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REVIEW ARTICLE

Lack of Standard Definitions of Primary and Secondary (Non)responders After Primary Gastric Bypass and Gastric Sleeve: a Systematic Review

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Abstract

Lack of standard definitions of primary and secondary (non)responders after RYGB and SG makes it impossible to compare the literature. The aim was to analyze the different definitions used. MEDLINE® was searched for literature published between 01-07-2014 and 01-07-2017 concerning (1) patients who received a primary RYGB or SG and (2) the outcomes of primary and secondary (non)responders. One hundred twelve out of 650 papers were eligible. Forty out of 47 papers described a definition of weight loss success. Sixty-seven out of 112 papers mentioned weight loss failure of which 42 described a definition, in total 23 different definitions. Weight regain was mentioned in 77 papers; only 21 papers provided a definition. The recent literature regarding definitions of these outcomes is highly inconsistent. To compare the literature international consensus is required.

Keywords Bariatric surgery · Roux-en-Y gastric bypass · Gastric sleeve · Weight loss success · Weight loss failure · Weight regain

Introduction

A basic rule in science is to describe outcome parameters in the methods section of an article. Each parameter has to be defined to make it comparable to other studies. In 1960, the International System of Units (SI) standardized the metric system which is the most widely used system of measurement [1].

In bariatric surgery, several standardized outcomes have been published to provide consistency and to be able to compare the literature [2]. However, not all outcomes after bariatric surgery are standardized. With the increase of long-term follow-up data, more information has become available about the proportion of patients with inadequate weight loss and weight regain [3–7]. In the current literature, authors often use the terminology of weight loss "success," weight loss "failure," and weight "regain." Terminology that we question, as the use of "failure" may be tactfully incorrect for patients, but more important the result of a bariatric procedure is not a success but a response. Therefore, we propose the following terminology: primary responder ("success"), primary non-responder ("failure"), and secondary non-responder ("weight regain") (Fig. 1). For these outcomes, no standardized definitions or systematic methods for reporting are published [8–10].

Mann et al. showed back in 2015, in a systematic review of the literature, that the majority of the studies did not define "failure" of bariatric surgery and that excess weight loss < 50% at eighteen months was the most frequent definition identified for "failure" [9]. Nevertheless, several authors have reported criteria regarding primary responders and primary non-responders (Table 1) [11–14]. However, none of these criteria are widely used and the differences between these definitions are extensive. The lack of uniform definitions may lead to alteration of results by adjusting the definition and thus creates bias. As an example, Diniz et al. reported that at five years postoperatively, the rates of success in their cohort, based on

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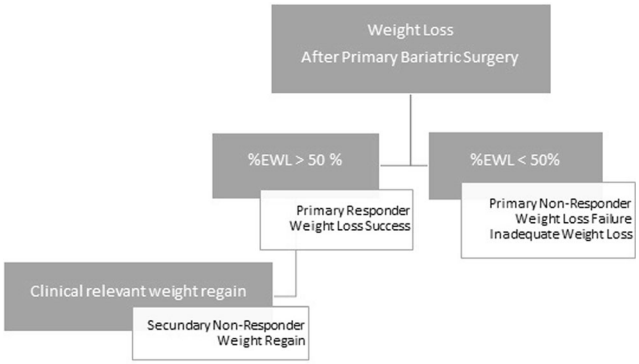

Fig. 1 Terminology Weight Loss Outcomes

the Biron criteria and the modified Reinhold Criteria, were 50.0% and 74.0% respectively [15].

The aim of this study was to analyze the currently used definitions of primary responders and primary and secondary non-responders after primary Roux-en-Y gastric bypass (RYGB) and primary sleeve gastrectomy (SG) in the recent literature, hereby determining if the situation Mann et al. described has improved. This in order to start an International System of bariatric outcomes to be able to compare future literature.

Materials and Methods

This systematic review is performed according to the PRISMA guideline, where applicable.

Eligibility Criteria

Studies that (1) included adult human patients who did receive either a primary RYGB or a primary SG procedure and (2) mentioned at least one of the three outcomes (weight loss success, weight loss failure, and weight regain) were included. Synonyms used for the outcomes that were eligible for inclusion are the following:

- Weight loss success–adequate weight loss–sufficient weight loss–optimal weight loss
- Weight loss failure–inadequate weight loss–insufficient weight loss–suboptimal weight loss
- Weight regain–weight gain–weight recidivism

Studies including patients who received other bariatric procedures (e.g., gastric banding, vertical banded gastroplasty, biliopancreatic diversion, duodenal switch) were considered not eligible. Studies about patients who underwent a primary banded RYGB or banded SG were also excluded because of the relative new technique and the limited data available concerning the long-term results. Multiple articles from one research group were included. All papers had to be written in English. There were no exclusion criteria regarding type of article and no other patient exclusion criteria than mentioned above, because in this review, we judge articles based on their methodology section instead of the results section.

