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ORIGINAL CONTRIBUTIONS

Adequate Multivitamin Supplementation after Roux-En-Y Gastric Bypass Results in a Decrease of National Health Care Costs: a Cost-Effectiveness Analysis

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Abstract

Introduction Patients with morbid obesity undergoing metabolic surgery are prone to develop vitamin and mineral deficiencies, which may worsen in time. In order to prevent these deficiencies after metabolic surgery, all patients are advised to take daily multivitamin supplementation. The aim of the study was to assess the cost-effectiveness of specially developed multivitamins (WLS Forte®) for metabolic surgery and over-the-counter (standard) multivitamin supplementation (sMVS).

Methods This cost-effectiveness analysis was preformed alongside an RCT for the Netherlands. Between June 2011 and March 2012, a total of 148 patients were randomized to one tablet daily of either WLS Forte® or sMVS. The patients were followed for 12 months. Data on costs within the health sector and outside the health sector were collected. The primary outcome is financial and logistic advantages, in terms of less patient visits to the outpatient department and the relevant costs to the employer due to absenteeism.

Results In total, 10 (14%) patients in the WLS Forte® group versus 23 (30%) patients in the sMVS group developed a deficiency. The costs for the WLS forte® supplement were €38 versus €23 for sMVS. Additional return visits and associated costs for medical staff were the largest costs, up to 43% in the sMVS group. Total costs for supplementation with sMVS were €243 versus €134 for WLS Forte®.

Conclusion Preventing deficiencies with WLS Forte® seem initially more expensive than sMVS. However, treatment with WLS Forte® resulted in less vitamin and mineral deficiencies, which eventually resulted in less overall costs.

Keywords Cost-effectiveness · Multivitamin supplementation · Morbid obesity · Roux-en-Y gastric bypass

Introduction

The Roux-en-Y gastric bypass (RYGB) and the sleeve gastrectomy are the two most frequently performed metabolic procedures worldwide [1]. Due to reduced dietary intake and, in case of the RYGB, surgically bypassing the areas of the gastrointestinal tract that is known to absorb many micronutrients, vitamin deficiencies may occur without proper supplementation. Especially deficiencies for iron (ID), vitamin B12, folic acid, vitamin D, and calcium are frequently diagnosed [2–6]. In order to prevent these post-surgical deficiencies, patients are advised to use lifelong multivitamin supplementation. Up to the present day, there has not as yet been a multivitamin supplement that meets the daily amount of vitamins and minerals which are needed after a RYGB. Based on the literature and pilot studies performed in our hospital, a new customized multivitamin supplement for RYGB patients was developed (WLS Forte® FitForMe, Rotterdam, the Netherlands). Besides the decrease in the number of deficiencies, it is expected that the use of WLS Forte® leads to financial and logistic advantages, in terms of less patient visits to the outpatient department and costs due to absenteeism for the employer.

A large randomized controlled trial (RCT) was initiated to investigate the effectiveness of WLS Forte®. In this RCT, patients were randomized between WLS Forte® and a standard MVS (sMVS, comparable with commercially available tablets containing 100% recommended daily allowance (RDA)). As part of the follow-up study this paper reports the

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cost-effectiveness analysis from the societal perspective of the Dutch Health Care of WLS Forte® versus sMVS supplementation.

Methods

Design

To perform this cost-effectiveness study, the patient records of all patients included in the RCT were used. The study protocol of this initial RCT was approved by the National Medical Ethics Review Committee and Local Ethical Committee. The protocol was registered at the clinical trials registry of the National Institutes of Health (ClinicalTrials.gov; identifier NCT 01609387). The protocol for this study (VITAAL II study) was approved by the national (CCMO Radboud Nijmegen) and local ethics committee (Rijnstate Hospital Arnhem). A detailed design of the RCT has been published elsewhere [7]. The original manuscript, published by Dogan et al. in 2014, describes in detail how patients were selected, randomized, and how the patients' daily intake of multivitamins was monitored. In brief, the study was a randomized double-blind, placebo-controlled trial. One hundred furty-eight patients, undergoing primary RYGB, were included between June 2011 and March 2012. Patients were randomized to either WLS Forte® ($n = 74$) or a sMVS ($n = 74$) and were followed for 1 year. Preoperatively diagnosed deficiencies for iron, folic aces, vitamin B12, and vitamin D were treated with predefined medication until 2 months preoperatively so that it would not intervene with the postoperative multivitamin supplements [7]. The content of each supplement is shown in Table 1. Both supplements were dosed as one capsule daily. No patients were lost to follow-up.

