders, Lovisenberg Diaconal Hospital, Oslo, Norway. The general flow of the examinations over a one-day visit included eye examinations, clinical examinations and interviews, questionnaires, physical performance tests, and, finally, oral health examinations.

Patient and public involvement statement

Two members of the Norwegian organization for BBS were closely involved in the planning of this study and were consulted to identify relevant research topics of interest to the organization. Both members were asked to test out the questionnaires.

Ethics

The study, registered at ClinicalTrials.gov, NCT05400278, was approved by the Regional Committee for Medical Research Ethics South East Norway (number 166639) and performed according to ethical guidelines [31].

Measurements

Demographics and clinical information

Demographic information was based on self-reports from participants. Information was collected regarding gender, age at diagnosis, education, employment, medical comorbidities and prior lifetime contact (yes, no) with health institutions (e.g., child and youth psychiatry,

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

services within education and psychology, district psychiatry, child habilitation, and national service for special needs education). Education was defined as high school or less (13 years or less) or more than 13 years of education. Employment, including paid full-time (100% employment), part-time (<100% employment), or self-employment, was classified as 'employed'. Any type of unpaid work, e.g., unemployed, support at the workplace, retirement, disability benefits, or home workers, was classified as 'unemployed'. In general, height and weight measurements were performed using a Seca 704 s (Seca GmbH & co. KG., Hamburg, Germany). Obesity was assessed by body mass index (BMI). BMI was calculated from the participants' height and body weight (BMI = kg/m^2). A BMI between 18.5 kg/m^2 and 25 kg/m^2 was considered normal weight, a BMI above 25 kg/m^2 but less than 30 kg/m^2 was considered overweight, and a BMI above 30 kg/m^2 was considered obese [32]. Renal disease included prenatally described kidney abnormalities, kidney tumours, increased kidney blood parameters, any stage of kidney failure or having had a kidney transplant. High blood pressure included measured systolic blood pressure above 140 mmHg, diastolic pressure above 90 mmHg and/or treatment with blood pressure-reducing medication. Diagnosis of diabetes mellitus was registered and/or medications for diabetes (yes/no). Oral/dental abnormalities (yes/no) were assessed by a dentist and included e.g., overbite, overjet, open bite, crowding of teeth, small teeth.

Needs for healthcare and social services

The Needs and Provision Complexity Scale (NPCS) [33] was used to evaluate the level of unmet needs for healthcare and social services. The NPCS was developed in the UK to identify healthcare and social support needs among individuals with neurological conditions [33]. It has been translated and recently validated in Norway [34, 35] and used in several populations, including individuals with Huntington's disease [34, 36], traumatic brain injuries [37] and

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

myotonic dystrophy [38]. The NPCS has not previously been used in adults with BBS. In this study, we used the Norwegian version 1.0. The NPCS has two parts: Part A (Needs, what the individual needs) was completed by two clinicians (authors CFR and SS) to evaluate each participant's needs for health and social care, and Part B (Gets, what the individual gets) was recorded by the clinician based on the information provided by the participants with BBS to evaluate care use (provision of healthcare). The NPCS has a total score ranging from 0–50 and contains five domains, which are scored as follows: healthcare scored from 0–6, personal care scored from 0–10, rehabilitation scored from 0–9, social and family support scored from 0–13 and environment scored from 0–12. The NPCS includes 15 items, which are scored according to highest level applicable as follows: medical care needs (0–3); skilled nursing needs (0–3); number of carers (0–2); care frequency (0–5); personal assistant/enabler (0–3); therapy disciplines (0–3); therapy intensity (0–3); vocational support/rehabilitation (0–3); social work case management (0–3); family carer support (0–3); respite residentially (0–3); respite as day care (0–2); advocacy (0–2); equipment (0–3); and accommodation (0–9). Higher scores indicate higher levels of needs. The total Needs score is the number of scores added together for the needs items. The total Gets score is the number of scores added together for the gets items. The total NPCS score is either the total score for Needs or the total score for Gets. Unmet Needs (Needs-Gets) were calculated for the total scores and the five domain scores. The percentage of participants needing the services (NPCS items) was converted to a binary variable (0 = no unmet need, 1 = unmet need) [33]. The Norwegian version of the NPCS has excellent interrater reliability for the total scores of the NPCS-Needs and the NPCS-Gets, with values of 0.911 and 0.987, respectively [35].

Physical performance evaluation

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

The Short Physical Performance Battery (SPPB) is a group of measures that combines the results of a 4.0 metre walking test at a normal pace (walking test), five-times rising from a chair as fast as possible (sit-to-stand test) and a standing balance test in a two-legged stance [39]. In this study, the SPPB was used to evaluate physical performance according to the standard guided procedure [39]. Each test was scored from 0 to 4, and the total score ranged from 0 to 12. A higher SPPB score signifies better physical performance. In the current study, the SPPB mean scores were compared to the mean normative scores in adults aged > 40 years from a Norwegian population-based study [40].

Self-reported health status

The EQ-5D-5L is a self-reported measure that is used to evaluate general health status. The EQ-5D-5L includes a visual analogue scale (EQ VAS) with scores ranging from 0 (the worst health you can imagine) to 100 (the best health you can imagine). Permission to use the EQ-5D-5L was obtained from the EuroQoL Group, and the Norwegian version was used [41]. The visual analogue scale was explained orally to each participant because of their reduced vision, and they were asked to rate their perceived health on the day of testing. The EQ-5D-5L consists of five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain has five levels ranging from 1 (no problems) to 5 (extreme problems/unable to). In this study, descriptive levels of each dimension were dichotomized to “no problems” (level one) or “any problems” (levels two to five) and compared to the Norwegian normative population [42]. Furthermore, the EQ-5D-5L index values, ranging from 0 (dead) to 1 (full health), were calculated based on the UK value set used in Norway [42].

Self-reported psychological distress

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

The Hospital Anxiety and Depression Scale (HADS) was used to assess symptoms of anxiety and depression within the last seven days [43]. The HADS includes an anxiety scale and a depression scale, each with seven items. Each item is scored on a 4-point scale, with the total scores for anxiety and depression ranging from 0 (best) to 21 (worst). A HADS score > 7 points was used to identify individuals with symptoms of anxiety or depression [44]. The HADS mean scores were compared to the mean Norwegian population scores from the HUNT-4 study [45].

Statistical analysis

Descriptions of the participants and questionnaires are provided with descriptive statistics, including means, medians and percentages. Shapiro–Wilk tests were performed to assess continuous data for normality. The NPCS domains, the EQ-5D-5L index score and the HADS score were not normally distributed, and these data were summarized as medians and interquartile ranges (IQRs). The mean and standard deviation (±SD) were also given for the NPCS to allow comparisons with previous studies. The chi-square test was used for the differences between categorical variables. Comparisons between normally distributed continuous variables were performed with Student's *t* test, whereas the Mann–Whitney U test was used for nonparametric variables. The Wilcoxon signed rank test for non-normally distributed variables was chosen to explore pairwise differences between the NPCS "Needs" and "Gets". Kendall's tau-b correlation coefficient (τ) was used to evaluate bivariate correlations between age, kidney disease, high blood pressure, obesity, the HADS subscales, the SPPB total score and the five domains of EQ-5D-5L with the five NPCS Gets subscales, with 1000 bootstrapped samples. All p values < 0.05 derived from two-sided tests were considered statistically significant. Because this study is observational with a small sample size, Bonferroni correction was not used, as it may overcorrect and increase the risk of type 2 error.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Statistical tests were conducted in SPSS, version 29.0 (SPSS Statistics, IBM Corporation, Chicago, IL).

Results

Study sample characteristics

Forty-six individuals were invited to participate. One person died shortly after the invitations were sent out, and one was excluded because of not having BBS. Thirty individuals participated in this study, a response rate of 68% (30/44). When those who consented to participate (n=30) and nonparticipants (n=14) were compared, no differences in age (p=0.660) or sex (p=0.88) were identified.

Table 1 shows the characteristics of the 30 adult participants (mean age (± SD) 39.8 ± 13.6, age range 20–69 years, 50% females). No sex differences were observed in any of the demographics (not shown). Overall, 17% of the participants were employed, either full- or part-time, one had retired, and the majority (80%) were receiving disability benefits. Four participants were offered the option of a home visit because they were unable to travel, they did not have an ophthalmology or oral exam.

All participants had retinal dystrophy (including self-reports from the four home visits), and 93% were overweight or obese (BMI above 25 kg/m^2). Oral/dental abnormalities were more common in males than in females. Almost two-thirds had high blood pressure, 27% had renal disease, and 23% were diagnosed with type 2 diabetes. Four individuals had both renal disease and type 2 diabetes. The need for mental health services during childhood was reported by 20% of the participants, and 70 % had been followed by educational-psychological services in the school system. Moreover, 13% reported follow-ups with psychiatric services during adulthood. The data for the NPCS are summarized in table 1. The median overall score for the NPCS (Needs) was 17.0 (IQR=8), and for the NPCS (Gets), it was 12.0 (IQR=6).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

273

274 Table 1. Demographics and characteristics of adults with Bardet-Biedl syndrome (*n*=30)

	Total
Males	15 (50)
Age at inclusion ǂ	39.8 (13.6)
Age diagnosed with BBS #	9 (13.5)
Marital status single	26 (87 %)
Living independently or with a spouse or partner	18 (60%)
Living with parents or in care home	12 (40%)
Education (≤13 years)	27 (90%)
Employed (full time, part time)	5 (17 %)
Disability benefits (full time)	24 (80 %)
Body mass index	37.9 (11.1)
Overweight or obesity	28 (93 %)
Retinal dystrophy*	30 (100 %)
Oral/dental abnormalities (*n*=26)	20 (77 %)
Renal disease	8 (27 %)
High blood pressure	20 (67 %)
Diabetes	7 (23 %)
Child mental health service	6 (20 %)
Educational-psychological service	21 (70 %)
Adult mental health clinic	4 (13%)
Needs and Provision Complexity Scale #	
Clinical version (Part A **Needs**)	
Total Needs score (score 0-50)	17.0 (8)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Healthcare (score 0-6)	2.0 (1)
Personal care (score 0-10)	5.0 (3)
Rehabilitation (score 0-9)	5.0 (3)
Social and family support (score 0-13)	1.5 (2)
Environment (score 0-12)	4.5 (3)
Patient version (Part B **Gets**)	
Total Needs score (score 0-50)	12.0 (6)
Healthcare (score 0-6)	2.0 (2)
Personal care (score 0-10)	3.0 (4)
Rehabilitation (score 0-9)	3.0 (2)
Social and family support (score 0-13)	0.0 (2)
Environment (score 0-12)	3.0 (3)

Notes.

