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Weight Management Interventions for Adults With Idiopathic Intracranial Hypertension: A Systematic Review and Practice Recommendations

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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 is to evaluate weight loss interventions in people with IIH to determine which intervention is superior in terms of weight loss, reduction in intracranial pressure, benefit to visual and headache outcomes, quality of life, and mental health.

Methods

A systematic review was carried out in accordance with PRISMA guidelines and registered with PROSPERO (CRD42023339569). MEDLINE and CINAHL were searched for relevant literature published from inception until 15th December 2022. Screening and quality appraisal was conducted by two independent reviewers. Recommendations were graded using Scottish Intercollegiate Guidelines Network (SIGN) methodology.

Results

A total of 17 studies were included. Bariatric surgery resulted in 27.2-27.8kg weight loss at 24 months (Level 1- to 1++). Lifestyle weight management interventions resulted in between 1.4 to 15.7kg weight loss (Level 2+ to 1++). Bariatric surgery resulted in the greatest mean reduction in ICP (-11.9cm H_2O) at 24 months (Level 1++), followed by multi-component lifestyle intervention + acetazolamide (-11.2cm H_2O) at 6 months (Level 1+), and then a very low energy diet intervention (-8.0cm H_2O) at 3 months (Level 2++). The least ICP reduction was shown at 24 months after completing a 12-month multi-component 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 BMI ≥35kg/m^2 since this had the most robust evidence for sustained weight management (Grade A). A multi-component lifestyle intervention (diet + physical activity + behaviour) had the most robust evidence for modest weight loss with a BMI <35kg/m^2 (Grade B). Longer term outcomes for weight management interventions in people with IIH are required, to determine if there is a superior weight loss intervention for IIH.

Introduction

Idiopathic intracranial hypertension (IIH) is characterized by raised intracranial pressure (ICP), pulse-synchronous tinnitus, headaches and papilloedema, 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 patients with BMI >40kg/m^2 were more likely to have severe papilloedema at the first neuro-ophthalmology visit and every 10kg/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 to the general population [9], which may result from common biological pathways related to hypothalamus-pituitary-adrenal cortex (HPA)-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 hard-wired to prevent weight loss [12,13]. This is a challenge for the treatment of IIH since 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 re-gain 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 summarise the relevant published studies relating to weight loss interventions for IIH in terms of their ability to deliver sustained weight loss and impact on key outcomes such as vision and headache. A second aim of the 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 (PRISMA) guidelines [17].

Search strategy

The databases MEDLINE and CINAHL were searched from inception up to 15th December 2022 via EBSCO using a comprehensive search strategy (eAppendix 1), which was tested and refined to maximise 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 (MeSH) 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 de-duplication and screening.

Inclusion and exclusion criteria

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

Papers selection and data extraction

Two reviewers (SA and SPM) 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, utilising Covidence. Disagreement was resolved by consensus between reviewers.

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 either by absolute weight (kg or %), excess weight (%) (calculated by absolute weight loss / (baseline weight – ideal body weight) x 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, papilloedema 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 (SA/SPM/FCh) and peer reviewed by the another (SA/SPM/FCh), using an electronic data extraction form.

Data analysis

Since the included studies were diverse, heterogeneity between studies in terms of the interventions, duration of follow-up and method of outcome measurement precluded pooling of results with meta-analysis. Instead, a narrative synthesis approach was employed to synthesise 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 the weight loss, ICP, headache and visual outcomes, based on Scottish Intercollegiate Guidelines Network (SIGN) methodology[19] (eAppendix 2), by two independent reviewers (SA and SPM).

Practice recommendations

The process of SIGN methodology[19] (eAppendix 2) was followed to formulate evidence-based clinical recommendations. A multi-disciplinary recommendation panel was formed of relevant professional groups with experience and expertise in IIH and weight management. The recommendation panel included a dietitian (SA), clinical psychologist (FCa), endocrinologist (AAT), bariatric surgeons (DJP, CP), neurologists (AJS, FCh), neuro-ophthalmologists (SPM, SW), and a patient representative (AD). The expert panel convened to discuss the 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 (GPP) were formulated to provide clinicians with short pieces of advice that the recommendation panel deemed were 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 a BMI <25kg/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 five studies [7,30–33] were reports of included studies. The study selection process is summarised in Figure 1.

