

# Changes in Cognitive Function Following Bariatric Surgery: An Updated Systematic Review

Isaac Hathaway<sup>1\*</sup>, Oshiokhe Momodu<sup>2</sup>, David M Williams<sup>1</sup>, Andrew J Beamish<sup>3</sup>, Jonathan Barry<sup>3</sup>, Jeffrey W Stephens<sup>1,4</sup>

<sup>1</sup>Diabetes Centre, Morriston Hospital, Swansea Bay University Health Board, Swansea, UK; <sup>2</sup>Swansea University Medical School, Swansea University, Swansea, UK; <sup>3</sup>Welsh Institute of Metabolic & Obesity Surgery, Morriston Hospital, Swansea Bay University Health Board, Swansea, UK; <sup>4</sup>Diabetes Research Group, Swansea University Medical School, Swansea University, Swansea, UK.

**\*Correspondence to:**

Dr Isaac Hathaway, Diabetes Centre, Morriston Hospital, Swansea, UK

Email: [Isaac.Hathaway3@wales.nhs.uk](mailto:Isaac.Hathaway3@wales.nhs.uk)

Tel: [REDACTED]

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## **Abstract**

Since a previous systematic review published in 2016, there have been further studies investigating the association of changes in cognitive function following bariatric surgery. All studies since the original review that reported at least one element of cognitive function before and after bariatric surgery were eligible. 137 additional studies were identified, 13 were included in addition to the 18 studies previously. Almost all studies reported improvements in at least one domain. Most revealed improvements were limited to a few domains and were not universal. Further findings investigated cognitive function improvement in relation to procedure choice, and mental health or quality of life post-surgery. Further high-powered studies are still necessary, but these findings support the impact of bariatric surgery on cognitive function in obesity.

## **Key Points**

- Cognitive function is likely to improve following bariatric surgery, however, the domains that improve are variable within the literature.
- The positive impact of bariatric surgery on quality-of-life measures and mental health is reassuring, although the mechanistic metabolic pathways that contribute to improvements are not well understood.
- Findings from cognitive assessments following adolescent bariatric surgery had mixed outcomes and further investigation is needed to determine if early intervention yields longer-term benefits.
- A large high-powered study is still absent in the literature and should be considered for further consolidation of these findings.

**Keywords:**

Alzheimer's disease; Bariatric surgery; Cognition; Cognitive function; Dementia; Gastric band; Gastric bypass; Gastric surgery; Metabolic surgery; Roux-en-Y gastric bypass; Sleeve gastrectomy.

**Introduction**

There is a direct relationship between increased body mass and cognitive impairment, leading to the hypothesis that weight loss interventions may reverse cognitive impairment in individuals living with obesity. Since neurocognitive deficits are associated with obesity, weight loss surgery may have a role in improving neurocognitive function. A previous systematic review published in 2016 identified a positive association between weight loss and improved cognitive function [1].

Neurocognition refers to one's ability to think and reason. It includes the ability to concentrate, memorise, process information, learn, speak, and understand. The main overarching domains are memory, language, executive function, and attention [2]. Obesity is associated with impairment of various aspects of neurocognitive function, with executive function skills being the most consistently reported deficits [3]. These deficits persist after adjusting for confounders and obesity-related conditions [4]. Overall, in the previous systematic review exploring the associations between neurocognitive function outcomes following bariatric surgery, executive function, language, memory, and attention each appeared to improve after weight loss [1]. However, at the time of this previous systematic review, studies exploring these associations were relatively few, and further studies have since been undertaken to further corroborate consistent benefits across various elements of neurocognitive function. Due to the association between obesity and impaired neurocognition, and

perceived benefits of bariatric surgery in the literature, there is growing interest in the impact of bariatric surgery on neurocognitive outcomes [5]. Cognitive testing is quite variable throughout literature, with no set testing modality being preferred to another.

This systematic review aims to update the findings of consistent measurable improvements in cognitive function following bariatric surgery with substantive new literature that has emerged since the initial publication.

### **Study objectives**

This systematic review aims to determine the effect of bariatric surgery on measures of cognition and determine whether weight loss surgery can help to reverse obesity-associated cognitive impairment, building on previously published conclusions.

### **Methods**

#### **Eligibility**

All studies measuring any aspect of cognitive function both before and after bariatric surgery until September 2023 were considered. No restrictions were placed on demographics, population, or duration of follow-up.

