RESEARCH ARTICLE OPEN ACCESS

Weight Management Interventions for Adults With Idiopathic Intracranial Hypertension

A Systematic Review and Practice Recommendations

Sally Abbott, MRes, Fiona Chan, MRCAP, Abd A. Tahrani, PhD, Sui Hsien Wong, MBBS, MD, FRCP, Fiona E.J. Campbell, PhD, Chetan Parmar, FRCS, Dimitri J. Pournaras, PhD, Amanda Denton, Msc, Alexandra Jean Sinclair, PhD, and Susan P. Mollan, MBChB, FRCOphth

Correspondence
Dr. Mollan
soozmollan@doctors.org.uk

Neurology® 2023;101:e2138-e2150. doi:10.1212/WNL.0000000000207866

Abstract

Background and Objectives

Idiopathic intracranial hypertension (IIH) is associated with obesity; however, there is a lack of clinical consensus on how to manage weight in IIH. The aim of this systematic review was to evaluate weight loss interventions in people with IIH to determine which intervention is superior in terms of weight loss, reduction in intracranial pressure (ICP), benefit to visual and headache outcomes, quality of life, and mental health.

Methods

A systematic review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and registered with PROSPERO (CRD42023339569). MEDLINE and CINAHL were searched for relevant literature published from inception until December 15, 2022. Screening and quality appraisal was conducted by 2 independent reviewers. Recommendations were graded using Scottish Intercollegiate Guidelines Network methodology.

Results

A total of 17 studies were included. Bariatric surgery resulted in 27.2–27.8 kg weight loss at 24 months (Level 1− to 1++). Lifestyle weight management interventions resulted in between 1.4 and 15.7 kg weight loss (Level 2+ to 1++). Bariatric surgery resulted in the greatest mean reduction in ICP (−11.9 cm H_2O) at 24 months (Level 1++), followed by multicomponent lifestyle intervention + acetazolamide (−11.2 cm H_2O) at 6 months (Level 1+) and then a very low-energy diet intervention (−8.0 cm H_2O) at 3 months (Level 2++). The least ICP reduction was shown at 24 months after completing a 12-month multicomponent lifestyle intervention (−3.5 cm H_2O) (Level 1++). Reduction in body weight was shown to be highly correlated with reduction in ICP (Level 2++ to 1++).

Discussion

Bariatric surgery should be considered for women with IIH and a body mass index (BMI) ≥35 kg/m^2 since this had the most robust evidence for sustained weight management (grade A). A multicomponent lifestyle intervention (diet + physical activity + behavior) had the most robust evidence for modest weight loss with a BMI <35 kg/m^2 (grade B). Longer-term outcomes for weight management interventions in people with IIH are required to determine whether there is a superior weight loss intervention for IIH.

From the Research Centre for Healthcare and Communities (S.A.), Coventry University; Birmingham Neuro-Ophthalmology (F.C.), University Hospitals Birmingham; Institute of Metabolism and Systems Research (A.A.T.), University of Birmingham, United Kingdom; Novo Nordisk (A.A.T.), Bagsvaerd, Denmark; Department of Neuro-Ophthalmology (S.H.W.), Moorfields Eye Hospital; Medical Eye Unit (S.H.W.), Guy's and St Thomas' NHSFT, London; School of Life Course & Population Sciences (S.H.W.), Kings College London; Department of Clinical and Movement Neurosciences (S.H.W.), University College London; Adult Weight Management (Bariatric Surgery) (F.E.J.C.), NHS Grampian; Department of Surgery (C.P.), University College London Hospitals; Department of Surgery (C.P.), Barts Health NHS Trust, London; Upper Gastrointestinal (D.J.P.), Bariatric and Metabolic Surgery, North Bristol NHS Trust; IIH UK (A.D.), London; Translational Brain Science (A.J.S., S.P.M.), Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham; and Birmingham Neuro-Ophthalmology (S.P.M.), University Hospitals Birmingham NHS Trust, United Kingdom.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

The Article Processing Charge was funded by the authors.

Glossary

BMI = body mass index; **GLP-1** = glucagon-like peptide-1; **GPP** = good practice point; **HIT** = Headache Impact Test; **HVF** = Humphrey visual field; **ICP** = intracranial pressure; **IIH** = idiopathic intracranial hypertension; **IIHTT** = IIH Treatment Trial; **IIHWT** = IIH Weight Trial; **OCT** = optic coherence tomography; **PMD** = perimetric mean deviation; **RCT** = randomized control trial; **SF-36** = Short Form-36; **SIGN** = Scottish Intercollegiate Guidelines Network; **VLED** = very low-energy diet.

Introduction

Idiopathic intracranial hypertension (IIH) is characterized by raised intracranial pressure (ICP), pulse-synchronous tinnitus, headaches, and papilledema, with the potential risk of permanent visual loss.[1] Most people living with IIH are also living with obesity.[2] Population studies have observed the increased incidence of IIH in those with an increased body mass index (BMI),[3] and an elevated BMI is shown to be directly associated with greater risk of a diagnosis of IIH.[2] Furthermore, a relationship between BMI and visual outcomes has been established. A study found that patients with BMI >40 kg/m^2 were more likely to have severe papilledema at the first neuro-ophthalmology visit and every 10 kg/m^2 increase in BMI increased the odds of severe visual loss by 1.4 times.[4]

IIH is emerging from being a disease of the neuro-ophthalmic axis to being a distinct metabolic disease, where the underlying pathophysiology may be modified by weight loss.[5-7] Moreover, IIH has been demonstrated to have a distinct pathophysiology that hinders weight loss and promotes further weight gain.[8] At the same time, psychiatric disorders are sevenfold more common in people with IIH compared with the general population,[9] that may result from common biological pathways related to hypothalamus-pituitary-adrenal cortex axis dysfunction,[10] which may mean weight management is more challenging for people living with IIH.

Obesity results from an interaction between innate biological and environmental factors, and there is a strong genetic component underlying interindividual variation in body weight.[11] As a result, the human body is biologically hardwired to prevent weight loss.[12,13] This is a challenge for the treatment of IIH because excess body weight has an impact on IIH development and improvement. Moderate weight gain of 5%–15% is associated with a greater risk of developing IIH among both people with and without obesity.[14] Meanwhile, weight loss in the range of 3%–24% has been reported to lead to remission,[5-7] and weight regain has been found to be a risk factor for disease recurrence.[15]

Sustained weight loss therefore is essential for long-term remission of the disease. However, clinical practice is varied in how to deliver the most effective weight loss strategies for IIH. Indeed, sustained weight loss has been demonstrated to be essential for long-term remission of the disease.[15] The optimal weight loss method for IIH is yet to be determined,[16] especially in the context of the chronic relapsing nature of obesity.

Hence, the aim of this study was to identify, evaluate, and summarize the relevant published studies relating to weight loss interventions for IIH for their ability to deliver sustained weight loss and impact on key outcomes, such as vision and headache. A second aim of this study was to convene a panel of experts in the field of IIH and weight management to review the evidence and provide practice points to help guide clinicians who may not have formal training in weight management.

Methods

This systematic review was registered on PROSPERO International Prospective Register of Systematic Reviews (identifier CRD42023339569) and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[17]

Search Strategy

The databases MEDLINE and CINAHL were searched from inception up to December 15, 2022, through EBSCO using a comprehensive search strategy (eAppendix 1, links.lww.com/WNL/D147), which was tested and refined to maximize sensitivity for retrieving relevant studies. There were no language restrictions. The Boolean operator "OR" was used to separate each term within each concept, and each concept was concatenated by the operator "AND." When possible, Medical Subject Heading terms were used to expand the search language. The search strategy was identical in both databases, with minor adaptation to the coding to suit individual database settings. References were imported into Covidence software for deduplication and screening.