Information Sources and Search

In October 2017, the electronic database MEDLINE® (PubMed®) was searched using the following combination of keywords with synonyms: gastric bypass, gastric sleeve, body weight, weight loss, fail*, *gain and success*. Only studies written in English concerning adult patients (19+ years) with a publication date between 01-07-2014 and 01-07-2017 were selected. This search was performed by two reviewers (DB and WL).

Study Selection

All articles identified with our search strategy were first screened for duplicates. Two reviewers (DB and WL) assessed relevance by independently screening titles and abstracts. In case of a discrepancy, the reviewers discussed the paper together until consensus was achieved. The articles thought to be relevant were eventually assessed in full text for eligibility based on the above stated criteria (DB and WL).

Table 1 Criteria of "success" and "failure" [11, 12, 13, 14]

	Reinhold	Lechner and Elliot	Christou et al.	Biron et al.	
Outcome measure	%excess weight	%EWL	BMI cutoff	Superobese BMI cutoff	Morbid obese BMI cutoff
Excellent	< 25%	≥ 80%	< 30 kg/m^2	–	–
Good	26–50%	50–80%	30–35 kg/m^2	< 40 kg/m^2	< 35 kg/m^2
Fair	51–75%	–	–	–	–
Poor	76–100%	< 50%	–	–	–
Failure	> 100%	< 25%	> 35 kg/m^2	–	–