#### **Search Criteria**

Searches for appropriate studies were conducted using the following databases: MEDLINE, PubMed, Scopus, and Cochrane Library. The following terms were used to describe weight loss surgery: bariatric surgery, gastric surgery, gastric bypass, Roux-en-Y, gastric band, sleeve gastrectomy, and weight loss surgery. Terms used to describe cognition were memory, cognition, cognitive function, dementia, Alzheimer's disease.

## **Study Selection**

Studies reporting at least one element of cognitive function before and after surgery were eligible. Following the literature search, each study was screened by title and abstract for selection. Studies were classified as irrelevant, relevant, or possibly relevant before a further selection process based on the full text. Reference lists for these studies were also screened for further potentially relevant literature. Each selected abstract was assessed by two reviewers (IH & DMW) for consideration and any indecision prompted review by a third reviewer (JWS).

## **Data Collection and Analysis**

Data were extracted for the following variables: age, gender, body mass index (BMI), surgery type, change in BMI pre- and post-operatively, and performance on cognitive testing. Study design and length were also sought to establish both power and the key strengths and limitations. The review was conducted in accordance with PRISMA 2020 protocols and registered through the PROSPERO international register of systematic reviews (ID: 487644). The risk of bias was also screened using the Cochrane Institution risk of bias tool [6]. The principal outcome measure was performance on cognitive testing, which while broad, allowed for a greater scope, bearing in mind the wide variation of methodologies used.

## **Results**

A total of 137 studies published since the previous original systematic review were screened from which 13 were included in the final review. Eighteen additional studies from the original review were also included for discussion, as summarised in Figure 1. Across all studies, 687 participants were involved, with a weighted mean age of

43.1±5.4 years. The weighted mean pre-surgery BMI was 46.2±1.6 kg/m<sup>2</sup>, while the weighted mean post-surgery BMI was 32.2.6±5.4 kg/m<sup>2</sup>. There was significant variation in the modalities of cognitive testing within the literature, with a total of 13 different batteries being used in different ways. Several studies used the same testing batteries, while others used single elements of larger testing frameworks.

### **The Effect of Bariatric Surgery on Cognitive Function**

Methods of cognitive assessment varied considerably through all studies, which limited a more detailed comparison. The breakdown of each study's variables is presented in Table 1. Table 2 highlights the key findings of each study.

Almost all studies reviewing the effect of bariatric surgery on cognition found improvements in at least one measured domain. Most revealed that improvements were in fact limited to a few select domains and were not typically universal. No domain improved significantly more than any other and, for several domains, positive outcomes reported within some studies were limited in others. Four studies found no improvement following bariatric surgery [7, 8, 20, 22].

While all included studies reviewed the effect of bariatric surgery on cognition and met the inclusion criteria, many studies included alternative themes, including the impact or effects of: biomarkers, metabolic changes, cerebro-vascularity, and adolescent bariatric surgery on cognitive outcomes. However, these findings were typically independent in the literature and little research has since followed relating to these themes.

### **Discussion**

The previous review noted a high degree of variation in the assessment process of cognitive performance. As a result, and due to the high proportion of well-designed but

comparatively small studies, it was suggested that there was a need for prospective longitudinal study designs. A study of this kind, focusing on cognition post-bariatric surgery, with both a large sample size and long-term follow-up, has not yet been conducted. The previous review highlighted improvements mainly in executive function and memory and raised the role of complex homeostatic mechanisms in cognitive improvement following bariatric surgery as an important, but poorly understood paradigm. Here, in this updated systematic review, we expand upon these findings with an additional 13 studies taken since the original publication. The findings presented continue to support a beneficial impact of bariatric surgery on neurocognitive outcomes, though studies including large populations with a long duration of follow-up are still lacking. Moreover, there continued to be significant heterogeneity with respect to study design and the reported neurocognitive outcomes which limited a meta-analysis of these outcomes.