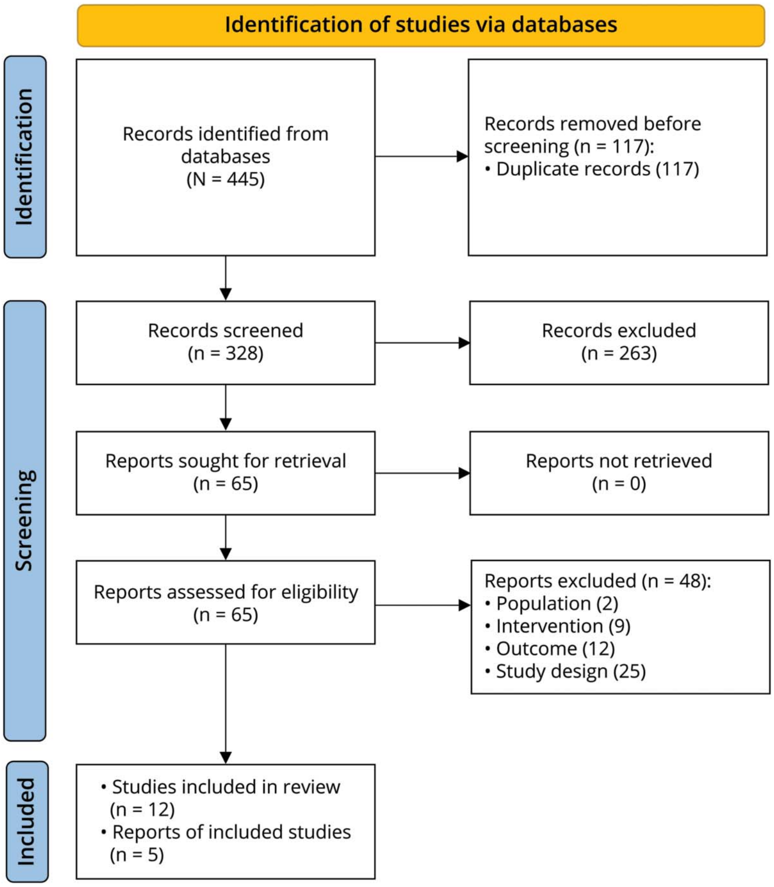
Inclusion and Exclusion Criteria

For studies to be included, the study population criteria were aged 16 years or older, diagnosed with IIH, and with a baseline BMI ≥25 kg/m^2. Studies were included if a weight management intervention was provided and weight change between preintervention and postintervention was reported. Reviews, expert opinions, case reports, and conference proceedings were excluded.

Papers Selection and Data Extraction

Two reviewers (S.A. and S.P.M.) independently and in duplicate screened titles and abstracts and then screened full-text reports for all identified studies. Reviewers were masked to each other's responses until each screening stage was complete, using Covidence. Disagreement was resolved by consensus between reviewers.

Figure PRISMA Flowchart



PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Data Extraction

Study characteristics were documented, and the criteria to which the participants were diagnosed with IIH were recorded. The primary outcome of interest in this systematic review was weight change, measured by absolute weight (in kilograms or %), excess weight (%) (calculated by absolute weight loss/[baseline weight − ideal body weight] × 100), or absolute BMI (kg/m^2) change. The secondary outcomes were changes in ICP, visual and headache outcomes, and self-reported quality of life measures (e.g., Short Form-36 [SF-36] Health Survey[18]). Specifically for visual outcomes, we documented visual acuity, visual field type and output, papilledema, and whether it was subjectively graded or quantified by optic coherence tomography (OCT) imaging. Headache outcomes included headache symptoms, headache phenotype assessment type, Headache Impact Test (HIT)-6, headache frequency, severity score, and analgesic usage. Data were extracted by one reviewer (S.A./S.P.M./F.C.) and peer reviewed by the another (S.A./S.P.M./F.C.), using an electronic data extraction form.

Data Analysis

Because the included studies were diverse, heterogeneity between studies for interventions, duration of follow-up, and method of outcome measurement precluded pooling of results with meta-analysis. Instead, a narrative synthesis approach was used to synthesize the findings from included studies.

Quality of Evidence

The quality and risk of bias of the included studies was assessed at the study level, and each study was assigned an evidence level for weight loss, ICP, headache, and visual outcomes, based on Scottish Intercollegiate Guidelines Network (SIGN) methodology[19] (eAppendix 2, links.lww.com/WNL/D148), by 2 independent reviewers (S.A. and S.P.M.).

Practice Recommendations

The process of SIGN methodology[19] (eAppendix 2, links.lww.com/WNL/D148) was followed to formulate evidence-based clinical recommendations. A multidisciplinary recommendation panel was formed of relevant professional groups with experience and expertise in IIH and weight management. The recommendation panel included a dietitian (S.A.), clinical psychologist (F.E.J.C.), endocrinologist (A.A.T.), bariatric surgeons (D.J.P., C.P.), neurologists (A.J.S., F.C.), neuro-ophthalmologists (S.P.M., S.W.), and a patient representative (A.D.). The expert panel convened to discuss the

Table 1 Study Design

Study	Setting	Study design	Inclusion criteria: IIH diagnosis	Inclusion criteria: Disease state	Inclusion criteria: Other	Exclusion criteria
Abdelbaki and Gomaa, 2020[27]	Egypt, single-center	Prospective cohort	—	—	Laparoscopic sleeve gastrectomy March 2016–March 2018 (BMI >40 or BMI >35 and at least 1 obesity related comorbidity)	
Ang et al., 2021[5]	Australia, multicenter	Retrospective cohort	Modified Dandy Criteria[53]	—	—	Incomplete weight records <3 follow-up visits
Egan et al., 2011[23]	UK, single-center	Prospective cohort	Neurologist diagnosis		Bariatric surgery database 2005–2011	
Glueck et al., 2006[25]	USA, multicenter	Nonrandomized interventional	Friedman Criteria (2002)[50]	—	Conventional pharmacotherapy treatment (acetazolamide, furosemide, or topiramate) Minimum 6 mo of follow-up on MET-diet combination or diet alone BMI >25	Previous shunt-fenestration surgery for IIH No evidence for IIH associated with secondary causes (Behcet disease, hypervitaminosis A, minocycline, recombinant human growth hormone therapy, or connective tissue disease)
Hermes et al., 2022[22]	Global, multicenter	Cross-sectional, retrospective	Revised Friedman Criteria (2013)[54]	—	Intracranial Hypertension Registry	Incomplete questionnaires Inadequate medical records to allow confirmation of IIH diagnosis Secondary intracranial hypertension Diagnosis during childhood Any bariatric surgery before IIH diagnosis Participants with >1 type of bariatric surgery Asymptomatic IIH <4 y of follow-up
Koc et al., 2018[26]	Turkey, single-centre	Retrospective, noninterventional, cross-sectional cohort	Modified Dandy Criteria[53]	—	Treatment for IIH limited to weight reduction and/or acetazolamide use only Single LP performed Consistent ophthalmic examination records and weight measurements throughout study period BMI >25 kg/m2 Referral to dietitian for weight reduction	Medications associated with raised ICP
Lainas et al., 2020[28]	France, multicentre	Prospective cohort (retrospective analysis)	Revised Friedman Criteria (2013)[54]	—	Laparoscopic sleeve gastrectomy (BMI >40 or BMI >35 and at least 1 obesity related comorbidity despite lifestyle and behavioral modifications with comprehensive motivation for surgery)	
Mollan et al., 2021[20] **Mollan et al. 2022**[7]	UK, multicentre	Randomized control trial	Revised Friedman Criteria (2013)[54]	Active disease Baseline LPOP >25 cm H_2O Papilledema at baseline	BMI >35 Weight gain	Previous optic nerve sheath fenestration
Sinclair et al., 2010[6] **Mulla et al., 2015**[30]	UK, multicentre	Nonrandomized, cross-over interventional	Dandy Criteria[51]	Active disease (LPOP >25 cm CSF, papilledema)	Disease duration of 3 mo	Previous CSF diversion Previous optic nerve sheath fenestration
Skau et al., 2011[29]	Denmark, single-centre	Prospective cohort	ICHD-II (Criteria B)[52]		>18 y LPOP >25 if BMI >30 LPOP >20 if BMI <30	Concurrent significant Medical disease Psychiatric disorders Ocular conditions

Continued

Table 1 Study Design *(continued)*

Study	Setting	Study design	Inclusion criteria			Exclusion criteria
			IIH diagnosis	Disease state	Other	
Sugerman et al., 1999[24]	USA, single-centre	Nonrandomised interventional	Persistent, severe headache, negative brain imaging study, and elevated CSF pressures (>20 cm H_2O)		Bariatric surgery (BMI >35 with severe obesity comorbidity or BMI >40)	
Wall et al., 2014[33] Weil et al., 2016[32] Friedman et al., 2017[31]	USA/ Canada, multicentre	Randomised control trial	Modified Dandy Criteria[53]	Active disease (elevated LPOP, papilledema)	Reproducible mild visual loss (−2 to −7 dB perimetric mean deviation)	Treated for IIH

Abbreviations: BMI = body mass index; ICHD-II = International Classification of Headache Disorders, 2nd edition; ICP = intracranial pressure; IIH = idiopathic intracranial hypertension; LP = lumbar puncture; LPOP = lumbar puncture opening pressure; MET = metformin.

evidence base identified from the systematic review and formulate draft recommendations. The draft recommendations together with their grading were circulated within the guideline group in an iterative process until consensus was achieved. Where an evidence base was lacking, good practice points (GPPs) were formulated to provide clinicians with short pieces of advice that the recommendation panel deemed was essential to good clinical practice.