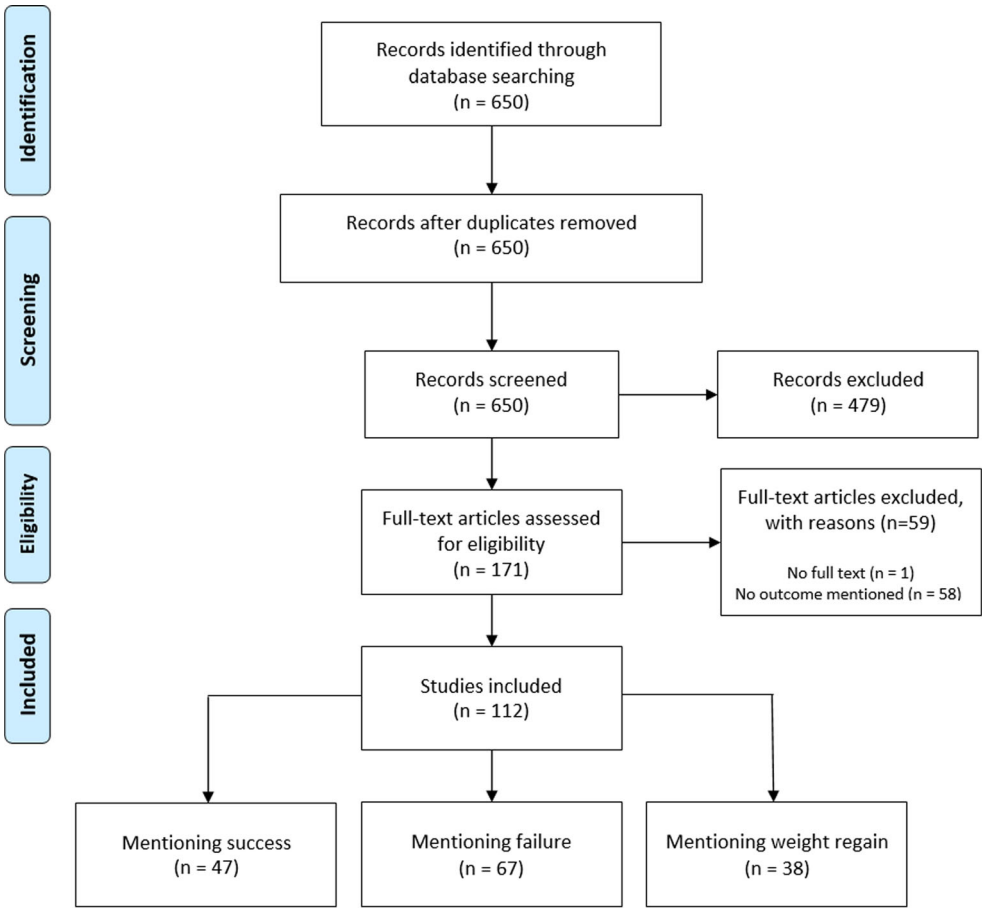

Fig. 2 Flowchart of the study selection according to PRISMA

Data Collection Process and Data Items

The following data was obtained from the included studies (DB and WL): year of publication, nationality, bariatric technique, outcomes (yes/no), and the definition(s) (if given). There was no assessment of bias in individual studies, as this was not relevant for the aim of the current study.

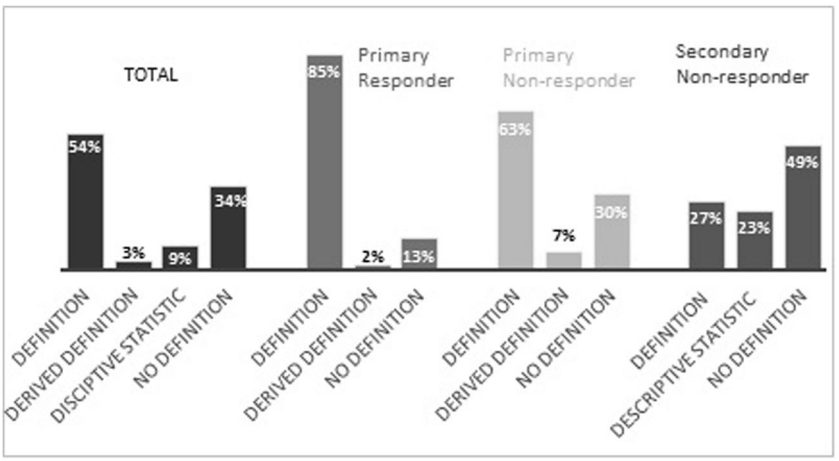

Fig. 3 Reporting of definitions

Table 2 Definitions

Definition of primary responder	Frequency of use[a]
2%EWL > 50%	XVI
%EWL > 50% 1 year after the surgery	IIII
%EWL > 50% 2 years after the surgery	III
%EWL > 50% during the whole follow-up after maximum weight loss	V
%EWL > 50% 1 year after the surgery to the end of the follow-up	I
%EWL > 50% at 5 years	I
%EWL > 60% 1 year after the surgery	I
%EWL > 60% and a BMI < 30 kg/m^2	I
%EBWL (excess body weight loss) ≥ 70% 2 years after the surgery	I
%EWL > 50% with resolution of comorbid health condition	II
%EWL > 50% and good glycemic control of T2DM to HbA1c lower than 6%	I
%EBL (excess BMI loss) > 50%	I
Adequate %EWL at 3 years = mean–1SD of the entire study's cohort	I
Definitions of primary non-responder	**Frequency of use[b]**
%EWL < 25%	IIII
%EWL < 25% at 1 year FU	I
%EWL < 30%	I
%EWL < 30% at the time of the last follow-up	I
%EWL < 50%	VII
%EWL< 50% 1 year after surgery	V
%EWL < 50% 18 months after the surgery	I
%EWL < 50% 2 years after the surgery	II
%EWL < 50% from 12 months FU to the end of FU	I
%EWL < 50% throughout FU	II
Excess body mass index loss (%EBMIL) < 25%	I
%EBMIL never exceeding 50%	I
< 25% weight loss (equivalent to > 50% EWL with BMI of 45–50)	I
No achievement of BMI < 35 kg/m^2 or after sufficient body weight reduction regained weight and exceeded BMI of 35 kg/m^2	I
%EWL < 50% and BMI > 35 kg/m^2	II
%EWL < 50% without weight regain or when the IFSO criteria for bariatric surgery were still met	I
BMI > 40 kg/m^2 - BMI > 35 kg/m^2 with co-morbidities or < 50% EWL or significant weight regain associated with inability to maintain %EWL of 50% 24 months after RYGB.	I
< 50%EWL or weight regain > 10 kg body weight	I
%EWL < 50% at nadir weight and thereafter or %EWL ≥ 50% at nadir weight, but < 50% at last FU visit (pronounced weight regain)	I
Patients weight was stable > 6 months with a %EWL < 50% or when a patient experienced weight regain	I
Significant weight regain	I
Excess weight loss < 50% at 2 years or weight gain > 15% from baseline	I
Unsatisfactory weight loss sustenance after the initial successful weight loss, with regain of > 50% of the weight lost	I
Definition of secondary non-responder	**Frequency of use**
Descriptive statistics (any weight regain)	XVIII
An increase in body weight of more than 5 kg	II
An increase in body weight of more than 10 kg from the nadir	II
An increase of at least 10% of the lowest postoperative weight	III
Any regain of lost weight from nadir weight	I
≥ 5% weight change between 1 and 2 years after surgery	I
Percentage excessive weight regain > 15%.	I
EWL regain > 25% with respect to the minimal weight or when patient met de criteria for bariatric surgery again established by the IFSO	I
> 25% rebound in EWL	I