Cognitive improvements following bariatric surgery were noted throughout the literature. The key point was that while there were generalised improvements, many studies conflicted on specific domains of improvement. Seven studies indicated widespread cognitive improvements, but the specific domains measured varied. Additionally, all 13 studies extracted from the LABS project showed cognitive improvements [25-37]. Shariati et al., measured nearly all domains of cognition and uncovered wholesale improvements, with only one element of working memory found not to improve [9]. The significance of this could be restricted to paradoxical age-related findings, but given the mean age is still only  $43.1 \pm 5.4$ , this is not likely [38,39]. Similarly, Smith et al., measured near all domains and yielded similar results, but with performance in visual attention and executive function testing limited; not surpassing Bonferroni correction on statistical analysis [8].

Tucker et al., and Anwar et al., used the same data sets for these studies and both used Integneuro Computerised Testing Battery (ICTB) with positive outcomes [11,16, 40]. This appeared to be a useful modality to measure generalised improvements in cognition but may be limited in its ability to determine specifics, as it is not an exhaustive tool. Four studies found a lack of improvement [14, 15, 20, 22]. Baskaran et al., used the Weschler Abbreviated Scale of Intelligence (WAIS), which is a broad testing modality with similar features to the ICTB [14, 41]. Walo-Syverse et al., however, used fewer modalities focusing on everyday working memory and verbal and non-verbal memory [15]. Georgiadou et al., and Sousa et al., also found no significant group differences across a range of cognitive assessments [20, 22]. While these studies had some of the larger cohorts in the literature, it is difficult to gauge whether these findings are significant or outliers, given the vast improvements expressed elsewhere; the results presented by Walo-Syverse et al., had a high degree of variability, while Baskaran et al., only included adolescent females.

Previously, Spitznagel et al., identified that pre-operative BMI was not an indicator for post-operative cognitive improvement in any of the tested domains [19]. This suggests that cognitive improvement was independent of increased pre-operative obesity among these participants. Though, it has been demonstrated that a higher pre-operative BMI results in higher BMI and increased incidence of comorbidity relapse at 5 years post-surgery [42], and that lower BMI and the absence of type 2 diabetes mellitus at baseline were associated with more favourable outcomes [43]. In contrast, a high-powered retrospective cohort study found that HbA1c had no bearing on peri-operative bariatric surgery outcomes [44].

The surgical procedure choice may affect cognitive outcomes. This was covered by several studies in the literature, however many of the outcomes differed, perhaps



suggesting that the findings may be incidental. Smith et al., found significant general cognitive improvements following VSG at one year, but not for the RYGB group [8], while Prehn et al., found that different surgery groups did not substantially differ when comparing cognitive function, mood or affect, or health related quality of life [17].

The verbal fluency of patients living with obesity may benefit following bariatric surgery, as per Spitznagel et al. The authors reported a 0.26 unit decrease in pre-operative verbal fluency for every 1.0 kg/m<sup>2</sup> increase in BMI at the age of 18 years [19]. Conversely, Baskaran, et al., did not find any significant difference in intelligence scores [14]. Already, studies in adolescent bariatric surgery from specialised adolescent centres, have found surgery outcomes comparable or superior to adults in the rate of complications and resolution of co-morbidities [45]. Perhaps bariatric surgery at a time when the brain is still in development could yield benefits relating to later adulthood cognition. The impact of adolescent bariatric surgery on cognitive function is currently being investigated within the Adolescent Morbid Obesity Surgery 2 (AMOS2) study, a randomised clinical trial comparing outcomes of adolescents undergoing bariatric surgery with those undergoing non-surgical weight management [46], which is due to report cognitive outcomes imminently. It is notable that Alosco et al., found that age did not influence change in cognitive performance among 95 bariatric surgery patients [29]. However, this finding was based on an adult, rather than an adolescent, population. Baskaran et al., highlighted that further research is necessitated to review the effect of age of onset of obesity and cognition [14].

An important factor relating to cognition is mental health and quality of life. It is widely theorised that depression and other mental health conditions have a negative impact on cognition [47, 48]. Equally, obesity is associated with an increased risk of mental health illness and weight loss negatively correlates with depression [49]. As a result,

the positive effects of bariatric surgery alleviating these depressive symptoms may improve cognition. Kotackova et al. found fewer depressive symptoms in patients post-bariatric surgery, along with improved verbal reasoning skills [10]. While reduced adiposity may not be the direct cause for both improvements, the extensive benefits of alleviating depressive symptoms should be considered as a beneficial outcome. Further, Ahmadzad-Asl et al. found significantly improved quality of life in the surgical group compared to the control group using the BAROS quality of life measurement tool [12]. This improvement could theoretically result in cognitive benefits, given the existent extensive literature, but needs further study.