Data Collection

All patients were followed for up to 12 months. The nutritional status was measured at baseline, 6 months, and 12 months. This included a complete blood count, calcium, phosphate, magnesium, zinc, albumin, iron, total-iron-binding-capacity (TIBC), ferritin, folic acid, vitamin B12, 25-hydroxyvitamin D (25-OHD), parathyroid hormone (PTH), vitamin B1, and vitamin B6. Calcium data are shown as calcium levels corrected for albumin (Ca_{corr}), according to the following equation: $Ca_{corr} = \text{Total calcium} - (0.025 \times \text{albumin}) + 1$. The detailed clinical outcome on vitamin or mineral deficiencies is reported elsewhere [7]. Data on nutritional deficiencies were extracted from the existing database of the initial RCT. The following deficiencies were included for cost analysis: ID, vitamin B11, vitamin B12, zinc, vitamin B1, and vitamin B6. Calcium and vitamin D deficiencies were excluded from analysis because it was unattainable to get the right quantities of calcium and cholecalciferol in the WLS Forte® supplement. For this reason, all patients also received calcium carbonate/cholecalciferol (CaD) 500/400 tablets three times daily (a total of 1500 mg calcium and 1200 IU vitamin D).

Table 1 The contents of standard multivitamin supplement versus WLS forte® used

Ingredients	Standard MVS		WLS Forte®	
	Dosage	*RDA (%)*	*Dosage*	*RDA(%)*
Biotin (μg)	25.00	50.0	600.00	1200.0
Calcium (mg)	91.43	11.4	0.0	0.0
Chloride (mg)	0.14	0.0	0.54	0.1
Chrome (μg)	40.00	100.0	160.00	400.0
Copper (μg)	999.60	100.0	3000.20	300.0
Folic acid (μg)	200.00	100.0	600.00	300.0
Iodine (μg)	153.70	102.5	225.04	150.0
Iron (mg)	14.00	100.0	70.00	500.0
Manganese (mg)	2.00	100.1	3.00	150.0
Magnesium (mg)	30.00	8.0	0.0	0.0
Molybdenum (μg)	50.00	100.0	112.40	224.8
Selenium (μg)	55.00	100.0	105.00	190.9
Vitamin A (μg)	599.70	75.0	1000.38	125.0
Vitamin B1 (mg)	1.10	99.7	2.75	249.7
Vitamin B2 (mg)	1.40	100.0	3.50	250.0
Vitamin B3 (mg)	16.0	100.0	32.00	200.0
Vitamin B5 (mg)	6.00	100.0	18.00	300.1
Vitamin B6 (mg)	1.40	100.2	2.80	199.7
Vitamin B12 (μg)	12.50	100.0	350.00	14,000.0
Vitamin C (mg)	80.00	100.0	120.00	150.0
Vitamin D (μg)	4.00	80.0	12.50	250.0
Vitamin E (mg)	10.00	83.4	24.00	200.0
Vitamin K1 (μg)	25.00	33.3	120.00	160.0
Zinc (mg)	10.00	100.0	22.50	225.0

RDA recommended daily allowance, *MVS* multivitamin supplement

Correction of Deficiencies

The vitamin and mineral deficiencies are treated by standard supplementation algorithms. These algorithms are shown in Table 2. When a patient was considered to be deficient, consultation was necessary to evaluate deficiency-related complaints and to initiate adequate treatment (Flowchart 1).