ǂ Scores presented as mean (±SD). # Scores presented as median (IQR).

Discrete variables presented as number (percentages).

* Including self-reported retinal dystrophy in four individuals.

Needs indicates that adults with BBS need this health service.

Gets indicate that adults receive this health service (provision).

Unmet needs

As shown in Table 2, clinicians (Needs) scored higher on all five domains compared to self-rated (Gets) scores. The Wilcoxon signed rank sum test confirmed the presence of significantly different pairwise comparisons between the measures of clinicians (NPCS Needs) compared with those of self-reports (NPCS Gets) (total: ($p < 0.001$); Healthcare: ($p = 0.002$); Personal care: ($p = 0.001$); Rehabilitation: ($p < 0.001$); Social and family support: ($p < 0.001$); and

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Environment; (p = 0.002); see Table 2). Most participants (97%) were found to have unmet needs. The majority had unmet needs for rehabilitation (83%), followed by unmet social and family support needs (63%), healthcare needs (50%), personal care needs (47%) and environmental needs (40%).

Table 2. Differences between health service needs (Part A) and gets (Part B) according to the Needs and Provision Complexity Scale (n = 30)

	Needs - Gets Median (IQR) / (range)	**Unmet Needs #** *n* (%)
Total NPCS (score 0-50)	4.0 (4.3) / (0-16)**	29/30 (97 %)
Healthcare (score 0-6)	0.5 (1) / (-1-2)*	15/30 (50 %)
Personal care (score 0-10)	0.0 (2) / (-1-5)*	14/30 (47 %)
Rehabilitation (score 0-9)	2.0 (2) / (0-8)**	25/30 (83 %)
Social and family support (score 0-13)	1.0 (1.3) / (-1-4)**	19/30 (63 %)
Environment (score 0-12)	0.0 (1) / (0-4)*	12/30 (40 %)

Notes.

Needs indicates that adults with BBS need this health service.

Gets indicate that adults receive this health service (provision).

Unmet needs are the difference between Needs and Gets.

Proportion of participants with a higher score on the NPCS Needs than the NPCS Gets.

* $p < 0.01$, ** $p < 0.001$ with the Wilcoxon signed rank test.

Figure 1 illustrates the proportions of unmet needs across all 15 items of the NPCS, using the binary variable described in the methods. Between 50% and 77% of the participants were found to have insufficient professional healthcare (e.g., medical care, social workers, physiotherapists, psychologists, occupational therapists, dieticians, and dentists).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

---Insert Figure 1 here---

Differences in outcome measures of health status, distress and physical performance

Table 3 presents the results for the EQ-5D-5L, HADS and SPPB in comparison with normative data, using online calculators for two sample *t*-tests and Chi-square tests. The BBS population reported significantly more health problems (EQ-5D-5L) in terms of mobility, self-care, and usual activities as well as significantly lower levels of general health (all $p < 0.001$) than the general Norwegian population [42]. The BBS population reported significantly lower scores (i.e., better mental health) on the three HADS scales ($p< 0.05$) than the adult population in the HUNT-4 study [45]. The HUNT-4 study has published data on the HADS and is considered representative of health problems of the total adult population in Norway [46]. Notably, four adults with BBS (13%) were identified as having potential anxiety (score > 7), and only one individual (3%) had potential depression (score > 7). Finally, significant differences ($p < 0.001$) were found for comparisons on levels of physical performance, the general population had much higher levels of physical functioning [40].

Notably, two participants with BBS were unable to perform the SPPB test because they were unable to stand without support and were therefore given a total score of zero.

Table 3. Comparisons for outcome measures (EQ-5D-5L, HADS, SPPB) for the BBS population (n = 30) and the Norwegian normative data

	BBS (n=30)	Normative data	p
EQ-5D-5L domains	**Any problems, n (%)**	**Any problems, n (%)** #	

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Mobility	16 (53 %)	562 (18.0 %) n=3120	< 0.001
Self-care	7 (23 %)	227 (7.3 %) n=3120	< 0.001
Usual activities	16 (53 %)	756 (24.2 %) n=3120	< 0.001
Pain / Discomfort	19 (63 %)	1937 (62.1 %) n=3120	0.888
Anxiety / Depression	13 (43 %)	1104 (35.4 %) n=3120	0.365
	BBS mean (SD)	**Expected mean (SD)** #	
EQ-5D-5L VAS scale (score 0-100)	63.8 (21.5)	77.9 (18.3) n=3120	< 0.001
EQ-5D-5L index score (score 0-1)	0.79 (0.18)	0.81 (0.20) n=3120	0.585
	BBS mean (SD)	**Expected mean (SD)** ǂ	
HADS-Total score	5.00 (6.01)	7.68 (5.66) n=40,648	< 0.01
HADS-Anxiety	3.13 (3.90)	4.40 (3.46) n=41,133	0.04
HADS Depression	1.87 (2.62)	3.30 (2.96) n=39,573	< 0.01
	BBS mean (SD)	**Expected mean (SD)** ≠	
SPPB-Total score	6.7 (3.5)	11.4 (1.3) n=7474	< 0.001

Notes.

Abbreviations: BBS = Bardet-Biedl syndrome; VAS = Visual Analogue Scale.; HADS = Hospital Anxiety and Depression Scale; SPPB = Short Physical Performance Battery

Comparisons between our BBS population and the general Norwegian population were conducted using online calculators for two sample *t*-tests and Chi-square tests.

Derived from Garratt et al. (2022) [42].

ǂ Derived from HUNT-4 study [45].

≠ Derived from Bergland et al. (2019) [40].

Correlations between care use (NPCS Gets) and health status outcomes

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

The Healthcare subscale of the NPCS (Table 4) was correlated with having more problems with usual activities (τ = .41, p = 0.01). The Personal Care subscale was correlated with worse physical performance (τ = -.34, p = < 0.01) and having more problems with self-care (τ = .47, p < 0.01). The correlation analyses revealed no associations between the provision of Rehabilitation, Social/family support and Environment with any of the health status outcomes.

Table 4. Correlation analysis between NPCS (Gets), HADS, SPPB and EQ-5D-5L and demographics in the total sample (n = 30)

	Healthcare	**Personal care**	**Rehabilitation**	**Social/ family support**	**Environment**
	τ	τ	τ	τ	τ
Age	.27	.10	.15	.01	-.21
Kidney disease (0=no, 1=yes)	.27	-.10	-.16	-.17	-.24
High blood pressure (0=no, 1=yes)	.27	.21	.04	-.14	.17
BMI	.09	.15	-.21	-.13	.18
HADS Anxiety	-.20	.10	.16	-.03	-.11
HADS Depression	-.21	.14	.04	.05	-.14
SPPB Total score	-.20	-.34*	-.09	-.24	-.05
EQ-5D-5L Mobility	.28	.07	-.12	.03	-.14
EQ-5D-5L Self-care	.14	.47**	.14	.21	.22
EQ-5D-5L Usual activity	.41*	.21	.02	.12	-.17
EQ-5D-5L Pain / Discomfort	.21	-.03	-.28	.01	-.11
EQ-5D-5L Anxiety / Depression	-.08	.25	.08	.09	-.10

Notes.

Abbreviations: NPCS = Needs and Provision Complexity Scale; HADS = Hospital Anxiety and Depression Scale; SPPB = Short Physical Performance Battery.

Correlation calculated with Kendall's tau beta correlation coefficient (τ). Bootstrapping with 1000-samples.

* p < 0.05; ** p < 0.01

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

Discussion

This study focused on the healthcare needs of adults with BBS in Norway. In this nationally representative cross-sectional study, we found that a substantial proportion of adults with BBS who need supportive health services do not receive such services. Significant discrepancies were identified between needs (clinicians' ratings) and gets (participants' ratings), indicating that a majority had unmet needs related to the domains of health and personal care as well as social and supportive care. Several key findings are noteworthy. First, rehabilitation needs were rated as the greatest unmet needs overall. This demonstrates that rehabilitation is a key need identified in this rare disorder and should be considered a central part of health care delivery for BBS. Due to the obesity problems in BBS, and in particular higher risk of high blood pressure, diabetes and kidney failure, people with BBS need to have access to assessment of rehabilitation needs. Compared with the general population [40], adults with BBS had significantly lower levels of physical functioning on objective tests. This indicates that training is an area of need and multidisciplinary care services working jointly with physical therapists could make the difference to better BBS-related outcomes, as addressed in other studies (16, 18).

Second, higher levels of medical healthcare and personal care services (care gets) were significantly and meaningfully correlated with greater difficulty with physical balance (SPPB), self-care and usual activities (EQ-5D-5L). This may indicate that healthcare services were able to meet the individual needs and that the adults with BBS received help for the identified difficulties with physical functioning, self-care and usual activities. Problems with mobility and usual activities (EQ-5D-5L) were reported in just over half of the participants and statistically more often than in the general Norwegian population [42]. However, adults with BBS had less distress (anxiety, depression) compared to the normative data. It may be that adults with BBS

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

have resources to address their mental problems (e.g., family members, personal assistant) contributing to less psychological needs, but these were not addressed in our study.

Third, no significant correlation was identified between the most prevalent unmet needs (i.e., rehabilitation and social/family support) and the disease-related and self-reported variables (kidney, high blood pressure, BMI, physical functioning, HADS, EQ-5D-5L). For adults with BBS experiencing disease progression (e.g., kidney, vision, obesity) and chronicity of the condition, considerable unmet needs are to be expected. Therefore, we speculate that the relationship of health services (gets) and the complexity of BBS if difficult to detect in a small sample. To overcome this limitation, larger studies could help address the unique rehabilitation needs and the unmet health needs in BBS. Given that people with BBS may underestimate the rehabilitation needs, future studies should combine clinical assessments, objective tests and self-reports.