Alosco et al., determined that preoperative history of major depression did not influence baseline or post-operative changes to performance in any cognitive domain among 67 patients [27]. In addition, a history of binge-eating disorders did not influence changes in BMI or cognitive follow-up in another study [34], indicating that mental health disorders should not necessarily contraindicate bariatric surgery, and further supports both mental health and cognitive outcomes associated with metabolic surgery.

Metabolic changes secondary to bariatric surgery were investigated in several new studies [7, 11, 13, 16]. These found that gut microbiome and other biomarkers may be linked with cognitive ability and as a result, surgeries which preserve or retract these compounds can affect cognition. Both studies recorded positive outcomes. Lammert et al., raised the theory of the importance of gut-brain relationships [7], highlighting that in patients who responded well to bariatric surgery in cognitive tests, there were much stronger dynamics of gut peptides, including glucagon-like peptide-1 (GLP-1), which is theorised to be neuroprotective and improve cognition [50, 51]. While this is the first study of its kind, and there was statistical insignificance in the differences

measured by some of the tests, it has raised an interesting topic of future research as one of the main mechanisms by which obesity and cognition are closely related. Similarly, Enaud, et al., measured bacterial diversity following bariatric surgery and found that alongside a 5% improvement in cognition, the bacterial alpha-diversity was also significantly higher [13]. The same could not be said for beta-diversity, however, alongside the findings from Lammert et al., and other research studies, a question is raised of the role of microbiota and biomarkers in cognition.

Another pair of studies looked at cerebrovascular responses following bariatric surgery [11, 16]. They found between 17-21% improvements in cognition function scoring post-operatively and that the cerebro-metabolic rate of oxygen was comparable to that of a healthy control. While the sample size was only six patients, it raises interesting questions around the true mechanistic changes that result in improved cognition.

From the previous review, the LABS study publications investigated a variety of these metabolic and hormonal changes [25, 26, 30]. Two studies found that decreases in leptin and increases in ghrelin, as well as decreases in alkaline phosphatase and a lower baseline cystatin C, were associated with better cognitive outcomes post-operatively [26, 30]. Conversely, a further study found that C-reactive protein levels were not associated with cognitive changes at follow up [25]. In addition, Gulstrand et al., found reduced hormonal counter regulatory response during prolonged hypoglycaemia [24]. While these specific domains have not been further investigated, the widespread positive influence of various metabolic changes on cognition have continued to be investigated since the previous review.

### **Limitations from the Literature**

It should be noted that in both the previous and more recent literature, the removal of potential participants with co-morbidities was extensive and included both physical

and psychological disorders. These confounders may certainly impact on findings across the board but are also integral elements of multi-faceted decision making when it comes to surgical candidate selection. While cognitive benefits may arise from a non-comorbid patient, assuming this application for comorbid groups is not possible. This is a key point that should be drawn from this update.

As aforementioned, there were also difficulties in analysis secondary to the variation of the cognitive assessment tools used across studies. All studies operating with different cohorts used different measurement tools to determine cognitive outcomes, challenging a robust large-scale analysis. A generalised consensus on cognitive tools is not possible due to accessibility and the international nature of the studies included, but continuity of measurement areas and breakdown of cognitive domains would be beneficial for future reviews or larger-scale and longer-term studies to support reproducibility and comparability across cohorts internationally.

Further, sample size was typically low, and no high-powered studies were found in the search. The largest cohort included 109 patients, while some studies had cohorts as low as 6 and 13 participants. In turn, this limits the ability of this review to draw reliable conclusions, but it remains a systematic summary of all collected data to date.

A larger, longitudinal study with robust cognitive measurements should be completed. This should involve means tested cognitive batteries with wide scope and ideally cover multiple centres with wider demographics. Additional considerations for future work should include more detailed examination of the effects of pre-operative BMI and co-morbid status on cognitive outcomes, where there is currently mixed evidence in the literature, as well as adolescent bariatric surgery and the best type of bariatric surgery for cognitive outcomes because the existing literature is both inconsistent and thin.