Results

After removal of duplicates, database searches yielded 328 studies. Of these, 263 were excluded based on their titles and abstracts. Forty-seven publications were then excluded after full-text review, due to participants having BMI <25 kg/m^2 (n = 2), study design (n = 25), weight change not reported (n = 12), and the absence of weight loss intervention (n = 8). A total of 17 studies were included, of which 12 studies[5,6,20-29] were original studies and 5 studies[7,30-33] were reports of included studies. The study selection process is presented in Figure.

Study Characteristics

Study characteristics can be found in Table 1. There were 6 studies[7,20,21,31-33] of randomized control trials (RCTs), 4 prospective nonrandomized interventional studies,[6,24,25,30] and 2 prospective[27,29] and 4 retrospective observational studies.[5,22,23,26,28] Prescribed concomitant IIH pharmacotherapy is presented in eTable 1 (links.lww.com/WNL/D149).

Participant Characteristics

There were a total of 496 patients included in this review, and studies generally had small sample sizes, ranging from 4 to 165 participants (Table 2). Most studies (n = 10) included only female participants in their inclusion criteria. Only 7 studies included male participants,[5,21,26,29,31-33] who were the minority of the study populations (ranging from 2.4% to 7.7%), and no male participants received a bariatric surgery intervention. The mean age of participants ranged between 27 and 39 years, and the mean baseline BMI ranged between 36 and 47 kg/m^2. Participants undergoing bariatric surgery also had a higher mean BMI (range 42.1–47.0 kg/m^2) than lifestyle interventions (30.6–40.0 kg/m^2). In the 9 studies that reported ethnicity,[6,7,20-22,25,30-33] most participants were White (range 65%–94%). Nine studies[6,7,20,21,27,30-33] recorded or defined the IIH disease duration, with a wide range from acute disease within 6 weeks of diagnosis to established disease beyond 11 years.

Weight Loss Interventions

Eight studies (n = 122 participants) reported on bariatric surgery interventions, including gastric band[7,20,22-24,34] (n = 6 studies), sleeve gastrectomy[7,20,22,27,28,34] (n = 6 studies), and gastric bypass[7,20,22,24,34] (n = 5 studies). Twelve studies reported on lifestyle weight management interventions (n = 374 participants), of which 4 studies[6,25,29,30] were dietary interventions alone, 7 studies[20,21,26,31-34] were multicomponent interventions (diet + physical activity + behavioral interventions), and in 1 study[5] patients independently sourced a weight management intervention of their choosing (eTable 1, links.lww.com/WNL/D149).

Weight Loss Outcomes

In studies where outcomes were pooled across bariatric surgery procedures (gastric band, gastric bypass, and sleeve gastrectomy), the mean weight loss was 27.2–27.8 kg at 24 months (Level 1− to 1++[20,34]) (Table 3). However, where weight loss outcomes were reported at the procedure level, the greatest weight loss was seen for gastric bypass procedures (n = 37 participants) with a significant weight reduction of 42.5–45.0 kg at 12–24 months and excess weight loss of 69.9%–71.0% at 24 months to a median of 91 months (Level 2− to 1−[7,22,24]). Sleeve gastrectomy (n = 42 participants)

Table 2 Baseline Participant Characteristics

Study	n	Sex	Female, n (%)	Age, y	BMI	Ethnicity, n (%)
Abdelbaki and Gomaa, 2020[27]	16	Female only	16 (100.0)	31 (SD 2)	46 (SD 4)	—
Ang et al., 2021[5]	39	Female Male	37 (94.9)	Median 35.0 (IQR 10.5)	36.0 (SD 7.6)	—
Egan et al., 2011[23]	4	Female only	4 (100.0)	Mean 32 (range 29–39)	Mean 46.1 (38.2–54)	—
Glueck et al., 2006[25]	36	Female only	36 (100.0)	35 (SD 9)	Diet: 37.2 (SD 8.1) PCOS: 38.2 (SD 5.7) Hyperinsulinemia: 36.8 (SD 5.5)	White: 34 (94.4), Black: 2 (5.6)
Hermes et al., 2022[22]	30	Female only	30 (100.0)	37.3 (SD 7.3)	Median 45 (IQR 7.2)	White: 28 (93.3), Black: 1 (3.3), other: 1 (3.3)
Koc et al., 2018[26]	19 20	Female Male	18 (94.7) 18 (90.0)	36.5 (SD 0.5) 39.6 (SD 1.7)	32.6 (SD 0.6) 32.4 (SD 0.1)	—
Lainas et al., 2020[28]	15	Female only	15 (100.0)	Median 31 (range 22–53)	Median 42.1 (36.7–53.5)	—
Mollan et al., 2021[20] **Mollan et al., 2022[7]** **Yiangou et al., 2022[34]**	66	Female only	66 (100.0)	32.0 (SD 7.9)	Mean Lifestyle: 43.7 (7.1) Surgical: 44.2 (7.1)	White: 55 (83.3), Black: 5 (7.6), South Asian: 1 (1.5), mixed: 5 (7.6)
Sinclair et al., 2010[6] **Mulla et al., 2015[30]**	25	Female only	25 (100.0)	34.4 (SD 9.2)	38.2 (SD 5)	White: 20 (80), Black: 3 (12), South Asian: 2 (8)
Skau et al., 2011[29]	37	Female Male	16 (94.1) Controls 19 (95%)	27.2 (SD 8.2)	36.1 (SD 7.4)	—
Sugerman et al., 1999[24]	24	Female only	24 (100.0)	34.0 (SD 10)	47.0 (SD 6)	—
Wall et al., 2014[33] **Weil et al., 2016[32]** **Friedman et al., 2017[31]**	165	Female Male	161 (97.6)	Acetazolamide: 28.2 (SD 6.9) Placebo: 30.0 (SD 8.0)	Mean Acetazolamide: 40.0 (SD 8.5) Placebo: 39.9 (SD 8.1)	White: 108 (65), Black: 41 (25), Other: 16 (10)

Abbreviations: BMI = body mass index; IQR = interquartile range; PCOS = polycystic ovary syndrome.

resulted in weight loss of 32.2–39.0 kg at 12–24 months (Level 3 to 1–[7,28]). Excess weight loss ranged from 75.2% to 87.4% at 12 months (Level 3[27,28]) and 40.2% excess weight loss at a median follow-up of 68 months (Level 2–[22]); statistical significance was not reported. Weight loss outcomes after gastric banding (n = 27 participants) varied. In one study, a mean 1.0 kg weight gain observed 24 months post-gastric band procedure (Level 1–[7]). In other studies, excess weight loss was 64.1% at a mean of 20 months and a lesser 27.1% at a median of 108 months (Level 3 to 2–[22,23]), although statistical significance was not reported for either study.

At 24 months (Level 1–[7]), gastric bypass was shown to result in the greatest weight loss (in kilograms) compared with both sleeve gastrectomy and gastric band ($p \le 0.001$) at 24 months. At longitudinal follow-up (Level 2–[22]), weight loss was greater for gastric bypass (median follow-up of 91 months) compared with gastric banding (median follow-up of 108 months) ($p = 0.007$), but there was no difference between gastric bypass and sleeve gastrectomy (median follow-up of 68 months) ($p = 0.069$).