Many of the health issues presented in our study could be addressed in a multidisciplinary team setting by relevant professionals, e.g., physicians, physical therapists, social workers, ophthalmologists, dentists, registered dietitians and psychologists; however, none of the participants taking part in this study received such services. A consensus statement study recommended that people with BBS had lifelong follow-ups, treatments for neurological and endocrinological diseases as well as rehabilitation sessions for visual handicap [47]. Present study builds on earlier studies of rare diseases, showing a need for supportive care in a broad range of domains and unmet needs in primary health care [2, 11, 48]. The BBS-related health problems represent broad types of healthcare needs and require multidisciplinary interventions in addition to pharmacological treatments (e.g., blood pressure, diabetes, obesity). Therefore, ensuring the delivery of healthcare and preventative measures to people diagnosed with BBS is important.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

BBS lacks pathognomonic signs or symptoms at birth or later, which, combined with a lack of knowledge about BBS, might cause diagnostic delay [16, 49]. The age at diagnosis was 9 years in the present study, and the majority of participants had been in contact with educational-psychological services during childhood. Furthermore, 20% of the participants had been referred to child and adolescent mental health services, indicating that children with BBS need treatment for their mental and/or behavioural problems. This finding highlights the importance of early disease intervention. Increased accessibility of genetic testing today may reduce the age at diagnosis compared with when our participants were diagnosed several decades ago.

Only 17% of adults with BBS were employed, which is notably lower than the rate reported in people with various eye diseases (44%) in Norway [50] and lower than the work participation in rare diseases (55%) reported in a recent scoping review [51]. The complexity of BBS makes it difficult to pinpoint the exact reasons for unemployment. Our findings may be limited because the analyses were exploratory and based on a small sample, and further research is needed to evaluate this in more detail. Complex conditions such as BBS with reduced vision, possible cognitive challenges and obesity pose difficulties to the working environment, which needs to be addressed to improve work participation.

The strengths of this study are the high response rate (68%). Also, this sample of responders appears to be largely representative of adults with BBS in the country (Norway). Evaluations were performed by a multidisciplinary research team, including different healthcare professionals working in hospitals and resource centres for rare conditions in Norway. This study could subsequently contribute to increasing awareness of BBS among professionals working in primary care but also in mental health and specialist health services, where treatments may be administered. No previous study has focused on describing healthcare needs and the provision of and access to healthcare in BBS. Based on present findings, substantial

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

physical and social healthcare needs are currently not addressed, and this study can serve as a starting point for future research on BBS or other rare diseases.

The small sample size may be considered a limitation because it significantly reduces the statistical power. The data were self-reported, which might have resulted in participants underestimating their problems because of a lack of self-awareness or having cognitive difficulties understanding the questions. Because individuals under 16 years of age were excluded, the study has limited generalizability to children. In addition, adults with BBS who did not participate in this study might have other healthcare needs. The cross-sectional design limits the assessments of longitudinal changes and causal associations between healthcare use (gets) and health outcomes.

Conclusions

Adults with BBS were found to have unmet physical, social and medical needs, which may contribute to health concerns. Rehabilitation needs were the greatest unmet needs and require special attention. Difficulties with physical functioning, self-care and usual activities were related with access to health services, indicating that the services were able to meet these needs. Given the complexity and heterogeneity of BBS, effective management requires a multidisciplinary approach that focuses not only on medical follow-up but also on functional mobility and social care to provide optimal personalized care and rehabilitation for all individuals with BBS.

Acknowledgement

The research team is deeply grateful to all the individuals with Bardet-Biedl syndrome for their time and investment in taking part in this study. We would like to thank the two

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

representatives of the Norwegian Organization for Bardet-Biedl syndrome for their involvement: Richard Ødegaard and Lill Susann Lerudsmoen.

Funding

This study was supported by grants from Raagholtstiftelsen in Norway (to Solrun Sigurdardottir).

Author contributions

All the authors meet the criteria for authorship stated in the requirements for manuscript submitted to BMJ Open and all four ICJME criteria. In particular, the authors' contributions to the manuscript were as follows: conceptualization and methodology: all the authors. Formal data analyses and writing of the original draft: CFR, SS. Supervision: SS, CvdL, RB. Review of the manuscript and editing and validation of the final text: all the authors. SS is the guarantor.

Competing interests

Solrun Sigurdardottir has received speaker fees from Sanofi. The other authors have no competing interests to declare.

Availability of data and materials

Norwegian ethical and legal restrictions prevent the authors from uploading or sharing data with public repositories. Individuals with Bardet–Biedl syndrome in Norway belong to a relatively small group, and very little personal data are needed to indirectly identify individual study participants.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Ethics approval and consent to participate

The Norwegian Regional Committee for Medical Research Ethics in Southeast Norway (number 166639) and the Data Protection officer at Oslo University Hospital (number 20/21045) approved the study. Written informed consent was obtained from all the included individuals.

Figure title

Figure 1. Percentage of unmet and met needs of the 15 items of the Needs and Provision Complexity Scale.

Figure 1. Notes. HC = Healthcare domain; PC = Personal care domain; REH = Rehabilitation domain; SF = Social and family support domain; E = Environment domain.

References

1. Austin CP, Cutillo CM, Lau LPL, Jonker AH, Rath A, Julkowska D, et al. Future of Rare Diseases Research 2017-2027: An IRDiRC Perspective. Clin Transl Sci. 2018;11(1):21-7.
2. Long JC, Best S, Nic Giolla Easpaig B, Hatem S, Fehlberg Z, Christodoulou J, et al. Needs of people with rare diseases that can be supported by electronic resources: a scoping review. BMJ Open. 2022;12(9):e060394.
3. Haendel M, Vasilevsky N, Unni D, Bologa C, Harris N, Rehm H, et al. How many rare diseases are there? Nat Rev Drug Discov. 2020;19(2):77-8.
4. products. UERENotEPaotCoDoom. 2000.
5. Ferreira CR. The burden of rare diseases. Am J Med Genet A. 2019;179(6):885-92.
6. Chung CCY, Hong Kong Genome P, Chu ATW, Chung BHY. Rare disease emerging as a global public health priority. Front Public Health. 2022;10:1028545.
7. Evans WR, Rafi I. Rare diseases in general practice: recognising the zebras among the horses. Br J Gen Pract. 2016;66(652):550-1.
8. Vandeborne L, van Overbeeke E, Dooms M, De Beleyr B, Huys I. Information needs of physicians regarding the diagnosis of rare diseases: a questionnaire-based study in Belgium. Orphanet J Rare Dis. 2019;14(1):99.
9. Fredwall S, Allum Y, AlSayed M, Alves I, Ben-Omran T, Boero S, et al. Optimising care and follow-up of adults with achondroplasia. Orphanet J Rare Dis. 2022;17(1):318.
10. Groft SC, Posada M, Taruscio D. Progress, challenges and global approaches to rare diseases. Acta Paediatr. 2021;110(10):2711-6.
11. Depping MK, Uhlenbusch N, von Kodolitsch Y, Klose HFE, Mautner VF, Lowe B. Supportive care needs of patients with rare chronic diseases: multi-method, cross-sectional study. Orphanet J Rare Dis. 2021;16(1):44.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

12. Zelihic D, Hjardemaal FR, Lippe CV. Caring for a child with Bardet-Biedl syndrome: A qualitative study of the parental experiences of daily coping and support. Eur J Med Genet. 2020;63(4):103856.
13. Pelentsov LJ, Fielder AL, Laws TA, Esterman AJ. The supportive care needs of parents with a child with a rare disease: results of an online survey. BMC Fam Pract. 2016;17:88.
14. Benito-Lozano J, Arias-Merino G, Gomez-Martinez M, Ancochea-Diaz A, Aparicio-Garcia A, Posada de la Paz M, et al. Diagnostic Process in Rare Diseases: Determinants Associated with Diagnostic Delay. Int J Environ Res Public Health. 2022;19(11).
15. Chandra B, Tung ML, Hsu Y, Scheetz T, Sheffield VC. Retinal ciliopathies through the lens of Bardet-Biedl Syndrome: Past, present and future. Prog Retin Eye Res. 2022;89:101035.
16. Forsythe E, Kenny J, Bacchelli C, Beales PL. Managing Bardet-Biedl Syndrome-Now and in the Future. Front Pediatr. 2018;6:23.
17. Forsythe E, Beales PL. Bardet-Biedl syndrome. Eur J Hum Genet. 2013;21(1):8-13.
18. Kenny J, Forsythe E, Beales P, Bacchelli C. Toward personalized medicine in Bardet-Biedl syndrome. Per Med. 2017;14(5):447-56.
19. Meyer JR, Krentz AD, Berg RL, Richardson JG, Pomeroy J, Hebbring SJ, et al. Kidney failure in Bardet–Biedl syndrome. Clin Genet. 2022;101(4):429-41.
20. Tomlinson JW. Bardet-Biedl syndrome: A focus on genetics, mechanisms and metabolic dysfunction. Diabetes Obes Metab. 2024.
21. Forsythe E, Haws RM, Argente J, Beales P, Martos-Moreno GA, Dollfus H, et al. Quality of life improvements following one year of setmelanotide in children and adult patients with Bardet-Biedl syndrome: phase 3 trial results. Orphanet J Rare Dis. 2023;18(1):12.
22. Melluso A, Secondulfo F, Capolongo G, Capasso G, Zacchia M. Bardet-Biedl Syndrome: Current Perspectives and Clinical Outlook. Ther Clin Risk Manag. 2023;19:115-32.
23. Denniston AK, Beales PL, Tomlins PJ, Good P, Langford M, Foggensteiner L, et al. Evaluation of visual function and needs in adult patients with bardet-biedl syndrome. Retina. 2014;34(11):2282-9.
24. Panny A, Glurich I, Haws RM, Acharya A. Oral and Craniofacial Anomalies of Bardet-Biedl Syndrome: Dental Management in the Context of a Rare Disease. J Dent Res. 2017;96(12):1361-9.
25. Smith BB, Barbara DW, Hyder JA, Smith MM. Anesthetic considerations for patients with Bardet-Biedl syndrome: a case series and review of the literature. Paediatr Anaesth. 2016;26(4):429-37.
26. Pomeroy J, Krentz AD, Richardson JG, Berg RL, VanWormer JJ, Haws RM. Bardet-Biedl syndrome: Weight patterns and genetics in a rare obesity syndrome. Pediatr Obes. 2021;16(2):e12703.
27. Mujahid S, Hunt KF, Cheah YS, Forsythe E, Hazlehurst JM, Sparks K, et al. The Endocrine and Metabolic Characteristics of a Large Bardet-Biedl Syndrome Clinic Population. J Clin Endocrinol Metab. 2018;103(5):1834-41.
28. Keifer E, Berg RL, Richardson JG, Haws RM. Early development and adaptive functioning in children with Bardet-Biedl syndrome. Am J Med Genet A. 2024;194(1):31-8.
29. Forsythe E, Mallya UG, Yang M, Huber C, Cala ML, Greatsinger A, et al. Burden of hyperphagia and obesity in Bardet-Biedl syndrome: a multicountry survey. Orphanet J Rare Dis. 2023;18(1):182.
30. McColl MA, Shortt S, Gignac M, Lam M. Disentangling the effects of disability and age on health service utilisation. Disabil Rehabil. 2011;33(13-14):1253-61.
31. World Medical A. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191-4.
32. Moyer VA, Force USPST. Screening for and management of obesity in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2012;157(5):373-8.
33. Turner-Stokes L, McCrone P, Jackson DM, Siegert RJ. The Needs and Provision Complexity Scale: a multicentre prospective cohort analysis of met and unmet needs and their cost implications for patients with complex neurological disability. BMJ Open. 2013;3(2).