Thirteen of the 18 studies included in the original review were from the Longitudinal Assessment of Bariatric Surgery (LABS) consortium, which led to over-representation and impaired the generalisability of the review findings. None of the additional reports included in this updated review were from this dataset, thereby reducing this effect. Small sample sizes limit the power of the findings from the newer studies. However, the updated review benefits from additional international perspectives and a wider breadth of demographic representation.

## **Conclusions**

Overall, the findings of this study support those of the previous. Cognition appears generally likely to improve following bariatric surgery. The domain of cognitive improvement is somewhat variable, and the literature has inconsistencies that limit the ability to interpret the change of domains relative to one another. Further research is necessary to determine the areas of improvement, while other research may be necessary to determine the best type of surgery for cognitive improvement, the effect of adolescent bariatric surgery, the relationship between cognitive improvement and mental health or quality of life post-bariatric surgery and, the mechanistic metabolic pathways that result in improvements.

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## **Ethics declarations**

### **Ethical Approval**

For this type of study, formal consent is not required.

## **Informed Consent**

Informed consent does not apply.

### **Conflict of Interest**

The authors declare no competing interests.

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**Table 1 summarises the population characteristics, surgical intervention and cognitive testing explored in each of the included studies.** Data are presented as the mean  $\pm$  standard deviation when available. Abbreviations: *BMI* body mass index; PR poor response group; GR good response group; GB gastric band; RYGB Roux-en-Y gastric bypass; gastric band SG sleeve gastrectomy; VSG vertical sleeve gastrectomy; LAGB laparoscopic adjustable gastric banding.

First Author	Year	Country	Participants	Age (years)	Gender	Pre-surgery BMI (kg/m <sup>2</sup> )	Post-surgery BMI (kg/m <sup>2</sup> )	Type of Surgery	Cognitive tests
Lammert[10]	2023	Germany	47	51.8 $\pm$ 10.1	F 36, M 21	PR 54.6 $\pm$ 8.4 GR 46.7 $\pm$ 7.4	PR 47.1 $\pm$ 6.2 GR 28.9 $\pm$ 3.1	RYGB	Digit span task, Memory impairment screen
Shariati[12]	2023	Iran	80	62.8 $\pm$ 2.3	F 56, M 24	41.15 $\pm$ 0.79	n/a	RYGB, GS	Digit span task, Wisconsin card sorting test, trail making test A/B
Smith[11]	2023	USA	36	VSG 38.4 $\pm$ 1.7, RYGB 39.8 $\pm$ 2.0	F only	VSG 43.9 $\pm$ 1.4, RYGB 44.5 $\pm$ 1.2	VSG 36.9 $\pm$ 1.3, RYGB 36.7 $\pm$ 1.3	VSG, RYGB	Letter Number Sequencing Test, Hopkins Verbal Learning Test, Stroop Test, Symbol Digit Modalities Test, Trail Making Test A
Kotackova[13]	2023	Czechia	18	48.6 $\pm$ 10.6	F 15, M 3	43.3 $\pm$ 6.7	32.7 $\pm$ 4.68	n/a	Digit Span Task, Trail Making Test, Verbal Reasoning Test, Stroop Test, Flag Attention Test
Anwar[14]	2022	USA	6	52.0 $\pm$ 10.0	F 5, M 1	41.9 $\pm$ 3.9	39.7 $\pm$ 3.4	SG	Integneuro Computerised Testing Battery
Ahmadzad-Asl[15]	2022	Canada/Iran	40	38.9 $\pm$ 11.2	F 25, M 5	45.1 $\pm$ 0.3	36.1 $\pm$ 1.2	n/a	Weschler Clinical Memory Scale,