Outcomes on Costs

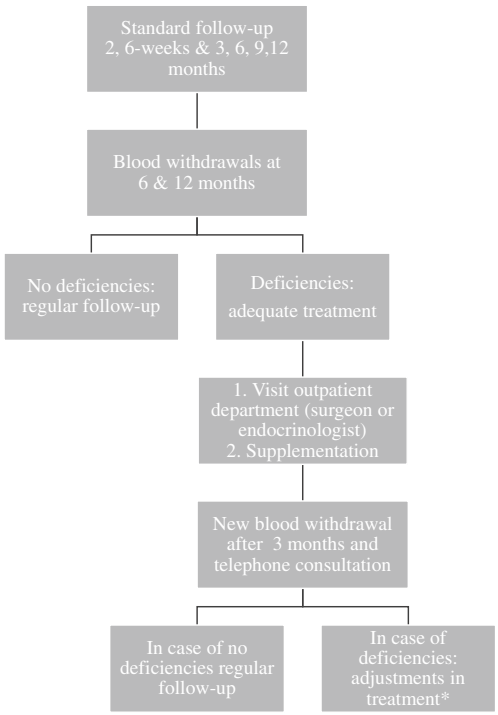
Direct Medical Cost The costs for vitamin deficiency after metabolic surgery were calculated by using a cost approach according to the Dutch guidelines for economic research in health care [8]. The Dutch health care system uses a registration and declaration system for hospitals that is based on

Table 2 Deficiencies and treatment

Deficiency	Treatment	Frequency
Iron	Ferrous gluconate 695 mg	3 times a day
Vitamin B11 (folic acid)	Folic acid 5 mg	1 time a day
Vitamin B12	Hydroxocobalamin 1000 μg intramuscular	Every 2 months
Zinc	Zinc sulfate 220 mg	2 times a day
Vitamin B1	Thiamin 25 mg	1 time a day
Vitamin B6	Pyridoxine 50 mg	1 time a day

diagnosis-treatment-combinations (DTC's). A DTC includes the total route, from diagnosis to (possible) treatment, which is set by the physician. All activities carried out in the hospital during this period lead to one billable product with an average price (hospital costs and fees). Each DTC is formed by a combination of a diagnosis, type of care, and treatment. For example, a DTC can include visits to the outpatient department, telephone consultations, blood withdrawals, surgery, materials, and overhead costs. The price for a DTC depends on the indication for consulting a specialist. The cost for the DTC associated with a vitamin deficiency after metabolic surgery is €335. In other words, every patient with a diagnosed vitamin or mineral deficiency costs the health care system €335.

Other costs are costs for daily multivitamin supplements, supplementation to treat a deficiency, and costs for the general practitioner to perform the hydroxocobalamin (vitamin B12) injections (Table 3). The costs for vitamin and mineral supplements are based on the wholesale price for the pharmacy department of our hospital. We assume that a newly diagnosed deficiency can be treated adequately within 3 months. Therefore, we calculated the costs per 3 months. The costs for multivitamin supplements are for a 1-year period since this is the studied period. Costs for the sMVS are based on a mean price of five commercially available tablets in the Netherlands.



Flowchart 1. The sequence of follow-up and treatment in relation to vitamin and mineral deficiencies after metabolic surgery. *In case of a persisting deficiency, adjustments in treatment have to be made with additional follow up

Indirect Medical Costs These are consisted of traveling expenses (including parking costs) and production losses caused by absenteeism. For traveling expenses, the assumption was made that all patients came to the hospital by car. The cost price for traveling was calculated on a base of €0.20 per kilometer [8]. Mean kilometers were extracted by calculating the distance between our hospital and the patients' home address. Parking costs were agreed on at €3.00 [8]. The costs resulting from production losses in terms of absence were calculated on the assumption that 75% of the patients had paid work, and the other 25% were unpaid volunteers or unemployed. The productivity costs for patients that have a job are per hour of paid work and depend on the age and sex of the patient. The mean age in the current study was 44 years and 45% was male. Based on these numbers, the costs per hour of paid work is €32 (2014; available at: statline.cbs.nl) [8]. The mean duration

Table 3 Costs for multivitamin supplements and drugs

Variables	Medicine	Average unit cost per 3 months (Euro's)
Multivitamin supplement	WLS Forte®	30
	sMVS	21
Deficiency		
Iron	Ferrous gluconate	82
Vitamin B11 (folic acid)	Folic acid	17
Vitamin B12	Hydroxocobalamin	55[a]
Zinc	Zinc sulfate	180
Vitamin B1	Thiamin 25 mg	16
Vitamin B6	Pyridoxine 50 mg	19

sMVS standard multivitamin supplement

[a] Price included costs for injection at the general practitioner

of absenteeism due to a visit to the outpatient department is estimated at 4 h, the mean duration for blood withdrawals after treatment at 3 h, and for a telephone consultation 30 min. In order to make sure the patient will achieve adequate treatment in case of a vitamin deficiency, a total of 7 h and 30 min of production time is lost due to absenteeism.