Study Characteristics

Study characteristics can be found in Table 1. There were six studies[7,20,21,31–33] of randomised control trials (RCTs), four of prospective non-randomised interventional studies[6,24,25,30]; and two prospective[27,29] and four retrospective observational studies [5,22,23,26,28]. Prescribed concomitant IIH pharmacotherapy was noted in eTable 1.

Participant characteristics

There were total of 496 patients included in this review and studies generally had small sample sizes, ranging from four to 165 participants (Table 2). Most studies (n=10) included only females in their inclusion criteria. Only seven 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 males received a bariatric surgery intervention. The mean age of participants ranged between 27 and 39 years old and the mean baseline BMI ranged between 36 to 47kg/m^2. Participants undergoing bariatric surgery also had a higher mean BMI (range 42.1 to 47.0kg/m^2) than lifestyle interventions (30.6 to 40.0kg/m^2). In the nine studies that reported ethnicity[6,7,20–22,25,30–33], most participants were white (range 65 to 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 four studies[6,25,29,30] were dietary interventions alone, seven studies [20,21,26,31–34] were multi-component interventions (diet + physical activity + behavioural interventions) and in one study[5] patients independently sourced a weight management intervention of their choosing (eTable 1).

Weight loss outcomes

In studies where outcomes were pooled across bariatric surgery procedures (gastric band, gastric bypass and sleeve gastrectomy), mean weight loss was 27.2 to 27.8kg 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 to 45.0kg at 12 to 24 months and excess weight loss of 69.9 to 71.0% at 24 months to a median of 91 months (Level 2- to 1- [7,22,24]). Sleeve gastrectomy (n=42 participants) resulted in weight loss of 32.2 to 39.0kg at 12 to 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 1.0kg 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 (kg) compared to both sleeve gastrectomy and gastric band (p=<0.001) at 24 months. At longitudinal follow-up (Level 2- [22]), weight loss was greater for gastric bypass (median follow-up 91 months) compared to gastric banding (median follow-up 108 months) ($p=0.007$), but there was no difference between gastric bypass and sleeve gastrectomy (median follow-up 68 months) ($p=0.069$).

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

Intracranial pressure outcomes

While ten studies recorded baseline ICP measured by lumbar puncture opening pressure[5,6,20,21,24,27–29,33] (Table 4), only three studies [6,20,33] measured change in ICP following weight management intervention. Bariatric surgery offered the greatest mean reduction (-11.9cm H_2O) in ICP at 24 months (Level 1++ [20]), followed by a 6-month multi-component lifestyle intervention + acetazolamide (-11.2cm H_2O) (Level 1+ [33]), and then a 3-month VLED (diet only) intervention (-8.0cm H_2O) (Level 2++ [6]), then a 6-month multi-component lifestyle intervention (-5.2cm H_2O) (Level 1+ [33]). The least ICP reduction was shown at 24 months after completing a 12-month multi-component 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 five studies reported the visual acuity [6,20,26,29,33] (eTable 2). 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] while one study did not report visual field outcomes[20]. Six studies reported the perimetric mean deviation (PMD) from the 24-2 Humphrey visual field analyser (Level 3 to 1+ [5,6,20,26,29,33]). Five studies commented on the presence or absence of papilloedema (Level 4 [23,24,27,28]), whereas formal Frisén grading, and OCT imaging were recorded in six studies (level 2- to 1+ [6,20,26,29,31,33]).

Only one 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). In 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; $P < .001$) (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 IIHWT RCTs [3,33] therefore did not find visual parameters that were directly associated with 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). Only one 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 two RCTs [20,31] there was no supporting evidence of a significant reduction of headache following 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 two studies [20,30] reported on quality-of-life; both used the Short Form 36 (SF-36) Health Survey[18] (Level 1++). After bariatric surgery [20], there were significant improvements in physical (p=<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=<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 one study[20] reported changes in self-reported anxiety and depression, assessed using the Hospital Anxiety and Depression Scale (HADS)[35]. There was no significant change in anxiety in either the multi-component 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 upon the evidence identified within the systematic review and graded according to the quality of available evidence. Where evidence was not available for IIH populations, GPP were formulated based upon evidence extrapolated from obesity literature. The graded recommendations are shown 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 recognised 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 upon the evidence identified by this systematic review, and detailed clinical guidance in good practice points from the obesity literature (Table 5).