Enaud[16]	2021	France	13	48.0±12.0	F 11, M 2	43.1±1.3	34.2±0.8	SG, GB	Wisconsin Card Sorting Test
Baskaran[17]	2021	USA	21	18.7±0.49	F only	47.5	31.8	n/a	Rey Auditory Verbal Learning Test, Weschler Clinical Memory Scale
Walo-Syverse[18]	2021	Norway	48	42.4±10.5	F 35, M 13	43.2±4.6	29.6±5.7	RYGB, GB, GS	Weschler Abbreviated Scale of Intelligence Paired Associate Learning, California Memory Test, Everyday Memory Questionnaire
Smith[21]	2020	USA	36	VSG 38.4±1.7, RYGB 39.8±2.0	F only	VSG 43.9±1.4, RYGB 44.5±1.2	VSG 36.9±1.3, RYGB 36.7±1.3	VSG, RYGB	Letter Number Sequencing Test, Hopkins Verbal Learning Test, Stroop, Symbol Digit Modalities Test, Trail Making Test A
Tucker[19]	2020	USA	6	52.0±10.0	F 5, M 1	41.9±3.9	39.7±3.4	SG	Integneuro Computerised Testing Battery
Prehn[20]	2020	Germany	40	46.0±11.0	F 28, M 12	49.3±7.8	38.8±7.4	VSG, RYGB, GB	Trail Making Test A & B, Stroop Test, Auditory Verbal Learning Test, Digits Span Task
Spitznagel[22]	2016	USA	78	43.22±10.5	F 65, M 13	46.7±5.3	30.66±5.39	RYGB, GB, GS	Integneuro Computerised Testing Battery, Verbal Interference, Maze Task, Verbal List Learning, Letter and Animal Fluency

Original review paper studies

Marques <sup>[24]</sup>	2014	Brazil	17	40.5±10.1	F only	50.1±4.7	37.2±4.1	RYGB	Trail Making Test A
Guldstrand <sup>[27]</sup>	2003	Sweden	6	40.0	F 7, M 1	45.0±4.5	30.7±2.7	VSG	Perceptual Maze Test
<b>Longitudinal Assessment of Bariatric Surgery (LABS) project publications</b>									
Alosco <sup>[35]</sup>	2014	USA	50	44.1±10.8	F 46, M 4	46.6±5.27	32.4±6.6	RYGB, LAGB	Cognitive Test Battery, Verbal List Learning, Digit Span Task, Verbal Interference, Maze Task, Letter Fluency, Animal Fluency, Switching of Attention
Alosco <sup>[34]</sup>	2014	USA	63	42.3±11.4	F 57, M 6	46.5±5.3	31.3±6.4	RYGB, LAGB	Cognitive Test Battery, Verbal List Learning, Digit Span Task, Verbal Interference, Maze Task, Letter Fluency, Animal Fluency, Switching of Attention
Miller <sup>[39]</sup>	2013	USA	95	43.2±10.9	F 85, M 10	46.2±5.9	30.2±5.2	RYGB, LAGB	Cognitive Test Battery, Verbal List Learning, Digit Span Task, Verbal Interference, Maze Task, Letter Fluency, Animal Fluency, Switching of Attention
Gunstad <sup>[40]</sup>	2011	USA	109	44.7±11.0	F 91, M 18	46.6±6.6	38.6±6.3	RYGB, LAGB	Cognitive Test Battery, Verbal List Learning, Digit Span Task, Verbal Interference, Maze Task, Letter Fluency, Animal Fluency, Switching of Attention

**Table 2 summarises the key findings from the included studies**

<b>First Author , Key findings Year</b>	
Lammert, 2023 <sup>[10]</sup>	In patients with a good response there was a significant improvement in Maths item Sequencing ( $p = 0.048$ ), while Item Sequencing and the digit span task failed in statistical significance In patients in the good response group there are stronger dynamics of gut peptides, including GLP-1 compared to the poor response group post-surgery
Smith, 2023 <sup>[11]</sup>	There were overall cognitive improvements at one-year post-op for VSG patients [t(16) = -3,015, $p=0.008$ ] but not for the RYGB group [t(17) = -1.475, $p=0.159$ ]. Memory remained unchanged pre- and post-operatively in both groups Differences in bariatric surgery type and impact on select cognitive outcomes
Shariati, 2023 <sup>[12]</sup>	Bariatric surgery patients performed significantly better than obese controls nearly all cognitive tests post-operatively, thereby demonstrating widespread improvements in cognitive ability. No improvement was found in the backward digit span task, which may indicate that specific elements of working memory do not improve, but this may be a consequence of the increased age of the sample
Kotackova, 2023 <sup>[13]</sup>	There were fewer depressive symptoms and improved verbal reasoning skills after surgery, but no improvement on digit span, trail making or Stroop and Flag Attention tests Reduced adiposity may be the cause of reduced incidence of depressive symptoms post-bariatric surgery, but verbal reasoning improvements are deemed to benefit through alternative mechanisms
Anwar, 2022 <sup>[14]</sup>	14 weeks post-op, cerebro-metabolic rate of oxygen was comparable to that of a healthy control ( $p=0.17$ )
Ahmadzad-Asl, 2022 <sup>[15]</sup>	Immediate auditory and working memory was significantly improved compared to the control group ( $p = 0.042$ ) ( $p = 0.003$ ) Mean BAROS and quality of life scores were also significantly higher
Enaud, 2021 <sup>[16]</sup>	AVLT and SS scores were significantly improved after bariatric surgery ( $p = 0.02$ ) ( $p= 0.05$ ) Bacterial alpha-diversity was significantly higher in surgery patients who performed well on AVLT
Baskaran, 2021 <sup>[17]</sup>	No significant difference in intelligence, verbal memory, and executive function scores between surgical and non-surgical groups, these persist with variable adjustments
Walo-Syverse, 2021 <sup>[18]</sup>	Visual and verbal memory performance was poorer after 1 year and returned to baseline at 2 years Verbal memory impairment rates were unchanged at 1 year follow-up Post-operative memory improvements are not universal