Table 2 (continued)

Any regain of lost weight after 2 years	I
Regained all their lost weight within 5% of baseline	I
> 15% regain of maximum total weight loss	I
> 20% regain of maximum total weight loss	I
> 25% regain of maximum total weight loss	I
Any regained weight after achievement of %EWL > 50%	II
Any weight regain after successful loss (defined as achievement of body mass index ≤ 35 kg/m^2)	I
Weight regain resulting in failure to maintain an %EWL ≥ 50% over time	I
Regained all their lost weight within 5% of baseline	I

[a] Definitions repeatedly used by the same research group were just recorded ones

[b] Definitions repeatedly used by the same research group were just recorded ones

Summary Measures and Synthesis of Results

All results are stated as absolute number or percentage. There is no comparative statistical analysis performed.

Results

Study Selection

The literature search identified 650 articles with limits applied. There were no duplicates. All 650 articles were screened on title and abstract for relevance. In total, 171 studies were assessed in full text of which 112 articles were included (Fig. 2).

Reporting of Definitions

In the 112 articles selected, 191 outcome parameters were described. One hundred three out of 191 outcomes (54%) gave a definition and in one-third (64/191), no definition or description was given (Fig. 3). In total, thirteen different definitions of primary responders were described and 23 different definitions of primary non-responders were found (Table 2). Eighteen out of 77 papers used descriptive statistics to describe weight regain and only 21 authors gave a clear definition. The remaining studies ($n = 38$) often mentioned "weight regain" as an indication for revisional bariatric surgery or as a consequence of pouch dilatation after SG and did not mention a definition or descriptive statistics.

Content of the Definitions

Primary responders were mainly defined using %EWL as outcome measure. %EWL was used in all but one of the definitions of primary responders and %EWL > 50% as cutoff point was used in 9/13 definitions ($n = 33/38$). Two definitions ($n = 3$) included the remission of a comorbidity in the definition of success. No definition contained a patient-reported outcome measure (PROM).

Primary non-responders were mainly defined using %EWL as outcome measure (16/23). However, different outcome measures were used, including BMI cutoff points, excess BMI loss, and total weight loss. Interestingly, primary non-responding was often combined with secondary non-responding as "failure" and used as an indication for revisional bariatric surgery (Table 2).

For secondary non-responders, many different weight loss outcome measures were used. Even within these outcome measures, the cutoff points were far apart. For example, by the outcome measure maximum total weight loss, cutoff points 15%, 20%, and 25% were used. The same applied for regain of a certain amount of kilograms and for the rebound in excess weight.

Follow-up Cutoff Point in Content of Definition

Only in 8/13 definitions of primary responders a timeframe was set in which the weight loss needed to be achieved in order to being defined successful. For primary non-responders, eight definitions set a clear timeframe. The follow-up cutoff point was a marked dissimilar. The values one year, eighteen months, two years, three years, five years, and during the whole follow-up were all used as cutoff points in the definitions.

Subgroups

There were no differences in definitions used for RYGB and SG. The same applied for the different nationalities. Within papers from the same research group, some papers reported a definition while others did not. Even more interestingly, sometimes different definitions were used by one and the same research group.

Conclusion

In the current study, a literature search regarding the definitions of primary and secondary (non)responders was performed and the recent literature is still comparing its own apples and

oranges about these outcomes. Since the study of Mann et al. in 2015, this practice has not changed [9]. In one-third of the papers found in the current study, no clear definition was given. If present, the definitions differed between papers as we found thirteen, 23, and seventeen definitions for primary responders, primary non-responders, and secondary non-responders respectively. No standard follow-up cutoff point was found.