While there was one 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 one cross over study (Level 2+) utilising a VLED for 3 months which demonstrated efficacy in terms of ICP, visual and headache outcomes, these two studies have not been replicated. The results of this analysis therefore demonstrated the shortage of high-quality evidence, as there were no studies that could be directly compared due to different weight management methods being used, and a lack of standardised 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 counselled 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 to 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 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. There was Level 2+ evidence that demonstrated a reduction of weight between 15-24% 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 papilloedema and favourable headache outcomes [6] and the IIHWT disease remission was defined as ICP to return to normal levels at 25 cmH_20 [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 via 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]. Behaviour therapy has been shown to be a useful adjunct when incorporated into treatment for weight loss and weight maintenance [40]. Licensed anti-obesity medications (AOMs) did not feature in this study, as 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 clinical 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 diarrhoea. 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 following 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, due to 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, in terms of 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 to other weight management programmes and has the highest quality-adjusted life year (QALY) 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 why in studies with long disease duration the visual field measures may not improve [45]. Likewise, papilloedema may acutely be present, and without intervention may regress to the mean.

Strengths of the study include the methodological rigour of the systematic review, which was prospectively registered on PROSPERO and all screening, data extraction and quality assessment was blinded and conducted by two reviewers. The evidence was translated into clinical recommendations which were made by multi-disciplinary experts in obesity and IIH, hence supporting the translation of the research for clinical application. There are certain limitations to the study. The included studies all used different outcome measures, and a variety of weight loss methods. This meant a meta-analysis was not able to be performed, due to 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, a reflection of IIH being less prevalent in males [47], however the findings are therefore not generalisable to males. 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 30-35kg/m^2. None of the studies included women who were pregnant, which is an area in need of evaluating, as 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 one 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 to 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 [49]. 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% [50]. 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.

Conclusions

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 seem 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, multi-component 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.

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Table 1: study design

Study	Setting	Study Design	Inclusion criteria			Exclusion Criteria
			IIH diagnosis	Disease State	Other	
Abdelbaki et al. 2020	Egypt. single-centre	Prospective cohort	-	-	Laparoscopic sleeve gastrectomy March 2016 – March 2018 (BMI > 40 or BMI >35 and at least 1 obesity related co-morbidity)	
Ang et al. 2021	Australia, multi-centre	Retrospective cohort	modified Dandy Criteria[4]	-	-	- Incomplete weight records - <3 follow up visits.
Egan et al. 2011	UK, single centre	Prospective cohort	Neurologist diagnosis		Bariatric surgery database 2005 - 2011	
Glueck et al. 2006	USA, multi-centre	Non-randomised interventional	Friedman Criteria (2002)[1]	-	– Conventional pharmacotherapy treatment (acetazolamide, furosemide or topiramate) – Minimum 6 months 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's disease, hypervitaminosis A, minocycline, recombinant human growth hormone therapy or connective tissue disease)
Hermes et al. 2022	Global, multi-centre	Cross-sectional, retrospective	Revised Friedman Criteria (2013)[5]	-	Intracranial Hypertension Registry	- Incomplete questionnaires - Inadequate medical records to allow confirmation of IIH diagnosis - Secondary intracranial hypertension - Diagnosis during childhood - Any bariatric surgery prior to IIH diagnosis - Participants with >1 type of bariatric surgery - Asymptomatic IIH - <4 years follow up
Koc et al. 2018	Turkey, single-	Retrospective, non-interventional, cross-sectional	modified Dandy Criteria[4]	-	- Treatment for IIH limited to weight reduction	Medications associated with raised ICP.