Tucker, 2020 <sup>[19]</sup>	17 % improvement in cognition at 2 weeks post-surgery and 21% at 14 weeks  No cerebro-vascular responses to hypercapnia were observed despite improvements in cognitive function
Prehn, 2020 <sup>[20]</sup>	Surgery groups did not differ substantially regarding changes in cognitive functions, mood/affect and health related quality of life Patients with higher executive functions test scores at first stage showed worse performance at follow up than patients with lower initial scores There were cognitive improvements in the surgery group over time (p= 0.01)
Smith, 2020 <sup>[21]</sup>	Bariatric surgery improves short term cognitive performance in individuals with obesity and the rate at which cognitive improvements are observed appear to depend on the type of surgery received Performance in cognition and executive function testing following RYGB compared to VSG (TMT) did not survive correction
Spitznagel, 2016 <sup>[22]</sup>	There were significantly improvements in attention, executive functions, and memory but not in verbal fluency  Pre-operative BMI did not predict pre- or post-operative function in any domain For each point increase in BMI at age 18, verbal fluency decreased by 0.26 U

### **Original review paper studies**

Georgiadou, 2014 <sup>[23]</sup>	This comparative cross-sectional study of 50 post-RYGB patients was unable to find any significant group differences for a range of cognitive assessments and non-food related impulsivity scores when compared with a pre-RYGB control group matched for age and gender
Marques, 2014 <sup>[24]</sup>	Improved postoperative scores on the Trail Making Test, a measure of executive function and cognitive flexibility
Sousa, 2012 <sup>[25]</sup>	There were no significant differences in performance on five neuropsychological tests of executive function between group of 30 obese participants seeking bariatric surgery and 30 post bariatric patient – both groups performed below their expected levels
Morton, 2009 <sup>[26]</sup>	Significant improvements in attention and memory (p < 0.002), processing speed (p < 0.03), and verbal learning (p < 0.04) were seen in 36 patients 6 months after laparoscopic gastric bypass
Guldstrand, 2003 <sup>[27]</sup>	Cognitive function appears to be clearly modified following weight loss from a more cautious accuracy preferring to a more impulsive speed preferring maze-solving strategy on the Perceptual Maze Test Insulin sensitivity improved post-operatively along with a decrease in plasma C-peptide. Insulin and glucagon There was also reduced hormonal counter regulatory responses during prolonged hypoglycaemia as shown by a decrease in epinephrine, norepinephrine, pancreatic polypeptide and cortisol