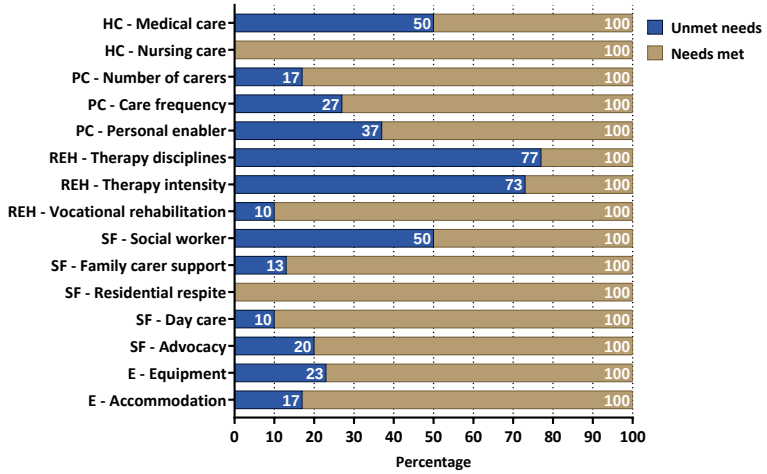
For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

34. van Walsem MR, Howe EI, Iversen K, Frich JC, Andelic N. Unmet needs for healthcare and social support services in patients with Huntington's disease: a cross-sectional population-based study. Orphanet J Rare Dis. 2015;10:124.
35. Forslund MV, Borgen IMH, Karic T, Kleffelgard I, Hauger SL, Lovstad M, et al. Validity of the Norwegian Version of the Needs and Provision Complexity Scale (NPCS) in Patients with Traumatic Brain Injury and Atraumatic Subarachnoid Hemorrhage. J Clin Med. 2024;13(3).
36. van Walsem MR, Howe EI, Ruud GA, Frich JC, Andelic N. Health-related quality of life and unmet healthcare needs in Huntington's disease. Health Qual Life Outcomes. 2017;15(1):6.
37. Laurie K, Foster MM, Borg DN, Gustafsson L. Perceived service adequacy and unmet need after discharge from brain injury rehabilitation. Disabil Rehabil. 2023;45(20):3252-61.
38. Holmoy AKT, Johannessen CH, Hope S, van Walsem MR, Aanonsen NO, Hassel B. Uncovering health and social care needs among myotonic dystrophy patients: Utility of the Needs and Provisions Complexity Scale. Acta Neurol Scand. 2019;139(6):526-32.
39. Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir GV, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci. 2000;55(4):M221-31.
40. Bergland A, Strand BH. Norwegian reference values for the Short Physical Performance Battery (SPPB): the Tromso Study. BMC Geriatr. 2019;19(1):216.
41. Nord E. EuroQol: health-related quality of life measurement. Valuations of health states by the general public in Norway. Health Policy. 1991;18(1):25-36.
42. Garratt AM, Hansen TM, Augestad LA, Rand K, Stavem K. Norwegian population norms for the EQ-5D-5L: results from a general population survey. Qual Life Res. 2022;31(2):517-26.
43. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res. 2002;52(2):69-77.
44. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361-70.
45. Forskningssenter H. HUNT Databank 2025 [Available from: https://hunt-db.medisin.ntnu.no/hunt-db/#variable/7259.
46. Asvold BO, Langhammer A, Rehn TA, Kjelvik G, Grontvedt TV, Sorgjerd EP, et al. Cohort Profile Update: The HUNT Study, Norway. Int J Epidemiol. 2023;52(1):e80-e91.
47. Dollfus H, Lilien MR, Maffei P, Verloes A, Muller J, Bacci GM, et al. Bardet-Biedl syndrome improved diagnosis criteria and management: Inter European Reference Networks consensus statement and recommendations. Eur J Hum Genet. 2024.
48. Bogart K, Hemmesch A, Barnes E, Blissenbach T, Beisang A, Engel P, et al. Healthcare access, satisfaction, and health-related quality of life among children and adults with rare diseases. Orphanet J Rare Dis. 2022;17(1):196.
49. Berezovsky A, Rocha DM, Sacai PY, Watanabe SS, Cavascan NN, Salomao SR. Visual acuity and retinal function in patients with Bardet-Biedl syndrome. Clinics (Sao Paulo). 2012;67(2):145-9.
50. Brunes A, Heir T. Visual impairment and employment in Norway. BMC Public Health. 2022;22(1):648.
51. Velvin G, Dammann B, Haagensen T, Johansen H, Stromme H, Geirdal AO, et al. Work participation in adults with rare genetic diseases - a scoping review. BMC Public Health. 2023;23(1):910.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .



bmjopen-2024-095986 on 22 April 2025. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . d by copyright, including for uses related to text and data mining, AI training, and similar technologies.

er review only

BMJ Open

Healthcare needs, care use, and health status outcomes in adults with Bardet–Biedl syndrome: a cross-sectional study in Norway

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-095986.R2
Article Type:	Original research
Date Submitted by the Author:	02-Apr-2025
Complete List of Authors:	Rustad, Cecilie Fremstad; Oslo University Hospital, Centre for Rare Disorders; University of Oslo, The Medical faculty Bragadottir, Ragnheidur; University of Oslo; Oslo University Hospital, Department of Ophthalmology Nordgarden, Hilde; Lovisenberg Diakonale Hospital, National Resource Centre for Oral Health in Rare Disorders Miller, Jeanette Ullmann; Oslo University Hospital, Centre for Rare Disorders Weedon-Fekjær, Mina ; Oslo University Hospital, Centre for Rare Disorders Arfa, Shahrzad; Oslo University Hospital, Centre for Rare Disorders Åsten, Pamela ; Lovisenberg Diakonale Hospital, National Resource Centre for Oral Health in Rare Disorders Tveten, Kristian; Telemark Hospital, Department of Medical Genetics von der Lippe, Charlotte; Telemark Hospital, Department of Medical Genetics Sigurdardottir, Solrun; Oslo University Hospital, Centre for Rare Disorders
Primary Subject Heading:	Patient-centred medicine
Secondary Subject Heading:	Genetics and genomics, Diabetes and endocrinology, General practice / Family practice, Health services research, Medical management
Keywords:	Quality of Life, Obesity, Disabled Persons, Health Services

SCHOLARONE™
Manuscripts

BMJ Open: first published as 10.1136/bmjopen-2024-095986 on 22 April 2025. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Healthcare needs, care use, and health status outcomes in adults with Bardet–Biedl syndrome: a cross-sectional study in Norway

Cecilie Fremstad Rustad[1,2], Ragnheidur Bragadottir[2,3], Hilde Nordgarden[4], Jeanette Ullmann Miller[1], Mina Susanne Weedon-Fekjær[1], Shahrzad Arfa[1], Pamela Marika Åsten[4], Kristian Tveten[5], Charlotte von der Lippe[5], Solrun Sigurdardottir[1]

[1] Centre for Rare Disorders, Oslo University Hospital, Oslo, Norway

[2] The Medical Faculty, University of Oslo, Oslo, Norway

[3] Department of Ophthalmology, Oslo University Hospital, Oslo, Norway

[4] National Resource Centre for Oral Health in Rare Disorders, Lovisenberg Diaconal Hospital, Oslo, Norway

[5] Department of Medical Genetics, Telemark Hospital Trust, Skien, Norway

Corresponding author:

Cecilie F. Rustad, MD, Centre for Rare Disorders, Oslo University Hospital, 4950 Nydalen, 0424 Oslo, Norway

Tel: +47 23 07 53 42

E-mail: cerus@ous-hf.no, cecilifr@uio.no

Word count: 4215, not including title page, abstract, keywords, references, figures and tables with titles and legends, acknowledgement, and statements on ethical approval, funding, competing interests, author contribution and availability of data.

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

Abstract

Objectives: This study aimed to determine healthcare needs and care use (provision of healthcare) in adults with Bardet–Biedl syndrome (BBS) and the associations between care use and physical functioning, health status outcomes and distress.

Design: Cross-sectional study.

Setting: Outpatient hospital visits.

Participants: Thirty adults with BBS were included (50% female, aged 20-69 years) and assessed with the Needs and Provision Complexity Scale (NPCS), Short Physical Performance Battery (SPPB), EQ-5D-5L, and Hospital Anxiety and Depression Scale (HADS).

Results: The majority (80%) received disability benefits, 93% were overweight or obese, and all had retinal dystrophy. Unmet needs (needs–gets) were found within the domains of rehabilitation (83%), social and family support (65%), healthcare (50%), personal care (47%) and the environment (40%). Significant correlations were observed between care use (gets) and worse physical performance (τ = -.34, p = < 0.01), more problems with self-care (τ = .47, p < 0.01) and more problems with usual activities (τ = .41, p = 0.01). Compared with those in the general population, adults with BBS reported significantly more problems (EQ-5D-5L) with mobility, self-care, and usual activities (all p < 0.001).

Conclusions: Most adults with BBS have unmet physical, social and medical needs, with the majority having unmet rehabilitation needs that require special attention. Physical mobility and usual activities were correlated with the provision of healthcare. The complexity of BBS requires a multidisciplinary approach that focuses not only on the medical follow-up of the condition but also on healthcare needs for functional mobility and social care.

This study was registered at ClinicalTrials.gov, NCT05400278.

Keywords: rare disease; medical needs; quality of life; disability; obesity; blindness

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

STRENGTHS AND LIMITATIONS OF THIS STUDY

- A multidisciplinary research team, including different healthcare professionals working in hospitals and resource centres for rare conditions, performed the evaluations.
- Generic, validated outcome measures were used to estimate and interpret physical and mental health in the BBS population.
- The small sample size limits the generalizability of the results and cannot be applied to children.
- Data were self-reported, which might result in participants underestimating their problems.