	centre	cohort			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	
Lainas et al. 2020	France, multi-centre	Prospective cohort (retrospective analysis)	revised Friedman Criteria (2013)[5]	-	Laparoscopic sleeve gastrectomy (BMI>40 or BMI > 35 and at least 1 obesity related co-morbidity despite lifestyle and behavioural modifications with comprehensive motivation for surgery)	
Mollan et al. 2021 Mollan at el. 2022	UK, multi-centre	Randomised Control Trial	revised Friedman Criteria (2013)[5]	Active disease - Baseline LPOP >25 cmH20 - Papilloedema at baseline	- BMI>35 - Weight gain	Previous optic nerve sheath fenestration
Sinclair et al. 2010 Mulla et al. 2015	UK, multi-centre	Non-randomised, cross-over interventional	Dandy Criteria[2]	Active disease (LPOP >25 cmCSF, papilloedema)	Disease duration of 3 months	- Previous cerebrospinal fluid diversion. - Previous optic nerve sheath fenestration.
Skau et al. 2011	Denmark, single centre	Prospective cohort	ICHD-II (Criteria B)[3]		- >18 years - LPOP > 25 if BMI >30 - LPOP > 20 if BMI < 30	Concurrent significant - medical disease. - psychiatric disorders. - ocular conditions
Sugerman et al.1999	USA, single centre	Non-randomised interventional	persistent, severe headache, negative brain imaging study, and elevated CSF pressures (>20 cm H2O).		- Bariatric surgery (BMI >35 with severe obesity co-morbidity or BMI>40)	
Wall et al. 2014 Weil et al. 2016 Friedman et al.	USA/Canada, multi-	Randomised Control Trial	modified Dandy Criteria[4]	Active disease (elevated LPOP, papilloedema)	Reproducible mild visual loss (-2 to -7 dB perimetric mean deviation)	Treated for IIH

2017	centre					

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Table 2: baseline participant characteristics

Study	n =	Gender	Females, n= (%)	Age, years	Body Mass Index (BMI),	Ethnicity, n= (%)
Abdelbaki et al. 2020	16	Female only	16 (100.0)	31 (SD 2)	46 (SD 4)	-
Ang et al.2021	39	Female Male	37 (94.9)	Median 35.0 (IQR 10.5)	36.0 (SD 7.6)	-
Egan et al. 2011	4	Female only	4 (100.0)	Mean 32 (range 29 – 39)	Mean 46.1 (38.2 – 54)	-
Glueck et al. 2006	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	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	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	15	Female only	15 (100.0)	Median 31 (range 22-53)	Median 42.1 (36.7 – 53.5)	-
Mollan et al.2021 Mollan et al.2022 Yiangou et al. 2022	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 Mulla et al. 2015	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	37	Female Male	16 (94.1) Controls 19 (95%)	27.2 (SD 8.2)	36.1 (SD 7.4)	-
Sugerman et al.1999	24	Female only	24 (100.0)	34.0 (SD 10)	47.0 (SD 6)	-
Wall et al. 2014 Weil et al. 2016 Friedman et al. 2017	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)

Table 3: Weight loss outcomes

Study	Time (months)	Excess weight loss (%), p-value	Weight loss (kg), p-value	Total weight loss (%), p-value	BMI loss (kg/m^2), p-value	Evidence level
Non-surgical (Patient choice)						
Ang 2021	24.7 (SD 13.5)	-	10 (IQR 8), <0.001	-	-	3
Non-surgical (Diet only)						
Glueck 2006	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 2018	6	-	-	-	2.0 (SD 3.1), NR	2-
Sinclair 2010 Mulla 2015	3	-	15.7 (SD 8.0), <0.001	15.3 (SD 7.0), <0.001	-	2+
Skau 2011	3	-	-	-	2.3 (SD NR), 0.005	2+
Non-surgical (Multi-component)						
Mollan 2021	12	-	2.1 (SE 2.0), 0.29	-	0.7 (SE 0.7), 0.35	1++
Mollan 2021	24	-	1.4 (SE 2.2), 0.53	-	0.4 (SE 0.8), 0.62	1++
Yiangou 2022	24	-	0.1 (95% CI 11.8, -4.0), 0.756	-	-0.1 (95% CI 1.3, -4.0), 0.824	1-
Wall 2014 Friedman 2017 Weil 2016	6	-	3.45 (SD NR)[d] 7.50 (SD NR)[e]	-	-	2+
Surgical (Pooled procedures)						
Mollan 2021	12	-	23.4 (SE 1.9), <0.001	-	8.5 (SE 0.7), <0.001	1++
Mollan 2021	24	-	27.8 (SE 2.1), <0.001	-	10.4 (SE 0.8), <0.001	1++
Yiangou 2022	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 2011	19.8 (SD NR)	64.1 (SD NR), NR	33.7 (SD NR), NR	-	12.7 (SD NR), NR	3
Hermes 2022	108 (IQR 48)	27.1 (IQR 40.6), NR	-	14.5 (IQR 17.0), NR	-	2-
Mollan 2022	24	-	-1.0 (SE 5.7), 0.868	-	0.0 (SE 2.1), 0.985	1-
Surgical (Gastric Bypass)						
Hermes 2022	91 (IQR 59)	69.9 (IQR 28.3), NR	-	34.7 (IQR 17.1), NR	-	2-
Mollan 2022	24	-	42.5 (SE 2.8), <0.001	-	16.0 (SE 1.0), <0.001	1-
Sugerman 1999[h]	12	71.0 (SD 18), <0.001	45.0 (SD 12), <0.001	-	-	2-
Surgical (Sleeve)						
Abdelbaki 2020	12	75.2 (SD 2.0), NR	-	-	-	3
Hermes 2022	68 (IQR 8)	40.2 (IQR 25.0), NR	-	24.9 (IQR 11.4), NR	-	2-