### **Longitudinal Assessment of Bariatric Surgery (LABS) project publications**

Hawkins, 2015 <sup>[28]</sup>	Changes to C-reactive protein (CRP) levels were not associated with changes to cognitive function in 77 bariatric surgery patients followed up at 12 months
Alosco, 2015 <sup>[29]</sup>	Decreases in leptin and increases in ghrelin were associated with improvements in attention and executive function in 84 bariatric surgery patients followed up at 12 months. These improvements were not influenced by BMI which may imply that resistance to leptin and decreased ghrelin may instead be responsible for obesity related declines in cognitive function.
Alosco, 2015 <sup>[30]</sup>	Preoperative history of major depressive disorder did not influence baseline or postoperative changes to performance in any cognitive domain in 67 bariatric surgery patients followed up at 12 months.
Alosco, 2014 <sup>[31]</sup>	Family history of Alzheimer 's disease was associated with postoperative cognitive impairment and a failure to exhibit improvement in memory in 94 bariatric surgery patients followed up at 12 weeks.
Alosco, 2014 <sup>[32]</sup>	Age did not influence changes to cognitive performance in 95 bariatric surgery patients followed up at 12 months.
Alosco, 2014 <sup>[33]</sup>	Postoperative decreases in alkaline phosphatase (ALP) and a lower baseline cystatin C were associated with better cognitive function in 78 bariatric surgery patients followed up at 12 months.
Alosco, 2014 <sup>[34]</sup>	Post bariatric surgery executive function and memory continued to improve over time up to 36 months whereas improvements in attention generally began to decline after 24 months. A smaller sample of 21 patients followed up to 48 months showed significant improvements from baseline for executive function and memory
Alosco, 2014 <sup>[35]</sup>	Significant improvements in various measures of memory were seen in 63 bariatric surgery patients followed up at 24 months.
Spitznagel, 2014 <sup>[36]</sup>	Better cognitive function at 12 weeks post-surgery predicted a lower BMI in 55 bariatric surgery patients followed up at 36 months
Lavender, 2014 <sup>[37]</sup>	Lifetime history of binge eating disorder did not influence changes in BMI or cognitive function in 68 bariatric surgery patients followed up at 12 months
Spitznagel, 2013 <sup>[38]</sup>	Better cognitive function at 12 weeks post-surgery predicted a lower body mass index (BMI) in 57 bariatric surgery patients followed up at 24 months – this was possibly due to greater adherence
Miller, 2013 <sup>[39]</sup>	Bariatric surgery patients performed significantly better than the obese controls at 12 months on the learning, long delay and recognition of memory indices Performance of obese controls on all indices at 12 months did not differ from baseline
Gunstad, 2011 <sup>[40]</sup>	Before bariatric surgery, there was an overall low to average performance in multiple cognitive domains including executive function and memory – twelve weeks post-surgery, this improved to within the average or above average ranges

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Patients without hypertension exhibited better postoperative cognitive performance than those without hypertension

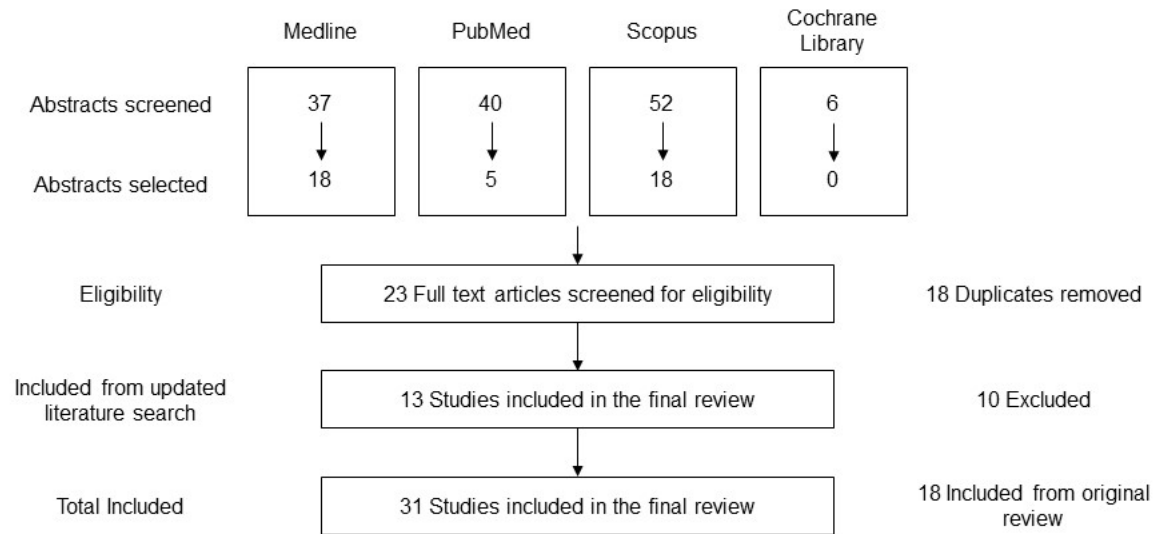


Figure 1: A breakdown of our comprehensive literature search and study selection