Introduction

Healthcare needs are an increasingly important issue in rare disease research. Frequent healthcare problems among people with rare diseases include a lack of appropriate access to diagnosis and a lack of treatment options [1, 2]. Rare diseases, defined in Europe as conditions with a prevalence of less than 1:2000 people, affect approximately 300 million individuals worldwide [3-5]. Many rare diseases are chronic, progressive, complex, and disabling, and the rarity of each of the ~7,000 rare diseases makes them difficult to diagnose [6]. Studies have shown that health professionals and general practitioners lack knowledge about rare diseases and lack confidence in providing care, transitioning care and coordinating the care of people with rare diseases [7-9]. Thus, individuals with rare diseases and their families unsurprisingly may face specific challenges when they seek information and support within health services. Delays in diagnosis and a lack of information about the diagnosis are shared challenges [10]. Furthermore, inequity in access to treatment and a lack of multidisciplinary care are health-related challenges that individuals with rare diseases may encounter [11-14].

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

One chronic, complex rare disease is the primary ciliopathy named Bardet–Biedl syndrome (BBS). This syndrome is characterized by retinal dystrophy, postaxial polydactyly, obesity, hypogonadism, renal abnormalities, and cognitive impairment [15, 16]. The prevalence of BBS is estimated to be 1 in 160,000 in Northern European populations [17]. The management of BBS poses challenges to health services because of the complexity of this condition, heterogeneity of the clinical phenotype, and limited treatment options [18]. Treatment for BBS-related rod-cone dystrophy is not available [15], whereas the treatment options for obesity, diabetes and kidney failure are the same for people with BBS as for those in the general population. More recently, individuals with BBS who are obese might be eligible for treatment with the melanocortin 4 receptor agonist setmelanotide if the treatment is available in the country where they live and if they fulfil the criteria for treatment [19-21]. Other management strategies are symptomatic, e.g., special education for cognitive impairment and training for visual loss [22]. Because treatment options for BBS are limited, a personalized clinical approach is relevant to match individual needs [18]. Therefore, diagnostics, prevention, treatment and follow-up are adapted to the biological condition of the individual. Multiple health needs have been identified in BBS, including vision-related needs [23], oral care needs [24], difficult airway management [25], type 2 diabetes mellitus needs [26], and problems accessing health services or treatments [27, 28]. Unmet needs have been recognized regarding targeted treatments for hunger, hyperphagia and obesity [29]. An unmet need can be defined as "difficulties receiving service in response to problems that significantly interfere with daily life" [30]. Adults with BBS might, for example, experience a need for physical activities to achieve weight loss before kidney transplantation but do not meet understanding for their obesity as one of the core features of BBS. The relationship between needs and health status in BBS needs to be better understood to address the unmet needs within the context of health status in order to improve healthcare. Despite the impact of BBS on the daily lives of individuals, to

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

the best of our knowledge, no research has documented their unmet needs for healthcare or the support they need. This study aimed to determine healthcare needs and care use in adults with BBS in Norway and associations between care use and physical functioning, health status outcomes and distress.

Methods

Participants

This study was performed to offer inclusion of all adults with BBS in Norway. Eligible individuals were recruited through a register at the Centre for Rare Disorders, Oslo University Hospital, Norway, and by advertisement on the Norwegian BBS Organization's webpage. The inclusion criteria were: (1) a clinical and/or genetic diagnosis of BBS; (2) ≥ 16 years of age; (3) residence in Norway; and (4) adequate knowledge of Norwegian for communication and understanding the questionnaires. The exclusion criterion was not having BBS. A clinical diagnosis meant fulfilling clinical criteria for Bardet-Biedl syndrome as outlined in Forsythe and Beales [17]. Informed consent was to be obtained from all participants prior to inclusion. Norway had a population of around 5.5 million individuals in 2022. The national resource centre for BBS had 46 adults registered and the Norwegian BBS Organization had approximately 50 adult members with BBS. Based on this information, half the number of adults with BBS was estimated to participate, that is 25 individuals.

Study design and data collection

This study was designed as a cross-sectional study and was conducted at the level of specialized healthcare in Norway from January 2022 to March 2023. Data were collected at the Oslo University Hospital and Lovisenberg Diaconal Hospital, Oslo, Norway. An eye examination was performed by an ophthalmologist (author RB). Clinical examinations and interviews were

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

conducted with a physician (author CFR or CvdL), including measuring height and weight and calculating body mass index (BMI = kg/m^2). The questionnaires were read aloud by one of the clinicians and answered orally, and a physical performance test was undertaken. These questionnaires and measures are described below. The oral health examinations were performed by a dentist and a speech and language pathologist (authors HN and PMÅ) at the National Resource Centre for Oral Health in Rare Disorders, Lovisenberg Diaconal Hospital, Oslo, Norway. The general flow of the examinations over a one-day visit included eye examinations, clinical examinations and interviews, questionnaires, physical performance tests, and, finally, oral health examinations.

Patient and public involvement statement

Two members of the Norwegian organization for BBS were closely involved in the planning of this study and were consulted to identify relevant research topics of interest to the organization. Both members were asked to test out the questionnaires.

Ethics

The study, registered at ClinicalTrials.gov, NCT05400278, was approved by the Regional Committee for Medical Research Ethics South East Norway (number 166639) and performed according to ethical guidelines [31].

Measurements

Demographics and clinical information

Demographic information was based on self-reports from participants. Information was collected regarding gender, age at diagnosis, education, employment, medical comorbidities and prior lifetime contact (yes, no) with health institutions (e.g., child and youth psychiatry,

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

services within education and psychology, district psychiatry, child habilitation, and national service for special needs education). Education was defined as high school or less (13 years or less) or more than 13 years of education. Employment, including paid full-time (100% employment), part-time (<100% employment), or self-employment, was classified as 'employed'. Any type of unpaid work, e.g., unemployed, support at the workplace, retirement, disability benefits, or home workers, was classified as 'unemployed'. In general, height and weight measurements were performed using a Seca 704 s (Seca GmbH & co. KG., Hamburg, Germany). Obesity was assessed by body mass index (BMI). BMI was calculated from the participants' height and body weight (BMI = kg/m^2). A BMI between 18.5 kg/m^2 and 25 kg/m^2 was considered normal weight, a BMI above 25 kg/m^2 but less than 30 kg/m^2 was considered overweight, and a BMI above 30 kg/m^2 was considered obese [32]. Renal disease included prenatally described kidney abnormalities, kidney tumours, increased kidney blood parameters, any stage of kidney failure or having had a kidney transplant. High blood pressure included measured systolic blood pressure above 140 mmHg, diastolic pressure above 90 mmHg and/or treatment with blood pressure-reducing medication. Diagnosis of diabetes mellitus was registered and/or medications for diabetes (yes/no). Oral/dental abnormalities (yes/no) were assessed by a dentist and included e.g., overbite, overjet, open bite, crowding of teeth, small teeth.

Needs for healthcare and social services

The Needs and Provision Complexity Scale (NPCS) [33] was used to evaluate the level of unmet needs for healthcare and social services. The NPCS was developed in the UK to identify healthcare and social support needs among individuals with neurological conditions [33]. It has been translated and recently validated in Norway [34, 35] and used in several populations, including individuals with Huntington's disease [34, 36], traumatic brain injuries [37] and

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

myotonic dystrophy [38]. The NPCS has not previously been used in adults with BBS. In this study, we used the Norwegian version 1.0. The NPCS has two parts: Part A (Needs, what the individual needs) was completed by two clinicians (authors CFR and SS) to evaluate each participant's needs for health and social care, and Part B (Gets, what the individual gets) was recorded by the clinician based on the information provided by the participants with BBS to evaluate care use (provision of healthcare). The NPCS has a total score ranging from 0–50 and contains five domains, which are scored as follows: healthcare scored from 0–6, personal care scored from 0–10, rehabilitation scored from 0–9, social and family support scored from 0–13 and environment scored from 0–12. The NPCS includes 15 items, which are scored according to highest level applicable as follows: medical care needs (0–3); skilled nursing needs (0–3); number of carers (0–2); care frequency (0–5); personal assistant/enabler (0–3); therapy disciplines (0–3); therapy intensity (0–3); vocational support/rehabilitation (0–3); social work case management (0–3); family carer support (0–3); respite residentially (0–3); respite as day care (0–2); advocacy (0–2); equipment (0–3); and accommodation (0–9). Higher scores indicate higher levels of needs. The total Needs score is the number of scores added together for the needs items. The total Gets score is the number of scores added together for the gets items. The total NPCS score is either the total score for Needs or the total score for Gets. Unmet Needs (Needs-Gets) were calculated for the total scores and the five domain scores. The percentage of participants needing the services (NPCS items) was converted to a binary variable (0 = no unmet need, 1 = unmet need) [33]. The Norwegian version of the NPCS has excellent interrater reliability for the total scores of the NPCS-Needs and the NPCS-Gets, with values of 0.911 and 0.987, respectively [35].

Physical performance evaluation

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

The Short Physical Performance Battery (SPPB) is a group of measures that combines the results of a 4.0 metre walking test at a normal pace (walking test), five-times rising from a chair as fast as possible (sit-to-stand test) and a standing balance test in a two-legged stance [39]. In this study, the SPPB was used to evaluate physical performance according to the standard guided procedure [39]. Each test was scored from 0 to 4, and the total score ranged from 0 to 12. A higher SPPB score signifies better physical performance. In the current study, the SPPB mean scores were compared to the mean normative scores in adults aged > 40 years from a Norwegian population-based study [40].

Self-reported health status

The EQ-5D-5L is a self-reported measure that is used to evaluate general health status. The EQ-5D-5L includes a visual analogue scale (EQ VAS) with scores ranging from 0 (the worst health you can imagine) to 100 (the best health you can imagine). Permission to use the EQ-5D-5L was obtained from the EuroQoL Group, and the Norwegian version was used [41]. The visual analogue scale was explained orally to each participant because of their reduced vision, and they were asked to rate their perceived health on the day of testing. The EQ-5D-5L consists of five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain has five levels ranging from 1 (no problems) to 5 (extreme problems/unable to). In this study, descriptive levels of each dimension were dichotomized to “no problems” (level one) or “any problems” (levels two to five) and compared to the Norwegian normative population [42]. Furthermore, the EQ-5D-5L index values, ranging from 0 (dead) to 1 (full health), were calculated based on the UK value set used in Norway [42].