The greatest weight loss with a lifestyle intervention was reported using a very low-energy diet (VLED) dietary intervention with a 15.7 kg at 3 months (Level 2+[6]). Short-term dietary interventions resulted in modest reductions in BMI of 2.0–2.3 kg/m^2 at 3–6 months (Level 2– to 2+[26,29]). At a median of 10–11 months of follow-up of a dietary intervention, weight loss was not significant; however, the addition of 2.25 g/d of metformin led to a mean weight loss of 6.9% and 8.2% in patients with hyperinsulinaemia and polycystic ovary syndrome, respectively (Level 2+[25]). A 6-month multicomponent intervention resulted in a mean weight loss of 3.5 kg and 7.5 kg for multicomponent intervention only and multicomponent intervention + acetazolamide, respectively (Level 2+[31-33]). A 12-month multicomponent intervention did not result in significant weight loss at either 12 or 24 months of follow-up (Level 1– to 1++[20,34]).

Table 3 Weight Loss Outcomes

Study	Time, mo	Excess weight loss (%), *p* value	Weight loss (kg), *p* value	Total weight loss (%), *p* value	BMI loss (kg/m²), *p* value	Evidence level
Nonsurgical (patient choice)						
Ang et al., 2021[5]	24.7 (SD 13.5)	—	10 (IQR 8), <0.001	—	—	3
Nonsurgical (diet only)						
Glueck et al., 2006[25]	10.0 (SD 1.9)[a] 11.0 (SD 2.5)[b] 10.1 (SD 3.2)[c]	—	—	3.9 (SD 6.7), 0.13[a] 8.2 (SD 6.9), 0.0015[b] 6.9 (SD 9.0), 0.04[c]	—	2+
Koc et al., 2018[26]	6	—	—	—	2.0 (SD 3.1), NR	2−
Sinclair et al., 2010[6] **Mulla et al., 2015**[30]	3	—	15.7 (SD 8.0), <0.001	15.3 (SD 7.0), <0.001	—	2+
Skau et al., 2011[29]	3	—	—	—	2.3 (SD NR), 0.005	2+
Nonsurgical (multicomponent)						
Mollan et al., 2021[20]	12	—	2.1 (SE 2.0), 0.29	—	0.7 (SE 0.7), 0.35	1++
Mollan et al., 2021[20]	24	—	1.4 (SE 2.2), 0.53	—	0.4 (SE 0.8), 0.62	1++
Yiangou et al., 2022[34]	24	—	0.1 (95% CI 11.8 to −4.0), 0.756	—	−0.1 (95% CI 1.3 to −4.0), 0.824	1−
Wall et al., 2014[33] **Friedman et al., 2017**[31] **Weil et al., 2016**[32]	6	—	3.45 (SD NR)[d] 7.50 (SD NR)[e]	—	—	2+
Surgical (pooled procedures)						
Mollan et al., 2021[20]	12	—	23.4 (SE 1.9), <0.001	—	8.5 (SE 0.7), <0.001	1++
Mollan et al., 2021[20]	24	—	27.8 (SE 2.1), <0.001	—	10.4 (SE 0.8), <0.001	1++
Yiangou et al., 2022[34]	24	—	27.2 (95% CI 34.7–16.8), 0.012	—	9.3 (95% CI 12.6–5.6), 0.012	1−
Surgical (gastric band)						
Egan et al., 2011[23]	19.8 (SD NR)	64.1 (SD NR), NR	33.7 (SD NR), NR	—	12.7 (SD NR), NR	3
Hermes et al., 2022[22]	108 (IQR 48)	27.1 (IQR 40.6), NR	—	14.5 (IQR 17.0), NR	—	2−
Mollan et al., 2022[7]	24	—	−1.0 (SE 5.7), 0.868	—	0.0 (SE 2.1), 0.985	1−
Surgical (gastric bypass)						
Hermes et al., 2022[22]	91 (IQR 59)	69.9 (IQR 28.3), NR	—	34.7 (IQR 17.1), NR	—	2−
Mollan et al., 2022[7]	24	—	42.5 (SE 2.8), <0.001	—	16.0 (SE 1.0), <0.001	1−
Sugerman et al., 1999[24,f]	12	71.0 (SD 18), <0.001	45.0 (SD 12), <0.001	—	—	2−
Surgical (sleeve)						
Abdelbaki and Gomaa, 2020[27]	12	75.2 (SD 2.0), NR	—	—	—	3
Hermes et al., 2022[22]	68 (IQR 8)	40.2 (IQR 25.0), NR	—	24.9 (IQR 11.4), NR	—	2−
Lainas et al., 2020[28]	12	87.4 (SD 9.4), NR	39.0 (IQR NR), 0.003	37.3 (SD 5.2), NR	14.4 (IQR NR), 0.003	3
Mollan et al., 2022[7]	24	—	32.2 (SE 4.6), <0.001	—	11.8 (SE 1.7), <0.001	1−

Abbreviations: IQR = interquartile range; PCOS = polycystic ovary syndrome; NR = not reported.
[a] Diet alone.
[b] Diet + metformin (PCOS).
[c] Diet + metformin (hyperinsulinemia).
[d] Placebo.
[e] Acetazolamide.
[f] Eleven of 12 participants had gastric bypass, negative values indicate weight gain.

Intracranial Pressure Outcomes

While 10 studies recorded baseline ICP measured by lumbar puncture opening pressure[5,6,20,21,24,27-29,33] (Table 4), only 3 studies[6,20,33] measured change in ICP after weight management intervention. Bariatric surgery offered the greatest mean reduction (−11.9 cm H_2O) in ICP at 24 months (Level 1++[20]), followed by a 6-month multicomponent lifestyle intervention + acetazolamide (−11.2 cm

Table 4 ICP Outcomes

	Intracranial pressure baseline measure, mean (SD), n (cm H_2O)	Intracranial pressure at end point, mean (SD), n (cm H_2O)	Time of end point	Difference (cm H_2O)	*p* Value	Notes	Level of evidence
Lifestyle intervention							
Abdelbaki and Gomaa, 2020[27]	41.2 (21), 16 (range 30–64)	—	—	—	—	—	Not graded
Ang et al., 2021[5]	Median (range), n 30 (5.5), 39	—	—	—	—	—	Not graded
Glueck et al., 2006[25]	—	—	—	—	—	—	Not graded
Koc et al., 2018[26]	32.2 (8.0), 19 34.6 (8.4), 20	—	—	—	—	—	Not graded
Mollan et al., 2021[20]	34.6 (5.6), 33	32.0 (5.2), 25	12 mo	Mean (SE) [95% CI] −2.5 (1.4) [−5.2 to 0.3]	0.084	—	1++
Mollan et al., 2021[20]	34.6 (5.6), 33	31.0 (5.7), 18	24 mo	Mean (SE) [95% CI] −3.5 (1.6) [6.6 to −0.3]	0.03	—	1++
Skau et al., 2011[29]	Median (range), n 31.0 (23.4 to >50), 13	Median (range), n 24.0 (20.2–42.5), 13	3 mo	Not reported	0.02	There was a positive linear association between proportional change in BMI and ICP (5.2 cm $H_2O/[m^2/kg]$), *p* = 0.0002	2++
Sinclair et al., 2010[6]	38.0 (5.0), 37	30.0 (4.9), 20	3 mo	Mean (SD) −8.0 (4.2)	<0.001	—	2++
Wall et al., 2014[33] Acetazolamide Placebo	34.9 (94.1), 86 34.2 (70.7), 79	24.5, 47 30.5, 38	6 mo	Mean −11.2 −5.2	—	Treatment effect −6.0 [95% CI −9.6 to 2.3] *p* = 0.002	1+
Surgical intervention							
Egan et al., 2011[23]	Not reported	—	—	—	—	—	Not graded
Hermes et al., 2022[22]	Not reported	—	—	—	—	—	Not graded
Lainas et al., 2020[28]	Median (range) 31 (25–50)	Not reported	—	—	—	—	Not graded
Mollan et al., 2021[20]	34.8 (5.8), 33	Mean (SD), n 26.9 (8.1), 18	2 wk	Mean (SE) [95% CI] −7.9 (2.0) [−11.8 to −4.0]	0.0002	—	1−
Mollan et al., 2021[20]	34.8 (5.8), 33	Mean (SD), n 26.4 (8.7), 29	12 mo	Mean (SE)[95% CI] −8.7 (1.3) [−11.3 to −6.1]	<0.001	—	1++
Mollan et al., 2021[20]	34.8 (5.8), 33	Mean (SD), n 22.8 (7.8), 22	24 mo	Mean (SE) [95% CI] −11.9 (1.5) [−14.8 to −9.0]	<0.001	—	1++
Sugerman et al., 1999[24]	32.4 (8.3) (range 23.0–52.0)	Not reported	—	—	—	—	Not graded

Abbreviations: BMI = body mass index; ICP = intracranial pressure.