Lainas 2020	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 2022	24	-	32.2 (SE 4.6), <0.001	-	11.8 (SE 1.7), <0.001	1-

[a] diet alone, [b] diet + metformin (PCOS), [c] diet + metformin (hyperinsulinemia), [d] placebo, [e] acetazolamide, [h] 11/12 participants had gastric bypass, negative values indicate weight gain, NR = not reported

Table 4: ICP outcomes

	Intracranial pressure baseline measure mean (SD), n (cm H_20)	**Intracranial pressure at end point** mean (SD), n (cm H_20)	**Time of end point**	**Difference** (cm H_20)		**Notes**	**Level of evidence**
Lifestyle intervention							
Abdelbaki 2020	41.2 (21), 16 (range 30–64)	-	-	-	-	-	Not graded
Ang 2021	median (range), n 30 (5.5), 39	-	-	-	-	-	Not graded
Glueck 2006	-	-	-	-	-	-	Not graded
Koc 2018	32.2 (8.0), 19 34.6 (8.4), 20	-	-	-	-	-	Not graded
Mollan 2021	34.6 (5.6), 33	32.0 (5.2), 25	12 months	mean (SE)[95% CI] -2.5 (1.4) [-5.2 to 0.3]	p=.084	-	1++
Mollan 2021	34.6 (5.6), 33	31.0 (5.7), 18	24 months	mean (SE)[95% CI] -3.5(1.6) [6.6 to -0.3]	p=.03	-	1++
Skau 2011	median (range), n 31.0 (23.4 to >50), 13	median (range), n 24.0 (20.2–42.5), 13	3 months	Not reported	p=.02	There was a positive linear association between proportional change in BMI and ICP (5.2 cmH20/(m^2/kg)), p=.0002	2++
Sinclair 2010	38.0 (5.0), 37	30.0 (4.9), 20	3 months	mean (SD) -8.0 (4.2)	P<0.001	-	2++
Wall 2014 Acetazolamide Placebo	34.9 (94.1), 86 34.2 (70.7), 79	24.5, 47 30.5, 38	6 months	mean -11.2 -5.2	..	Treatment effect -6.0 [95% CI, -9.6 to 2.3] p= .002	1+
Surgical intervention							

Egan 2011	Not reported	-	-	-	-	-	Not graded
Hermes 2020	Not reported	-	-	-	-	-	Not graded
Lainas 2020	median (range) 31 (25–50)	Not reported	-	-	-	-	Not graded
Mollan 2021	34.8 (5.8), 33	mean (SD), n 26.9 (8.1), 18	2 weeks	mean (SE)[95% CI] -7.9 (2.0) [-11.8 to -4.0]	p=.0002	-	1-
Mollan 2021	34.8 (5.8), 33	mean (SD), n 26.4 (8.7), 29	12 months	mean (SE)[95% CI] -8.7 (1.3) [-11.3, -6.1]	p<.001	-	1++
Mollan 2021	34.8 (5.8), 33	mean (SD), n 22.8 (7.8), 22	24 months	mean (SE)[95% CI] -11.9 (1.5) [-14.8, -9.0]	p<.001	-	1++
Sugerman 1999	32.4 (8.3) (range 23.0–52.0)	Not reported	-	-	-	-	Not graded