As long as there is no uniform definition, the literature regarding the outcomes is not comparable. Mann et al. showed that there was an inconsistency in reporting primary non-responders after primary bariatric procedure as 31 out of 51 papers did not gave a definition [9]. In addition, Lauti et al. showed that for secondary non-responders after SG, in nine out of the 21 papers, no definition was given [16]. In the current study, the percentage of articles that did not give a definition of primary non-responders was lower, 30%. However, out of the 42 definitions given, there were 23 different definitions. Looking at secondary non-responders, the results are even worse: in halve of the articles, no definition was given and in about a quarter only, descriptive statistics were given. Twenty-one articles gave a definition of secondary non-responders; in total, seventeen different definitions were found. To be able to compare the literature, all outcomes must be defined in the methods section of a paper and a uniform definition is required.

Moreover, due to the lack of a uniform definition, authors are able to manipulate their results by adjusting the definitions. Lauti et al. showed that, by applying six different definitions of secondary non-responders in a cohort of 96 patients receiving a SG, the percentage of secondary non-responders ranged from 9 to 91% [17]. When applying the 21 definitions of secondary non-responders, we found in the current study, on a cohort, the range of secondary non-responders would possibly not be that much different from Lauti et al., as the extremes of the definitions are comparable. This shows that the results of studies using different definitions will differ greatly. A standardized definition is needed to minimize bias and to be able to compare results and thereby determine the proportion of primary and secondary non-responders.

Another notable finding is that several authors used primary and secondary non-responders combined as "failure," as if these outcomes are equal. AlSabah et al. showed that primary non-responders achieved better results after revisional bariatric surgery compared secondary non-responders [18]. On the contrary, Uittenbogaart et al. reported a difference in achievement of weight loss success between these two groups after secondary gastric banding, as secondary non-responders (n = 15) were more likely to again reach %EWL > 50% and experienced significantly more weight loss compared to primary non-responders (n = 25) [19]. In the current study, three definitions of secondary non-responders mentioned that first, a %EWL of 50% must be achieved to be defined secondary non-responder. In these three papers, primary non-responders were defined separately. Primary non-responders (weight loss failure) and secondary non-responders (weight regain) are two different outcomes and should therefore be both defined and reported separately.

For the current study, a limited search was used in which papers could have been missed that gave a definition of one of the three outcomes. Only papers regarding primary RYGB and primary SG were searched because these procedures cover almost 90% of all the bariatric procedures which makes it the most relevant "subgroup" [20, 21]. Furthermore, only studies published the last three years were included. Even with this limited search, the current study shows the extreme diversity in the use of definitions and especially the lack of definitions in secondary non-responders.

Parallel to the differences in definitions, the outcome measures used are also diverse. To describe weight loss, some authors use %EWL while others use percentage total body weight loss (%TBWL) or just change in BMI to describe weight loss. Outcome measures are not comparable with each other. Several authors have questioned the use of %EWL, as it is not suitable to compare groups in non-randomized studies. The range differs depending on the formula used, the ideal weight is hard to determine, and it is difficult to understand for patients [22–25]. In addition, several authors recommend the use of another outcome measure, such as %TBWL which is independent of the initial BMI [23, 24]. The majority of the definitions of (non)responders in the current study contain the outcome measure %EWL, but many different outcome measures were used (Table 2).

Bariatric surgery is performed to improve cardiovascular risk profile/metabolic syndrome, extend the life expectancy, and improve quality of life (QoL). Striking is that 89.2% of the definitions did not include any of the previous mentioned factors and in the remaining 10.8% only remission of comorbidities was included. An interesting question is whether the cutoff point of the weight outcome measure in the definitions will change if there is remission of a weight-related comorbidity or improvement of another outcome, or for secondary non-responders whether there is a re-emergence of a weight-related comorbidity. DiGiorgi et al. reported that there is a relation between weight regain and the "re-emergence" of type II diabetes [26]. Results should not be about numbers but about the patients. Therefore, remissions of comorbidities, PROMs, and QoL should be taken into account when speaking about primary responders and primary and secondary non-responders (success, failure, and weight regain). However, for scientific purpose to compare the literature, uniform definitions of the outcomes purely based on a weight loss outcome measures should be defined.

The current study shows that definitions used in the recent literature regarding primary responders and primary and secondary non-responders are highly inconsistent. To be able to compare the literature, standardized outcomes regarding these

three outcomes should be formed and international consensus is required.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethics This paper does not contain any studies with human participants or animals performed by any of the authors.

Consent Statement For this type of study, formal consent was not required.

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