Self-reported psychological distress

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

The Hospital Anxiety and Depression Scale (HADS) was used to assess symptoms of anxiety and depression within the last seven days [43]. The HADS includes an anxiety scale and a depression scale, each with seven items. Each item is scored on a 4-point scale, with the total scores for anxiety and depression ranging from 0 (best) to 21 (worst). A HADS score > 7 points was used to identify individuals with symptoms of anxiety or depression [44]. The HADS mean scores were compared to the mean Norwegian population scores from the HUNT-4 study [45].

Statistical analysis

Descriptions of the participants and questionnaires are provided with descriptive statistics, including means, medians and percentages. Shapiro–Wilk tests were performed to assess continuous data for normality. The NPCS domains, the EQ-5D-5L index score and the HADS score were not normally distributed, and these data were summarized as medians and interquartile ranges (IQRs). The mean and standard deviation (±SD) were also given for the NPCS to allow comparisons with previous studies. The chi-square test was used for the differences between categorical variables. Comparisons between normally distributed continuous variables were performed with Student's *t* test, whereas the Mann–Whitney U test was used for nonparametric variables. The Wilcoxon signed rank test for non-normally distributed variables was chosen to explore pairwise differences between the NPCS "Needs" and "Gets". Kendall's tau-b correlation coefficient (τ) was used to evaluate bivariate correlations between age, kidney disease, high blood pressure, obesity, the HADS subscales, the SPPB total score and the five domains of EQ-5D-5L with the five NPCS Gets subscales, with 1000 bootstrapped samples. All p values < 0.05 derived from two-sided tests were considered statistically significant. Because this study is observational with a small sample size, Bonferroni correction was not used, as it may overcorrect and increase the risk of type 2 error.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Statistical tests were conducted in SPSS, version 29.0 (SPSS Statistics, IBM Corporation, Chicago, IL).

Results

Study sample characteristics

Forty-six individuals were invited to participate. One person died shortly after the invitations were sent out, and one was excluded because of not having BBS. Thirty individuals participated in this study, a response rate of 68% (30/44). When those who consented to participate (n=30) and nonparticipants (n=14) were compared, no differences in age (p=0.660) or sex (p=0.88) were identified.

Table 1 shows the characteristics of the 30 adult participants (mean age (± SD) 39.8 ± 13.6, age range 20–69 years, 50% females). No sex differences were observed in any of the demographics (not shown). Overall, 17% of the participants were employed, either full- or part-time, one had retired, and the majority (80%) were receiving disability benefits. Four participants were offered the option of a home visit because they were unable to travel, they did not have an ophthalmology or oral exam.

All participants had retinal dystrophy (including self-reports from the four home visits), and 93% were overweight or obese (BMI above 25 kg/m^2). Oral/dental abnormalities were more common in males than in females. Almost two-thirds had high blood pressure, 27% had renal disease, and 23% were diagnosed with type 2 diabetes. Four individuals had both renal disease and type 2 diabetes. The need for mental health services during childhood was reported by 20% of the participants, and 70 % had been followed by educational-psychological services in the school system. Moreover, 13% reported follow-ups with psychiatric services during adulthood.

The data for the NPCS are summarized in table 1. The median overall score for the NPCS (Needs) was 17.0 (IQR=8), and for the NPCS (Gets), it was 12.0 (IQR=6).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Table 1. Demographics and characteristics of adults with Bardet-Biedl syndrome (*n*=30)

	Total
Males	15 (50%)
Age at inclusion ǂ	39.8 (13.6)
Age diagnosed with BBS #	9 (13.5)
Marital status single	26 (87%)
Living independently or with a spouse or partner	18 (60%)
Living with parents or in care home	12 (40%)
Education (≤13 years)	27 (90%)
Employed (full time, part time)	5 (17%)
Disability benefits (full time)	24 (80%)
Body mass index	37.9 (11.1)
Overweight or obesity	28 (93%)
Retinal dystrophy*	30 (100%)
Oral/dental abnormalities (*n*=26)	20 (77%)
Renal disease	8 (27%)
High blood pressure	20 (67%)
Diabetes	7 (23%)
Child mental health service	6 (20%)
Educational-psychological service	21 (70%)
Adult mental health clinic	4 (13%)
Needs and Provision Complexity Scale #	
Clinical version (Part A **Needs**)	
Total Needs score (score 0-50)	17.0 (8)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

Healthcare (score 0-6)	2.0 (1)
Personal care (score 0-10)	5.0 (3)
Rehabilitation (score 0-9)	5.0 (3)
Social and family support (score 0-13)	1.5 (2)
Environment (score 0-12)	4.5 (3)
Patient version (Part B **Gets**)	
Total Needs score (score 0-50)	12.0 (6)
Healthcare (score 0-6)	2.0 (2)
Personal care (score 0-10)	3.0 (4)
Rehabilitation (score 0-9)	3.0 (2)
Social and family support (score 0-13)	0.0 (2)
Environment (score 0-12)	3.0 (3)

Notes.

ǂ Scores presented as mean (±SD). # Scores presented as median (IQR).

Discrete variables presented as number (percentages).

* Including self-reported retinal dystrophy in four individuals.

Needs indicates that adults with BBS need this health service.

Gets indicate that adults receive this health service (provision).

Unmet needs

As shown in Table 2, clinicians (Needs) scored higher on all five domains compared to self-rated (Gets) scores. The Wilcoxon signed rank sum test confirmed the presence of significantly different pairwise comparisons between the measures of clinicians (NPCS Needs) compared with those of self-reports (NPCS Gets) (total: ($p < 0.001$); Healthcare: ($p = 0.002$); Personal care: ($p = 0.001$); Rehabilitation: ($p < 0.001$); Social and family support: ($p < 0.001$); and

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Environment; (p = 0.002); see Table 2). Most participants (97%) were found to have unmet needs. The majority had unmet needs for rehabilitation (83%), followed by unmet social and family support needs (63%), healthcare needs (50%), personal care needs (47%) and environmental needs (40%).

Table 2. Differences between health service needs (Part A) and gets (Part B) according to the Needs and Provision Complexity Scale (n = 30)

	Needs - Gets Median (IQR) / (range)	**Unmet Needs #** *n* (%)
Total NPCS (score 0–50)	4.0 (4.3) / (0–16)**	29/30 (97%)
Healthcare (score 0–6)	0.5 (1) / (-1–2)*	15/30 (50%)
Personal care (score 0–10)	0.0 (2) / (-1–5)*	14/30 (47%)
Rehabilitation (score 0–9)	2.0 (2) / (0–8)**	25/30 (83%)
Social and family support (score 0–13)	1.0 (1.3) / (-1–4)**	19/30 (63%)
Environment (score 0–12)	0.0 (1) / (0–4)*	12/30 (40%)

Notes.

Needs indicates that adults with BBS need this health service.

Gets indicate that adults receive this health service (provision).

Unmet needs are the difference between Needs and Gets.

Proportion of participants with a higher score on the NPCS Needs than the NPCS Gets.

* $p < 0.01$, ** $p < 0.001$ with the Wilcoxon signed rank test.

Figure 1 illustrates the proportions of unmet needs across all 15 items of the NPCS, using the binary variable described in the methods. Between 50% and 77% of the participants were found to have insufficient professional healthcare (e.g., medical care, social workers, physiotherapists, psychologists, occupational therapists, dieticians, and dentists).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

---Insert Figure 1 here---

Differences in outcome measures of health status, distress and physical performance

Table 3 presents the results for the EQ-5D-5L, HADS and SPPB in comparison with normative data, using online calculators for two sample *t*-tests and Chi-square tests. The BBS population reported significantly more health problems (EQ-5D-5L) in terms of mobility, self-care, and usual activities as well as significantly lower levels of general health (all $p < 0.001$) than the general Norwegian population [42]. The BBS population reported significantly lower scores (i.e., better mental health) on the three HADS scales ($p< 0.05$) than the adult population in the HUNT-4 study [45]. The HUNT-4 study has published data on the HADS and is considered representative of health problems of the total adult population in Norway [46]. Notably, four adults with BBS (13%) were identified as having potential anxiety (score > 7), and only one individual (3%) had potential depression (score > 7). Finally, significant differences ($p < 0.001$) were found for comparisons on levels of physical performance, the general population had much higher levels of physical functioning [40].

Notably, two participants with BBS were unable to perform the SPPB test because they were unable to stand without support and were therefore given a total score of zero.

Table 3. Comparisons for outcome measures (EQ-5D-5L, HADS, SPPB) for the BBS population (n = 30) and the Norwegian normative data

EQ-5D-5L domains	BBS (n=30)	Normative data (n=3120)	*p*
	Any problems, *n* (%)	**Any problems, *n* (%)** #	

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

Mobility	16 (53%)	562 (18.0%)	< 0.001
Self-care	7 (23%)	227 (7.3%)	< 0.001
Usual activities	16 (53%)	756 (24.2%)	< 0.001
Pain / Discomfort	19 (63%)	1937 (62.1%)	0.888
Anxiety / Depression	13 (43%)	1104 (35.4%)	0.365
	BBS mean (SD)	**Expected mean (SD)** #	
EQ-5D-5L VAS scale (score 0–100)	63.8 (21.5)	77.9 (18.3)	< 0.001
EQ-5D-5L index score (score 0–1)	0.79 (0.18)	0.81 (0.20)	0.585
	BBS mean (SD)	**Expected mean (SD)** ǂ	
HADS-Total score	5.00 (6.01)	7.68 (5.66) *n*=40,648	< 0.01
HADS-Anxiety	3.13 (3.90)	4.40 (3.46) *n*=41,133	0.04
HADS Depression	1.87 (2.62)	3.30 (2.96) *n*=39,573	< 0.01
	BBS mean (SD)	**Expected mean (SD)** ≠	
SPPB-Total score	6.7 (3.5)	11.4 (1.3) *n*=7474	< 0.001

Notes.

Abbreviations: BBS = Bardet-Biedl syndrome; VAS = Visual Analogue Scale.; HADS = Hospital Anxiety and Depression Scale; SPPB = Short Physical Performance Battery

Comparisons between our BBS population and the general Norwegian population were conducted using online calculators for two sample *t*-tests and Chi-square tests.

Derived from Garratt et al. (2022) [42].

ǂ Derived from HUNT-4 study [45].

≠ Derived from Bergland et al. (2019) [40].