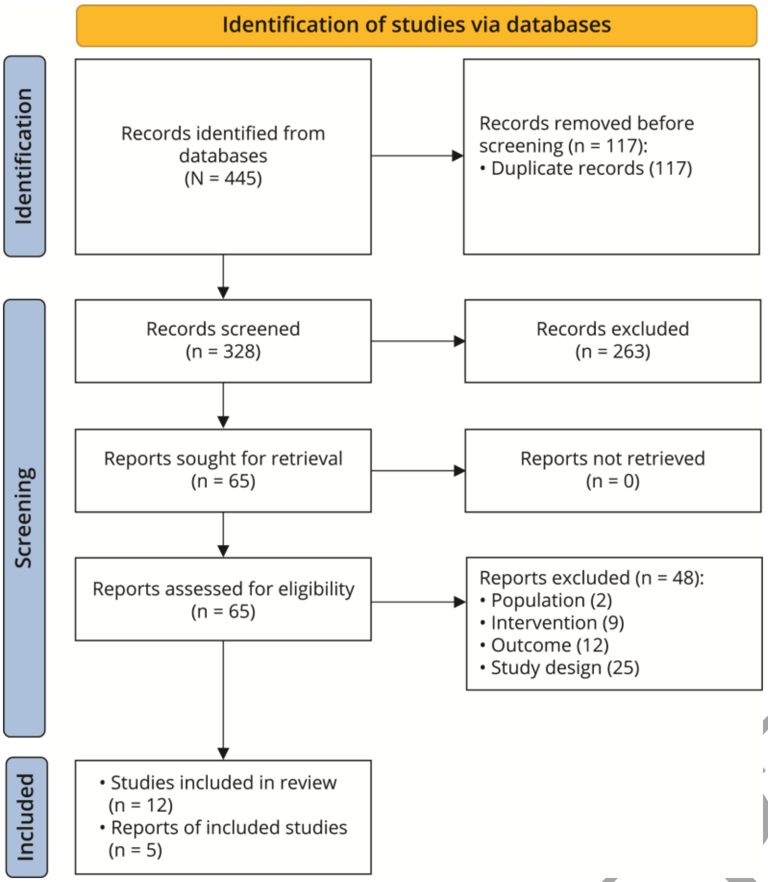
Table 5: **Graded recommendations for weight management in IIH**

Recommendations	**Grade (evidence level 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. Anti-psychotic 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 this may only be achieved via intervention with bariatric surgery.	C (EL 2+)
Advise patients a multi-component lifestyle intervention (dietary therapy + physical activity + behaviour) is an alternative treatment that may support a more modest weight loss of up to 5-10%	GPP
Lifestyle	
Advise patients that a multi-component intervention (diet + physical activity + behaviour) may be effective in the medium-term (up to 6 months) for modest weight loss, but weight loss may not be maintained in the longer-term (>24 months).	B (EL 1++ to 2+)
Advise patients that dietary approaches alone that create an energy deficit of 500-1,000kcals/day may be effective in the short-term for modest weight loss (up to 6 months).	C (EL 2+)
Only recommend very low energy diets (VLEDs) of <800kcals/day if the patient will have access to intensive dietary support and if the patient presents with immediate risk of worsening papilloedema.	C (EL 2+)
Pharmacotherapy	
Acetazolamide in conjunction with a multi-component lifestyle intervention may support weight management, however this may be due side-effects of the medication which can cause dysgeusia.	B (EL 1+)
Metformin in conjunction with a multi-component 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 counselled 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 >35kg/m^2, bariatric surgery should be considered.	A (EL 1++)
For men living with IIH and a BMI >35kg/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 weeks following 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 multi-disciplinary assessment of patient suitability for bariatric surgery should be undertaken by a bariatric specialist unit	GPP

EL = evidence level, GPP = Good Practice Point

Figure: PRISMA flowchart



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