H_2O) (Level 1+[33]), then a 3-month VLED (diet only) intervention (−8.0 cm H_2O) (Level 2++[6]), and then a 6-month multicomponent lifestyle intervention (−5.2 cm H_2O) (Level 1+[33]). The least ICP reduction was shown at 24 months after completing a 12-month multicomponent lifestyle intervention (−3.5 cm H_2O) (Level 1++[20]). Reduction in body weight was also shown to be highly correlated with reduction in ICP (Level 2++ to 1++[6,20]).

Visual Outcomes

Only 5 studies reported the visual acuity[6,20,26,29,33] (eTable 2, links.lww.com/WNL/D150). Five studies gave brief descriptions of visual field loss but did not detail the type of visual fields that were performed,[23-25,27,28] whereas 1 study did not report visual field outcomes.[20] Six studies reported the perimetric mean deviation (PMD) from the 24-2 Humphrey visual field (HVF) analyzer (Level 3 to 1+[5,6,20,26,29,33]). Five studies commented on the presence or absence of papilledema (Level 4[23,24,27,28]), whereas formal Frisén grading and OCT imaging were recorded in 6 studies (Level 2– to 1+[6,20,26,29,31,33]).

Only 1 study[6] noted significant improvements in visual acuity, low-contrast visual acuity, HVF, and OCT measures of papilledema with a 15% reduction in weight (Level 2++). Generally, visual parameters improved over time; however, when a direct comparison was made in between groups, there was no significance found in most studies (eTable 2, links.lww.com/WNL/D150). In IIH Treatment Trial (IIHTT),[33] there was a modest, but statistically significant, improvement in the visual field MD, in conjunction with a significant difference in the weight loss between those on placebo and multicomponent intervention and those in the acetazolamide and multicomponent intervention arm (acetazolamide −7.50 kg, from 107.72 kg to 100.22 kg; placebo −3.45 kg, from 107.72 kg to 104.27 kg; treatment effect −4.05 kg, 95% CI −6.27 to −1.83 kg; $p < 0.001$) (Level 1+). A mediation analysis of the primary outcome PMD was performed to determine the degree to which the effect of acetazolamide on PMD was mediated by its effect on weight, but this was found to be not significant ($p = 0.64$). The IIHTT and IIH Weight Trial (IIHWT) RCTs[3,33] therefore did not find visual parameters that were directly associated with the extent of weight loss (Level 2+ to 1+), and all the other studies reporting visual outcomes did not directly compare changes in visual outcomes with weight outcomes (Level 4 to Level 2++).

Headache Outcomes

Few studies provided detailed headache outcomes (Level 2++ to 2+, eTable 3, links.lww.com/WNL/D151). Only 1 study[6] noted significant reduction in headache frequency, severity, analgesic use, and HIT-6 scores with VLED also delivering a 15% reduction in weight at 3 months (Level 2++[6]). In the 2 RCTs,[20,31] there was no supporting evidence of a significant reduction of headache after weight loss (Level 2++ to 2+). Notably in the IIHTT study,[31] there was no correlation between headache burden, as assessed by HIT-6, and BMI at either baseline or subsequent follow-up at 6 months (Level 2+).

Quality of Life Outcomes

Only 2 studies[20,30] reported on quality of life; both used the SF-36 Health Survey[18] (Level 1++). After bariatric surgery,[20] there were significant improvements in physical ($p \leq 0.001$) but not mental component scores at 24 months (Level 1++). Immediately after a 3-month VLED (diet alone) intervention,[30] there was a significant improvement in both the physical ($p \leq 0.001$) and mental ($p = 0.020$) component scores (Level 2+). However, this improvement was not sustained at 3 months after the VLED intervention had ended.

Mental Health Outcomes

Only 1 study[20] reported changes in self-reported anxiety and depression, assessed using the Hospital Anxiety and Depression Scale.[35] There was no significant change in anxiety in either the multicomponent lifestyle intervention or bariatric surgery intervention groups; however, there was a significant ($p = 0.002$) reduction in depression scores (−2.7; 95% CI −1.0 to −4.4) at 24 months in the bariatric surgery intervention group only (Level 1++).

Graded Recommendations for Clinical Practice

The expert panel identified consensus-based recommendations for weight management in people with IIH based on the evidence identified within the systematic review and graded according to the quality of available evidence. Where evidence was not available for IIH populations, GPPs were formulated based on evidence extrapolated from obesity literature. The graded recommendations are presented in Table 5.

Discussion

The recommendation to treat overweight and obesity in people living with IIH is not only because weight loss reduces ICP but also that it reduces mortality[36] and reduces the burden of prevalent and incident obesity-related complications.[36] Weight loss is recognized as a modifiable factor in the treatment of IIH. This study sought to determine the optimal weight loss intervention for IIH, which was identified as research priority by the James Lind Alliance Priority Setting Partnership.[16] The panel made graded recommendations based on the evidence identified by this systematic review and detailed clinical guidance in GPPs from the obesity literature (Table 5).

Although there was 1 RCT demonstrating Level 1++ evidence for the directed use of bariatric surgery with sustained weight loss and reduction in ICP to 24 months[19] and 1 cross-over study (Level 2+) using a VLED for 3 months, which demonstrated efficacy for ICP, visual, and headache outcomes, these 2 studies have not been replicated. The results of this analysis therefore demonstrated the shortage of high-quality evidence because there were no studies that could be directly compared due to different weight management methods being used and a lack of standardized outcome measures.

Sustained long-term weight loss should be considered as a tool to improve the health and quality of life of patients with IIH. Patients with IIH with overweight or obesity should be counseled sensitively about the role of obesity and weight management in IIH. They should have their weight measured and BMI calculated to assess the weight management options and monitor the intervention efficacy. Although there are no RCTs that evaluated the measurement of overweight and obesity compared with not measuring these outcomes, the panel agreed that this aspect of IIH patient care was essential.

The degree of weight loss required for IIH symptom improvement was less clear as studies reported the amount of weight lost with a variety of outcome measures. There were no studies evaluating the time where the minimum amount of weight lost was correlated with the point of disease remission. Level 2+ evidence demonstrated that a reduction of