Correlations between care use (NPCS Gets) and health status outcomes

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

The Healthcare subscale of the NPCS (Table 4) was correlated with having more problems with usual activities (τ = .41, p = 0.01). The Personal Care subscale was correlated with worse physical performance (τ = -.34, p = < 0.01) and having more problems with self-care (τ = .47, p < 0.01). The correlation analyses revealed no associations between the provision of Rehabilitation, Social/family support and Environment with any of the health status outcomes.

Table 4. Correlation analysis between NPCS (Gets), HADS, SPPB and EQ-5D-5L and demographics in the total sample (n = 30)

	Healthcare	Personal care	Rehabilitation	Social/ family support	Environment
	τ	τ	τ	τ	τ
Age	.27	.10	.15	.01	-.21
Kidney disease (0=no, 1=yes)	.27	-.10	-.16	-.17	-.24
High blood pressure (0=no, 1=yes)	.27	.21	.04	-.14	.17
BMI	.09	.15	-.21	-.13	.18
HADS Anxiety	-.20	.10	.16	-.03	-.11
HADS Depression	-.21	.14	.04	.05	-.14
SPPB Total score	-.20	-.34*	-.09	-.24	-.05
EQ-5D-5L Mobility	.28	.07	-.12	.03	-.14
EQ-5D-5L Self-care	.14	.47**	.14	.21	.22
EQ-5D-5L Usual activity	.41*	.21	.02	.12	-.17
EQ-5D-5L Pain / Discomfort	.21	-.03	-.28	.01	-.11
EQ-5D-5L Anxiety / Depression	-.08	.25	.08	.09	-.10

Notes.

Abbreviations: NPCS = Needs and Provision Complexity Scale; HADS = Hospital Anxiety and Depression Scale; SPPB = Short Physical Performance Battery.

Correlation calculated with Kendall's tau beta correlation coefficient (τ). Bootstrapping with 1000-samples.

* p < 0.05; ** p < 0.01.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

Discussion

This study focused on the healthcare needs of adults with BBS in Norway. In this nationally representative cross-sectional study, we found that a substantial proportion of adults with BBS who need supportive health services do not receive such services. Significant discrepancies were identified between needs (clinicians' ratings) and gets (participants' ratings), indicating that a majority had unmet needs related to the domains of health and personal care as well as social and supportive care. Several key findings are noteworthy. First, rehabilitation needs were rated as the greatest unmet needs overall. This demonstrates that rehabilitation is a key need identified in this rare disorder and should be considered a central part of health care delivery for BBS. Due to the obesity problems in BBS, and in particular higher risk of high blood pressure, diabetes and kidney failure, people with BBS need to have access to assessment of rehabilitation needs. Compared with the general population [40], adults with BBS had significantly lower levels of physical functioning on objective tests. This indicates that training is an area of need and multidisciplinary care services working jointly with physical therapists could make the difference to better BBS-related outcomes, as addressed in other studies (16, 18).

Second, higher levels of medical healthcare and personal care services (care gets) were significantly and meaningfully correlated with greater difficulty with physical balance (SPPB), self-care and usual activities (EQ-5D-5L). This may indicate that healthcare services were able to meet the individual needs and that the adults with BBS received help for the identified difficulties with physical functioning, self-care and usual activities. Problems with mobility and usual activities (EQ-5D-5L) were reported in just over half of the participants and statistically more often than in the general Norwegian population [42]. However, adults with BBS had less distress (anxiety, depression) compared to the normative data. It may be that adults with BBS

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

have resources to address their mental problems (e.g., family members, personal assistant) contributing to less psychological needs, but these were not addressed in our study.

Third, no significant correlation was identified between the most prevalent unmet needs (i.e., rehabilitation and social/family support) and the disease-related and self-reported variables (kidney, high blood pressure, BMI, physical functioning, HADS, EQ-5D-5L). For adults with BBS experiencing disease progression (e.g., kidney, vision, obesity) and chronicity of the condition, considerable unmet needs are to be expected. Therefore, we speculate that the relationship of health services (gets) and the complexity of BBS if difficult to detect in a small sample. To overcome this limitation, larger studies could help address the unique rehabilitation needs and the unmet health needs in BBS. Given that people with BBS may underestimate the rehabilitation needs, future studies should combine clinical assessments, objective tests and self-reports.

Many of the health issues presented in our study could be addressed in a multidisciplinary team setting by relevant professionals, e.g., physicians, physical therapists, social workers, ophthalmologists, dentists, registered dietitians and psychologists; however, none of the participants taking part in this study received such services. A consensus statement study recommended that people with BBS had lifelong follow-ups, treatments for neurological and endocrinological diseases as well as rehabilitation sessions for visual handicap [47]. Present study builds on earlier studies of rare diseases, showing a need for supportive care in a broad range of domains and unmet needs in primary health care [2, 11, 48]. The BBS-related health problems represent broad types of healthcare needs and require multidisciplinary interventions in addition to pharmacological treatments (e.g., blood pressure, diabetes, obesity). Therefore, ensuring the delivery of healthcare and preventative measures to people diagnosed with BBS is important.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

BBS lacks pathognomonic signs or symptoms at birth or later, which, combined with a lack of knowledge about BBS, might cause diagnostic delay [16, 49]. The age at diagnosis was 9 years in the present study, and the majority of participants had been in contact with educational-psychological services during childhood. Furthermore, 20% of the participants had been referred to child and adolescent mental health services, indicating that children with BBS need treatment for their mental and/or behavioural problems. This finding highlights the importance of early disease intervention. Increased accessibility of genetic testing today may reduce the age at diagnosis compared with when our participants were diagnosed several decades ago.

Only 17% of adults with BBS were employed, which is notably lower than the rate reported in people with various eye diseases (44%) in Norway [50] and lower than the work participation in rare diseases (55%) reported in a recent scoping review [51]. The complexity of BBS makes it difficult to pinpoint the exact reasons for unemployment. Our findings may be limited because the analyses were exploratory and based on a small sample, and further research is needed to evaluate this in more detail. Complex conditions such as BBS with reduced vision, possible cognitive challenges and obesity pose difficulties to the working environment, which needs to be addressed to improve work participation.

The strengths of this study are the high response rate (68%). Also, this sample of responders appears to be largely representative of adults with BBS in the country (Norway). Evaluations were performed by a multidisciplinary research team, including different healthcare professionals working in hospitals and resource centres for rare conditions in Norway. This study could subsequently contribute to increasing awareness of BBS among professionals working in primary care but also in mental health and specialist health services, where treatments may be administered. No previous study has focused on describing healthcare needs and the provision of and access to healthcare in BBS. Based on present findings, substantial

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

physical and social healthcare needs are currently not addressed, and this study can serve as a starting point for future research on BBS or other rare diseases.

The small sample size may be considered a limitation because it significantly reduces the statistical power. The data were self-reported, which might have resulted in participants underestimating their problems because of a lack of self-awareness or having cognitive difficulties understanding the questions. Because individuals under 16 years of age were excluded, the study has limited generalizability to children. In addition, adults with BBS who did not participate in this study might have other healthcare needs. The cross-sectional design limits the assessments of longitudinal changes and causal associations between healthcare use (gets) and health outcomes. We have compared our data to normative data, this is for reference only and caution is needed due to differences in e.g., age distribution, sex, sample size, data collection, and other factors.

Conclusions

Adults with BBS were found to have unmet physical, social and medical needs, which may contribute to health concerns. Rehabilitation needs were the greatest unmet needs and require special attention. Difficulties with physical functioning, self-care and usual activities were related with access to health services, indicating that the services were able to meet these needs. Given the complexity and heterogeneity of BBS, effective management requires a multidisciplinary approach that focuses not only on medical follow-up but also on functional mobility and social care to provide optimal personalized care and rehabilitation for all individuals with BBS.

Acknowledgement

For peer review only

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Enseignement Superieur (ABES) .

The research team is deeply grateful to all the individuals with Bardet-Biedl syndrome for their time and investment in taking part in this study. We would like to thank the two representatives of the Norwegian Organization for Bardet-Biedl syndrome for their involvement: Richard Ødegaard and Lill Susann Lerudsmoen.

Funding

This study was supported by grants from Raagholtstiftelsen in Norway (to Solrun Sigurdardottir).

Author contributions

All the authors meet the criteria for authorship stated in the requirements for manuscript submitted to BMJ Open and all four ICJME criteria. In particular, the authors' contributions to the manuscript were as follows: conceptualization and methodology: all the authors. Formal data analyses and writing of the original draft: CFR, SS. Supervision: SS, CvdL, RB. Review of the manuscript and editing and validation of the final text: all the authors. SS is the guarantor.

Competing interests

Solrun Sigurdardottir has received speaker fees from Sanofi. The other authors have no competing interests to declare.

Availability of data and materials

Norwegian ethical and legal restrictions prevent the authors from uploading or sharing data with public repositories. Individuals with Bardet–Biedl syndrome in Norway belong to a

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

relatively small group, and very little personal data are needed to indirectly identify individual study participants.

Ethics approval and consent to participate

The Norwegian Regional Committee for Medical Research Ethics in Southeast Norway (number 166639) and the Data Protection officer at Oslo University Hospital (number 20/21045) approved the study. Written informed consent was obtained from all the included individuals.

Figure title

Figure 1. Percentage of unmet and met needs of the 15 items of the Needs and Provision Complexity Scale.

Figure 1. Notes. HC = Healthcare domain; PC = Personal care domain; REH = Rehabilitation domain; SF = Social and family support domain; E = Environment domain.

References

1. Austin CP, Cutillo CM, Lau LPL, Jonker AH, Rath A, Julkowska D, et al. Future of Rare Diseases Research 2017-2027: An IRDiRC Perspective. Clin Transl Sci. 2018;11(1):21-7.
2. Long JC, Best S, Nic Giolla Easpaig B, Hatem S, Fehlberg Z, Christodoulou J, et al. Needs of people with rare diseases that can be supported by electronic resources: a scoping review. BMJ Open. 2022;12(9):e060394.
3. Haendel M, Vasilevsky N, Unni D, Bologa C, Harris N, Rehm H, et al. How many rare diseases are there? Nat Rev Drug Discov. 2020;19(2):77-8.
4. products. UERENotEPaotCoDoom. 2000.
5. Ferreira CR. The burden of rare diseases. Am J Med Genet A. 2019;179(6):885-92.
6. Chung CCY, Hong Kong Genome P, Chu ATW, Chung BHY. Rare disease emerging as a global public health priority. Front Public Health. 2022;10:1028545.
7. Evans WR, Rafi I. Rare diseases in general practice: recognising the zebras among the horses. Br J Gen Pract. 2016;66(652):550-1.
8. Vandeborne L, van Overbeeke E, Dooms M, De Beleyr B, Huys I. Information needs of physicians regarding the diagnosis of rare diseases: a questionnaire-based study in Belgium. Orphanet J Rare Dis. 2019;14(1):99.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .

9. Fredwall S, Allum Y, AlSayed M, Alves I, Ben-Omran T, Boero S, et al. Optimising care and follow-up of adults with achondroplasia. Orphanet J Rare Dis. 2022;17(1):318.
10. Groft SC, Posada M, Taruscio D. Progress, challenges and global approaches to rare diseases. Acta Paediatr. 2021;110(10):2711-6.
11. Depping MK, Uhlenbusch N, von Kodolitsch Y, Klose HFE, Mautner VF, Lowe B. Supportive care needs of patients with rare chronic diseases: multi-method, cross-sectional study. Orphanet J Rare Dis. 2021;16(1):44.
12. Zelihic D, Hjardemaal FR, Lippe CV. Caring for a child with Bardet-Biedl syndrome: A qualitative study of the parental experiences of daily coping and support. Eur J Med Genet. 2020;63(4):103856.
13. Pelentsov LJ, Fielder AL, Laws TA, Esterman AJ. The supportive care needs of parents with a child with a rare disease: results of an online survey. BMC Fam Pract. 2016;17:88.
14. Benito-Lozano J, Arias-Merino G, Gomez-Martinez M, Ancochea-Diaz A, Aparicio-Garcia A, Posada de la Paz M, et al. Diagnostic Process in Rare Diseases: Determinants Associated with Diagnostic Delay. Int J Environ Res Public Health. 2022;19(11).
15. Chandra B, Tung ML, Hsu Y, Scheetz T, Sheffield VC. Retinal ciliopathies through the lens of Bardet-Biedl Syndrome: Past, present and future. Prog Retin Eye Res. 2022;89:101035.
16. Forsythe E, Kenny J, Bacchelli C, Beales PL. Managing Bardet-Biedl Syndrome-Now and in the Future. Front Pediatr. 2018;6:23.
17. Forsythe E, Beales PL. Bardet-Biedl syndrome. Eur J Hum Genet. 2013;21(1):8-13.
18. Kenny J, Forsythe E, Beales P, Bacchelli C. Toward personalized medicine in Bardet-Biedl syndrome. Per Med. 2017;14(5):447-56.
19. Meyer JR, Krentz AD, Berg RL, Richardson JG, Pomeroy J, Hebbring SJ, et al. Kidney failure in Bardet–Biedl syndrome. Clin Genet. 2022;101(4):429-41.
20. Tomlinson JW. Bardet-Biedl syndrome: A focus on genetics, mechanisms and metabolic dysfunction. Diabetes Obes Metab. 2024.
21. Forsythe E, Haws RM, Argente J, Beales P, Martos-Moreno GA, Dollfus H, et al. Quality of life improvements following one year of setmelanotide in children and adult patients with Bardet-Biedl syndrome: phase 3 trial results. Orphanet J Rare Dis. 2023;18(1):12.
22. Melluso A, Secondulfo F, Capolongo G, Capasso G, Zacchia M. Bardet-Biedl Syndrome: Current Perspectives and Clinical Outlook. Ther Clin Risk Manag. 2023;19:115-32.
23. Denniston AK, Beales PL, Tomlins PJ, Good P, Langford M, Foggensteiner L, et al. Evaluation of visual function and needs in adult patients with bardet-biedl syndrome. Retina. 2014;34(11):2282-9.
24. Panny A, Glurich I, Haws RM, Acharya A. Oral and Craniofacial Anomalies of Bardet-Biedl Syndrome: Dental Management in the Context of a Rare Disease. J Dent Res. 2017;96(12):1361-9.
25. Smith BB, Barbara DW, Hyder JA, Smith MM. Anesthetic considerations for patients with Bardet-Biedl syndrome: a case series and review of the literature. Paediatr Anaesth. 2016;26(4):429-37.
26. Pomeroy J, Krentz AD, Richardson JG, Berg RL, VanWormer JJ, Haws RM. Bardet-Biedl syndrome: Weight patterns and genetics in a rare obesity syndrome. Pediatr Obes. 2021;16(2):e12703.
27. Mujahid S, Hunt KF, Cheah YS, Forsythe E, Hazlehurst JM, Sparks K, et al. The Endocrine and Metabolic Characteristics of a Large Bardet-Biedl Syndrome Clinic Population. J Clin Endocrinol Metab. 2018;103(5):1834-41.
28. Keifer E, Berg RL, Richardson JG, Haws RM. Early development and adaptive functioning in children with Bardet-Biedl syndrome. Am J Med Genet A. 2024;194(1):31-8.
29. Forsythe E, Mallya UG, Yang M, Huber C, Cala ML, Greatsinger A, et al. Burden of hyperphagia and obesity in Bardet-Biedl syndrome: a multicountry survey. Orphanet J Rare Dis. 2023;18(1):182.
30. McColl MA, Shortt S, Gignac M, Lam M. Disentangling the effects of disability and age on health service utilisation. Disabil Rehabil. 2011;33(13-14):1253-61.

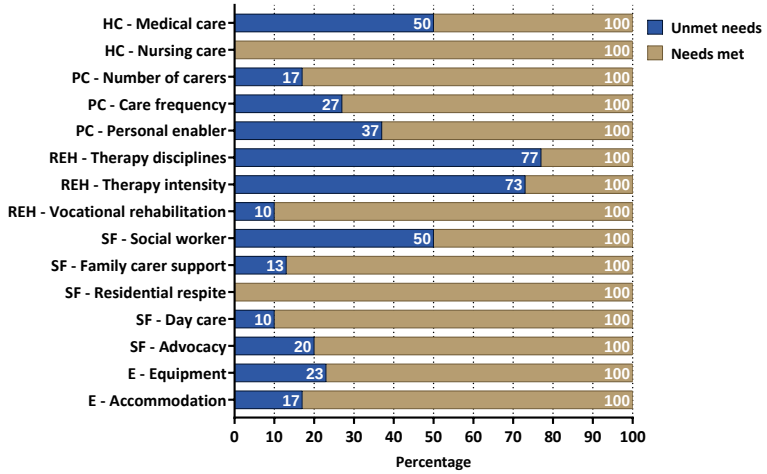
For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies. Enseignement Superieur (ABES) .

31. World Medical A. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310(20):2191-4.
32. Moyer VA, Force USPST. Screening for and management of obesity in adults: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2012;157(5):373-8.
33. Turner-Stokes L, McCrone P, Jackson DM, Siegert RJ. The Needs and Provision Complexity Scale: a multicentre prospective cohort analysis of met and unmet needs and their cost implications for patients with complex neurological disability. BMJ Open. 2013;3(2).
34. van Walsem MR, Howe EI, Iversen K, Frich JC, Andelic N. Unmet needs for healthcare and social support services in patients with Huntington's disease: a cross-sectional population-based study. Orphanet J Rare Dis. 2015;10:124.
35. Forslund MV, Borgen IMH, Karic T, Kleffelgard I, Hauger SL, Lovstad M, et al. Validity of the Norwegian Version of the Needs and Provision Complexity Scale (NPCS) in Patients with Traumatic Brain Injury and Atraumatic Subarachnoid Hemorrhage. J Clin Med. 2024;13(3).
36. van Walsem MR, Howe EI, Ruud GA, Frich JC, Andelic N. Health-related quality of life and unmet healthcare needs in Huntington's disease. Health Qual Life Outcomes. 2017;15(1):6.
37. Laurie K, Foster MM, Borg DN, Gustafsson L. Perceived service adequacy and unmet need after discharge from brain injury rehabilitation. Disabil Rehabil. 2023;45(20):3252-61.
38. Holmoy AKT, Johannessen CH, Hope S, van Walsem MR, Aanonsen NO, Hassel B. Uncovering health and social care needs among myotonic dystrophy patients: Utility of the Needs and Provisions Complexity Scale. Acta Neurol Scand. 2019;139(6):526-32.
39. Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir GV, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci. 2000;55(4):M221-31.
40. Bergland A, Strand BH. Norwegian reference values for the Short Physical Performance Battery (SPPB): the Tromso Study. BMC Geriatr. 2019;19(1):216.
41. Nord E. EuroQol: health-related quality of life measurement. Valuations of health states by the general public in Norway. Health Policy. 1991;18(1):25-36.
42. Garratt AM, Hansen TM, Augestad LA, Rand K, Stavem K. Norwegian population norms for the EQ-5D-5L: results from a general population survey. Qual Life Res. 2022;31(2):517-26.
43. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res. 2002;52(2):69-77.
44. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361-70.
45. Forskningssenter H. HUNT Databank 2025. Available from: https://hunt-db.medisin.ntnu.no/hunt-db/#variable/7259.
46. Asvold BO, Langhammer A, Rehn TA, Kjelvik G, Grontvedt TV, Sorgjerd EP, et al. Cohort Profile Update: The HUNT Study, Norway. Int J Epidemiol. 2023;52(1):e80-e91.
47. Dollfus H, Lilien MR, Maffei P, Verloes A, Muller J, Bacci GM, et al. Bardet-Biedl syndrome improved diagnosis criteria and management: Inter European Reference Networks consensus statement and recommendations. Eur J Hum Genet. 2024.
48. Bogart K, Hemmesch A, Barnes E, Blissenbach T, Beisang A, Engel P, et al. Healthcare access, satisfaction, and health-related quality of life among children and adults with rare diseases. Orphanet J Rare Dis. 2022;17(1):196.
49. Berezovsky A, Rocha DM, Sacai PY, Watanabe SS, Cavascan NN, Salomao SR. Visual acuity and retinal function in patients with Bardet-Biedl syndrome. Clinics (Sao Paulo). 2012;67(2):145-9.
50. Brunes A, Heir T. Visual impairment and employment in Norway. BMC Public Health. 2022;22(1):648.
51. Velvin G, Dammann B, Haagensen T, Johansen H, Stromme H, Geirdal AO, et al. Work participation in adults with rare genetic diseases - a scoping review. BMC Public Health. 2023;23(1):910.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.
Enseignement Superieur (ABES) .



bmjopen-2024-095986 on 22 April 2025. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) .
d by copyright, including for uses related to text and data mining, AI training, and similar technologies.

er review only