Table 5 Graded Recommendations for Weight Management in IIH

Recommendations	Grade (EL range)
Assessment	
Screen for OSA routinely using STOP-BANG due to the high prevalence of OSA in adults living with IIH	B (EL 1−)
Sleep studies for OSA should be considered at a low threshold of STOP-BANG score	B (EL 1−)
Screen for overweight and obesity by taking weight and height measurements to calculate BMI. Repeat measurements should be taken to determine long-term weight trajectory and effectiveness of weight management treatment	GPP
Obtain a complete drug history. Antipsychotic medications can cause weight gain and precipitate IIH. Where a temporal relationship is noted between weight gain and a causative medicine, the clinical team should discuss this with the mental health team and patient	GPP
Goal for weight loss and weight maintenance	
Discuss sensitively with patients that obesity is a complex metabolic disorder and weight management has been shown to improve some symptoms of IIH and may support IIH disease remission	GPP
Discuss with patients that the goal of weight management is to maintain a lower body weight over the long term	GPP
Counsel patients that obesity is a chronic, relapsing disease, and therefore, total lifelong remission from obesity may not be achievable	GPP
Advise patients that weight loss of 15%–24% contributes to IIH disease remission; however, counsel patients that this may only be achieved through intervention with bariatric surgery	C (EL 2+)
Advise patients a multicomponent lifestyle intervention (dietary therapy + physical activity + behavior) is an alternative treatment that may support a more modest weight loss of up to 5%–10%	GPP
Lifestyle	
Advise patients that a multicomponent intervention (diet + physical activity + behavior) may be effective in the medium-term (up to 6 mo) for modest weight loss, but weight loss may not be maintained in the longer term (>24 mo)	B (EL 1++ to 2+)
Advise patients that dietary approaches alone that create an energy deficit of 500–1,000 kcals/d may be effective in the short term for modest weight loss (up to 6 mo)	C (EL 2+)
Only recommend VLEDs of <800 kcals/d if the patient will have access to intensive dietary support and if the patient presents with immediate risk of worsening papilledema	C (EL 2+)
Pharmacotherapy	
Acetazolamide in conjunction with a multicomponent lifestyle intervention may support weight management; however, this may be due to side effects of the medication which can cause dysgeusia	B (EL 1+)
Metformin in conjunction with a multicomponent lifestyle intervention in patients with IIH and PCOS may support weight management	C (EL 2+)
GLP-1 RA licensed for weight management may be useful in immediate management of IIH requiring weight loss; however, cessation of GLP-1 RA is demonstrated to result in weight regain and therefore should be considered a long-term intervention. If GLP-1 RA is only prescribed short term, patients should be counseled that weight regain is likely once the medication is stopped	GPP
Topiramate prescribed for IIH may result in weight loss due to side effects appetite reduction; however, this should not be prescribed solely for the purpose of weight loss	GPP
Bariatric surgery	
For women living with IIH and a BMI >35 kg/m^2, bariatric surgery should be considered	A (EL 1++)
For men living with IIH and a BMI >35 kg/m^2, bariatric surgery should be considered	GPP
When considering selection of bariatric surgical procedure, a gastric bypass or sleeve gastrectomy may be preferential	C (EL 1− to 3)
Bariatric surgery may be considered as an early intervention for IIH as ICP has been demonstrated to reduce at 2 wk after the procedure	C (EL 2++)
Patients with active IIH may warrant priority referral for bariatric surgery given the importance of weight loss and maintenance in the disease	GPP
A multidisciplinary assessment of patient suitability for bariatric surgery should be undertaken by a bariatric specialist unit	GPP

Abbreviations: EL = evidence level; GLP-1 RA = glucagon-like peptide-1 receptor agonist; GPP = good practice point; ICP = intracranial pressure; IIH = idiopathic intracranial hypertension; OSA = obstructive sleep apnea; PCOS = polycystic ovary syndrome; VLED = very low-energy diet.

weight between 15% and 24% was required to achieve disease remission. In the VLED cross-over study, 15% of body weight loss was correlated with reduction in ICP, resolution of papilledema, and favorable headache outcomes,[6] and the IIHWT disease remission was defined as ICP to return to normal levels at 25 cm H_2O.[7] It is therefore important to acknowledge that while some lifestyle interventions delivered in the community setting may be effective for weight loss,[37] they may not deliver the magnitude of weight loss required to induce remission of IIH. The panel considered this evidence and recommended the target weight loss should be 15% for IIH disease remission. However, the panel acknowledged that this goal is unlikely to be achieved through a lifestyle intervention alone, and a realistic goal may be 5%–10% weight loss,[38] which may still offer some improvement in IIH symptoms.

There were no studies evaluating solely physical activity interventions in IIH. Physical activity could be recommended as part of a weight control program because it may contribute to maintenance of weight loss.[39] Behavior therapy has been shown to be a useful adjunct when incorporated into treatment for weight loss and weight maintenance.[40] Licensed antiobesity medications did not feature in this study because there were no studies with primary aims of using pharmacotherapy for weight loss in IIH. It was noteworthy that there was inadvertent evidence for the beneficial effect of acetazolamide on weight reduction.[31] Carbonic anhydrase inhibitors, such as acetazolamide and topiramate, and to a lesser extent zonisamide, are used to manage IIH[1] and have previously been clinically observed to reduce weight. The method by which acetazolamide causes weight loss could be due to the propensity to cause dysgeusia (a salty, rancid, or metallic taste sensation that persists in the mouth), nausea, dyspepsia, vomiting, and diarrhea. Acetazolamide is not well tolerated in this patient group with up to 40% of people discontinuing the medicine.[41] In our systematic review, it was interesting to observe the magnitude of reduction of weight and ICP at 6 months after the directed use of acetazolamide.[33]

Bariatric surgery had the greatest sustained weight loss up to 24 months.[20] Clinicians managing IIH may be reluctant to refer patients for bariatric surgery because of funding access and misconceptions regarding the safety of bariatric surgery, such as operative mortality, excess skin, and nutritional optic atrophy. Physicians may be concerned about CSF shunting and subsequent bariatric surgery; however, bariatric surgery has been shown to be safer and more cost-effective than CSF shunting.[42]

Gastric bypass and sleeve gastrectomy surgical procedures were superior to gastric banding for weight loss and ICP reduction in people with IIH. For obesity, gastric bypass has been found to be the most clinically effective and most cost-effective intervention compared with other weight management programs and has the highest quality-adjusted life year gains.[43] Superiority of gastric bypass over sleeve gastrectomy in IIH may be explained by the enhanced postprandial glucagon-like peptide-1 (GLP-1) secretion, as emerging data found that exogenously administered GLP-1 significantly reduces ICP without weight loss.[44]

Another key consideration when understanding the impact of an intervention is the natural history of the disease, including disease duration. This could have an impact on outcomes; for example, in people who have had the disease for many years, it may not be possible to reverse visual loss that has occurred due to axonal loss, and hence, in studies with long disease duration, the visual field measures may not improve.[45] Similarly, papilledema may acutely be present and without intervention may regress to the mean.

Strengths of this study include the methodological rigor of the systematic review, which was prospectively registered on PROSPERO, and all screening, data extraction, and quality assessment were blinded and conducted by 2 reviewers. The evidence was translated into clinical recommendations which were made by multidisciplinary experts in obesity and IIH, hence supporting the translation of the research for clinical application. There are certain limitations to this study. The included studies all used different outcome measures and a variety of weight loss methods. This meant that meta-analysis was not able to be performed because of study heterogeneity. This heterogeneity in IIH studies evaluating weight loss methods needs to be considered when planning future clinical trials in IIH. We also only included published studies, which means there was potential for publication bias. As meta-analysis was precluded, it was not appropriate to quantify any potential publication bias using funnel plot.[46]

The study populations of our included studies were predominately female population and a reflection of IIH being less prevalent in male population[47]; however, the findings are therefore not generalizable to male population. Specifically, there is a need for research to examine the effectiveness of bariatric surgery in IIH in a male population and for both genders at a lower BMI of 30–35 kg/m^2. None of the studies included women who were pregnant, which is an area in need of evaluating, because it has been recommended that weight management in pregnancy should receive specialist weight management input.[44]

Most of the studies were of short duration, with only 1 study reporting outcomes longitudinally at 9 years. The longer the reporting period, the more missing data occurred. However, future studies should be encouraged to include long-term outcomes, to determine cost-effectiveness and intervention durability. People with IIH who have obesity, compared with healthy weight, have significantly lower health-related quality of life scores.[48] Moreover, obesity and weight gain have been found to be independent predictors of poorer mental health-related quality of life.[14] Psychiatric symptoms in association with IIH are usually poorly described and underestimated in the literature, but the prevalence is reported to be as high as 86%.[49] Given that psychiatric symptom control and can influence patients' engagement and adherence to weight management interventions and indeed IIH treatments, this requires investigation. Hence, future studies should collect quality of life and psychiatric outcome measures to evaluate the influence of weight management interventions and include long-term outcome data collection to assess durability of the intervention.

We advocate for obesity to be viewed as a chronic disease with complex contributory associations and prognostic implications to IIH, rather than merely a risk factor. Weight loss should be seen as an important tool in the management of IIH. The biological drivers of obesity may explain why short-term weight management interventions are often insufficient for long-term disease remission. The hierarchy of effect in weight loss methods seems to be analogous to the reduction of ICP, with bariatric surgery having the most robust evidence for effective treatment of obesity in the IIH population. However, not all patients will qualify for bariatric surgery intervention. In such case, multicomponent lifestyle interventions should be provided, but it should be acknowledged that weight loss is likely to be modest, and IIH disease remission is therefore unlikely but may still offer improvement in IIH symptoms.

Study Funding

IIH UK charity provided funding for the Open Access publication cost.

Disclosure

S. Abbott consultancy fees from Johnson & Johnson. A.A. Tahrani report Grants from Novo Nordisk and Sanofi; personal fees from Novo Nordisk, Janssen, AZ, Eli Lilly, BI, BMS, NAPP, MSD, Nestle, Gilead, Sanofi as well as nonfinancial support from Novo Nordisk, Eli Lilly, AZ, Impeto medical, Resmed, Aptiva, BI, BMS, NAPP, MSD. A.A. Tahrani is currently an employee of Novo Nordisk. Novo Nordisk had no involvement in this work. D.J. Pournaras has been funded by the Royal College of Surgeons of England. He receives consulting fees from Johnson & Johnson and payments for lectures, presentations, and educational events from Johnson & Johnson, Medtronic, and Novo Nordisk. A.J. Sinclair reports personal fees from Invex therapeutics in her role as Director with stock holdings, during the conduct of the study, other from Allergan, Novartis, Cheisi, and Amgen outside the submitted work. S.P. Mollan reports consulting fees from Invex Therapeutics, the Velux foundation, and Neurodiem; advisory board compensation from Janssen, Santhera, GenSight Biologics, and Chugai-Roche Ltd.; and speaker fees from Chiesi, Heidelberg engineering, Allergan, Chugai-Roche Ltd, Santen, Santhera, Roche, and Teva; and all conflicts of interest are outside the submitted work. All other authors declare no competing interests. Go to Neurology.org/N for full disclosures.

Publication History

Received by *Neurology* May 11, 2023. Accepted in final form August 15, 2023. Submitted and externally peer reviewed. The handling editor was Associate Editor Rebecca Burch, MD.

Appendix Authors

Name	Location	Contribution
Sally Abbott, MRes	Research Centre for Healthcare and Communities, Coventry University, United Kingdom	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data
Fiona Chan, MRCAP	Birmingham Neuro-Ophthalmology, University Hospitals Birmingham, United Kingdom	Drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data
Abd A. Tahrani, PhD	Institute of Metabolism and Systems Research, University of Birmingham, United Kingdom; Novo Nordisk, Bagsvaerd, Denmark	Analysis or interpretation of data
Sui Hsien Wong, MBBS, MD, FRCP	Department of Neuro-Ophthalmology, Moorfields Eye Hospital; Medical Eye Unit, Guy's and St Thomas' NHSFT, London; School of Life Course & Population Sciences, Kings College London; Department of Clinical and Movement Neurosciences, University College London, United Kingdom	Analysis or interpretation of data
Fiona E.J. Campbell, PhD	Adult Weight Management (Bariatric Surgery), NHS Grampian, United Kingdom	Analysis or interpretation of data
Chetan Parmar, FRCS	Department of Surgery, University College London Hospitals; Department of Surgery, Barts Health NHS Trust, London, United Kingdom	Analysis or interpretation of data
Dimitri J. Pournaras, PhD	Upper Gastrointestinal, Bariatric and Metabolic Surgery, North Bristol NHS Trust, United Kingdom	Analysis or interpretation of data
Amanda Denton, Msc	IIH UK, London, United Kingdom	Analysis or interpretation of data
Alexandra Jean Sinclair, PhD	Translational Brain Science, Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, United Kingdom	Analysis or interpretation of data
Susan P. Mollan, MBChB, FRCOphth	Birmingham Neuro-Ophthalmology, University Hospitals Birmingham NHS Trust, United Kingdom	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data

References

1. Mollan SP, Davies B, Silver NC, et al. Idiopathic intracranial hypertension: consensus guidelines on management. *J Neurol Neurosurg Psychiatry*. 2018;89(10):1088-1100. doi:10.1136/jnnp-2017-317440
2. Adderley NJ, Subramanian A, Nirantharakumar K, et al. Association between idiopathic intracranial hypertension and risk of cardiovascular diseases in women in the United Kingdom. *JAMA Neurol*. 2019;76(9):1088-1098. doi:10.1001/jamaneurol.2019.1812
3. Mollan SP, Mytton J, Tsermoulas G, Sinclair AJ. Idiopathic intracranial hypertension: evaluation of admissions and emergency readmissions through the hospital episode statistic dataset between 2002-2020. *Life*. 2021;11(5):417. doi:10.3390/life11050417
4. Szewka AJ, Bruce BB, Newman NJ, Biousse V. Idiopathic intracranial hypertension: relation between obesity and visual outcomes. *J Neuroophthalmol*. 2013;33(1):4-8. doi:10.1097/WNO.0b013e31823f852d
5. Ang JL, Teo KZ, Fraser CL. Weight loss in idiopathic intracranial hypertension: a retrospective review of outcomes in the clinical setting. *J Neuroophthalmol*. 2021; 41(4):e458-e463. doi:10.1097/WNO.0000000000001107
6. Sinclair AJ, Burdon MA, Nightingale PG, et al. Low energy diet and intracranial pressure in women with idiopathic intracranial hypertension: prospective cohort study. *BMJ*. 2010;341:c2701. doi:10.1136/bmj.c2701
7. Mollan SP, Mitchell JL, Yiangou A, et al. Association of amount of weight lost after bariatric surgery with intracranial pressure in women with idiopathic intracranial hypertension. *Neurology*. 2022;99(11):e1090-e1099. doi:10.1212/WNL.0000000000200839
8. Westgate CSJ, Botfield HF, Alimajstorovic Z, et al. Systemic and adipocyte transcriptional and metabolic dysregulation in idiopathic intracranial hypertension. *JCI Insight*. 2021;6(10):e145346. doi:10.1172/jci.insight.145346
9. Puustinen T, Tervonen J, Avellan C, et al. Psychiatric disorders are a common prognostic marker for worse outcome in patients with idiopathic intracranial hypertension. *Clin Neurol Neurosurg*. 2019;186:105527. doi:10.1016/j.clineuro.2019.105527
10. Kim YK, Na KS, Myint AM, Leonard BE. The role of pro-inflammatory cytokines in neuroinflammation, neurogenesis and the neuroendocrine system in major depression. *Prog Neuropsychopharmacol Biol Psychiatry*. 2016;64:277-284. doi:10.1016/j.pnpbp.2015.06.008
11. Loos RJF, Yeo GSH. The genetics of obesity: from discovery to biology. *Nat Rev Genet*. 2022;23(2):120-133. doi:10.1038/s41576-021-00414-z
12. Hall KD, Kahan S. Maintenance of lost weight and long-term management of obesity. *Med Clin North Am*. 2018;102(1):183-197. doi:10.1016/j.mcna.2017.08.012
13. Greenway FL. Physiological adaptations to weight loss and factors favouring weight regain. *Int J Obes*. 2015;39(8):1188-1196. doi:10.1038/ijo.2015.59
14. Daniels AB, Liu GT, Volpe NJ, et al. Profiles of obesity, weight gain, and quality of life in idiopathic intracranial hypertension (pseudotumor cerebri). *Am J Ophthalmol*. 2007;143(4):635-641. doi:10.1016/j.ajo.2006.12.040
15. Ko MW, Chang SC, Ridha MA, et al. Weight gain and recurrence in idiopathic intracranial hypertension: a case-control study. *Neurology*. 2011;76(18):1564-1567. doi:10.1212/WNL.0b013e3182190f51
16. Mollan S, Hemmings K, Herd CP, Denton A, Williamson S, Sinclair AJ. What are the research priorities for idiopathic intracranial hypertension? A priority setting partnership between patients and healthcare professionals. *BMJ Open*. 2019;9(3): e026573. doi:10.1136/bmjopen-2018-026573
17. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi:10.1136/bmj.n71
18. Ware JE, Gandek B. Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) project. *J Clin Epidemiol*. 1998;51(11):903-912. doi:10.1016/s0895-4356(98)00081-x
19. Scottish Intercollegiate Guidelines Network. *SIGN 50: A Guideline Developer's Handbook [online]*. SIGN; 2019. Accessed May 3, 2023. sign.ac.uk/media/2038/sign50_2019.pdf.
20. Mollan SP, Mitchell JL, Ottridge RS, et al. Effectiveness of bariatric surgery vs community weight management intervention for the treatment of idiopathic intracranial hypertension: a randomized clinical trial. *JAMA Neurol*. 2021;78(6):678-686. doi:10.1001/jamaneurol.2021.0659
21. Wall M, Kupersmith MJ, Kieburtz KD, et al. The idiopathic intracranial hypertension treatment trial: clinical profile at baseline. *JAMA Neurol*. 2014;71(6):693-701. doi:10.1001/jamaneurol.2014.133
22. Hermes S, Bharadwaj M, Miller N, et al. Long-term outcomes of bariatric surgery in idiopathic intracranial hypertension patients. *Neurologist*. 2023;28(2):87-93. doi:10.1097/NRL.0000000000000446
23. Egan R, Meredith H, Coulston J, Bennetto L, Morgan J, Norton S. The effects of laparoscopic adjustable gastric banding on idiopathic intracranial hypertension. *Obes Surg*. 2011;21(2):161-166. doi:10.1007/s11695-010-0307-8
24. Sugerman H, Felton W, Sismanis A, Kellum J, DeMaria E, Sugerman E. Gastric surgery for pseudotumor cerebri associated with severe obesity. *Ann Surg*. 1999; 229(5):634-640; discussion 640-642. doi:10.1097/00000658-199905000-00005
25. Glueck CJ, Golnik KC, Aregawi D, Goldenberg N, Sieve L, Wang P. Changes in weight, papilledema, headache, visual field, and life status in response to diet and metformin in women with idiopathic intracranial hypertension with and without concurrent polycystic ovary syndrome or hyperinsulinemia. *Transl Res*. 2006;148(5): 215-222. doi:10.1016/j.trsl.2006.05.003
26. Koc F, Isik MR, Sefi-Yurdakul N. Weight reduction for a better visual outcome in idiopathic intracranial hypertension. *Arq Bras Oftalmol*. 2018;81(1):18-23. doi:10.5935/0004-2749.20180006
27. Abdelbaki TN, Gomaa M. Outcome of idiopathic intracranial hypertension after laparoscopic sleeve gastrectomy. *Surg Obes Relat Dis*. 2020;16(9):1195-1201. doi:10.1016/j.soard.2020.03.032
28. Lainas P, El Soueidy T, Amor IB, et al. Laparoscopic sleeve gastrectomy for the treatment of idiopathic intracranial hypertension in patients with severe obesity. *Surg Obes Relat Dis*. 2020;16(12):1971-1977. doi:10.1016/j.soard.2020.07.034
29. Skau M, Sander B, Milea D, Jensen R. Disease activity in idiopathic intracranial hypertension: a 3-month follow-up study. *J Neurol*. 2011;258(2):277-283. doi:10.1007/s00415-010-5750-x
30. Mulla Y, Markey KA, Woolley RL, Patel S, Mollan SP, Sinclair AJ. Headache determines quality of life in idiopathic intracranial hypertension. *J Headache Pain*. 2015;16: 521. doi:10.1186/s10194-015-0521-9
31. Friedman DI, Quiros PA, Subramanian PS, et al. Headache in idiopathic intracranial hypertension: findings from the idiopathic intracranial hypertension treatment trial. *Headache*. 2017;57(8):1195-1205. doi:10.1111/head.13153
32. Weil R, Kovacs B, Miller N, et al. A 6-month telephone-based weight loss intervention in overweight and obese subjects with idiopathic intracranial hypertension. *Obes Sci Pract*. 2016;2:95-103. doi:10.1002/osp4.34
33. Wall M, McDermott MP, Kieburtz KD, et al. Effect of acetazolamide on visual function in patients with idiopathic intracranial hypertension and mild visual loss: the idiopathic intracranial hypertension treatment trial. *JAMA*. 2014;311(16):1641-1651. doi:10.1001/jama.2014.3312
34. Yiangou A, Mitchell JL, Nicholls M, et al. Obstructive sleep apnoea in women with idiopathic intracranial hypertension: a sub-study of the idiopathic intracranial hypertension weight randomised controlled trial (IIH: WT). *J Neurol*. 2022;269(4): 1945-1956. doi:10.1007/s00415-021-10700-9
35. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361-370. doi:10.1111/j.1600-0447.1983.tb09716.x
36. Ma C, Avenell A, Bolland M, et al. Effects of weight loss interventions for adults who are obese on mortality, cardiovascular disease, and cancer: systematic review and meta-analysis. *BMJ*. 2017;359:j4849. doi:10.1136/bmj.j4849
37. Madigan CD, Graham HE, Sturgiss E, et al. Effectiveness of weight management interventions for adults delivered in primary care: systematic review and meta-analysis of randomised controlled trials. *BMJ*. 2022;377:e069719. doi:10.1136/bmj-2021-069719
38. National Institute of Health and Care Excellence. *Weight Management: Lifestyle Services for Overweight or Obese Adults*. NICE; 2014. Accessed March 27, 2018. nice.org.uk/guidance/ph53/chapter/1-Recommendations.
39. Paixão C, Dias CM, Jorge R, et al. Successful weight loss maintenance: a systematic review of weight control registries. *Obes Rev*. 2020;21(5):e13003. doi:10.1111/obr.13003
40. LeBlanc ES, Patnode CD, Webber EM, Redmond N, Rushkin M, O'Connor EA. Behavioral and pharmacotherapy weight loss interventions to prevent obesity-related morbidity and mortality in adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2018;320(11):1172-1191. doi:10.1001/jama.2018.7777
41. Ball AK, Howman A, Wheatley K, et al. A randomised controlled trial of treatment for idiopathic intracranial hypertension. *J Neurol*. 2011;258(5):874-881. doi:10.1007/s00415-010-5861-4
42. Merola J, Selezneva L, Perkins R, Lang J, Barry J, Leach P. Cerebrospinal fluid diversion versus bariatric surgery in the management of idiopathic intracranial hypertension. *Br J Neurosurg*. 2020;34(1):9-12. doi:10.1080/02688697.2019.1698012
43. Boyers D, Retat L, Jacobsen E, et al. Cost-effectiveness of bariatric surgery and non-surgical weight management programmes for adults with severe obesity: a decision analysis model. *Int J Obes*. 2021;45(10):2179-2190. doi:10.1038/s41366-021-00849-8
44. Mitchell JL, Lyons HS, Walker JK, et al. The effect of GLP-1RA exenatide on idiopathic intracranial hypertension: a randomized clinical trial. *Brain*. 2023;146(5): 1821-1830. doi:10.1093/brain/awad003
45. Mollan SP, Bodoza S, Ní Mhéalóid Á, et al. Visual field pointwise analysis of the idiopathic intracranial hypertension weight trial (IIH:WT). *Transl Vis Sci Technol*. 2023;12(5):1. doi:10.1167/tvst.12.5.1
46. Mueller KF, Meerpohl JJ, Briel M, et al. Methods for detecting, quantifying, and adjusting for dissemination bias in meta-analysis are described. *J Clin Epidemiol*. 2016; 80:25-33. doi:10.1016/j.jclinepi.2016.04.015
47. Al Abdulsalam HK, Ajlan AM. Idiopathic intracranial hypertension in males. *Neurosciences*. 2017;22(3):220-223. doi:10.17712/nsj.2017.3.20170005
48. Kleinschmidt JJ, Digre KB, Hanover R. Idiopathic intracranial hypertension: relationship to depression, anxiety, and quality of life. *Neurology*. 2000;54(2):319-324. doi:10.1212/wnl.54.2.319
49. de Oliveira MF, Yamashita RHG, Boa Sorte AA, et al. Psychiatric symptoms are frequent in idiopathic intracranial hypertension patients. *Neurosurg Rev*. 2021;44(2): 1183-1189. doi:10.1007/s10143-020-01321-3
50. Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. *Neurology*. 2002;59(10):1492-1495. doi:10.1212/01.wnl.0000029570.69134.1b
51. Dandy WE. Intracranial pressure without brain tumor. *Ann Surg*. 1937;106(4): 492-513. doi:10.1097/00000658-193710000-00002
52. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders, 2nd edition. *Cephalalgia*. 2004; 24(suppl 1):9-160. doi:10.1111/j.1468-2982.2003.00824.x
53. Smith JL. Whence pseudotumor cerebri? *J Clin Neuroophthalmol*. 1985;5(1):55-56.
54. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology*. 2013;81(13):1159-1165. doi:10.1212/WNL.0b013e3182a55f17