Results

Demographics

In the original population of 148 patients (74 patients in each group), 45% ($n = 66$) was male. The median age was 44 years (range 22–65). Mean weight and BMI at baseline were respectively 134 kg (range 89–202) and 45 kg/m^2 (range 28–60). After 12 months follow-up, a median percentage excess weight loss (%EWL) of 72% (range 21–136) was achieved. Both groups were similar with respect to age, sex, weight, BMI, and preoperative deficiencies (data shown in the original article).

Deficiencies

A total of 44 different deficiencies were found: 14 deficiencies in 10 patients in the WLS Forte® group versus 30 deficiencies in 23 patients in the sMVS group.

Costs

The summary of the total cost is presented in Table 4. This table summarizes both resource use and costs for the entire patient group. The costs are based on a treatment period of 3 months in which we assume a deficiency can be treated adequately. Treatment with WLS Forte® was more expensive (€8.880) compared to sMVS (€6.216). DTC's were the largest cost items within the health sector, with a portion up to 34% of the total costs in the sMVS group. The largest cost item outside the health sector are the costs due to absenteeism, which accounts for up to 24% of the total costs in the sMVS group.

Incremental Costs and Deficiencies per Patient (Table 5)

The total costs per year for our group of patients for were €15.962 for WLS Forte® and €22.610 for sMVS, respectively. Total costs per patient for preventing and treating nutritional deficiencies were €306 for sMVS versus €216 for WLS Forte® every 3 months. The chance of developing any kind of vitamin or mineral deficiency is 14% for WLS Forte® versus 30% for sMVS. In terms of incremental costs per patient, the WLS Forte® was less costly and more effective.

Discussion

The use of an optimal multivitamin supplement (WLS Forte®) seems to be more cost effective in this population compared to a multivitamin supplement that is available over the counter (sMVS). In the WLS Forte® algorithm, less deficiencies occurred which consequently resulted in less visits to the outpatient department. Most of the costs are related to the number of deficiencies that were treated. The use of a specialized multivitamin resulted in less overall costs compared to sMVS.

The need for standardized multivitamin supplementation after metabolic surgery is an important topic. Especially since the number of procedures is rapidly increasing [1]. Due to different pathways, such as restriction of caloric intake and partial bypassing of the upper intestinal tract, patients are prone to developing vitamin and mineral deficiencies. The most common deficiencies after metabolic surgery are in iron, vitamin B12, folic acid, and vitamin D [5, 6]. In order to prevent patients from developing these deficiencies, patients are advised to take multivitamin supplementation on a daily basis. However, it is known that the current multivitamin supplements are not sufficient enough to prevent most deficiencies [6]. Therefore, a new multivitamin supplement for RYGB patients was developed which was able to reduce the number of deficiencies if taken consequently. This reduction is the most important aspect of the specialized multivitamin but on the other hand, these supplements are more expensive compared to the supplements that are already available.

The reduction in the number of deficiencies resulted in less patient visits to the outpatient clinic. This reduction in visits to the outpatient clinic has a number of advantages from different perspectives. From the perspective of the hospital personnel (including nurses and medical specialists), the reduction saves time in which we assume personnel can treat other patients or will be deployed elsewhere in the hospital. To a lesser extent, this also applies to the general practitioner, who also might be consulted for deficiencies after metabolic surgery. The perspective of an employer should not be underestimated. Costs due to absenteeism for a visit to the outpatient clinic are a major expense, up to 31% of the total costs in the sMVS group. It may be assumed that this percentage is an underestimation of the actual costs made by the employer. For example, this paper does not include the costs for absenteeism due to symptoms of a deficiency and costs for temporarily replacing personnel.

For patients, the costs of a supplement are an important issue since multivitamin supplements are not reimbursed. For this reason, patients often resort to the cheapest supplement, although this probably is not the most effective supplement. Many patients are not aware of the adverse effects of vitamin and mineral deficiencies. Therefore, patients should be well informed and advised to take their supplementation

Table 4 Financial cost estimates and probabilities per patient in the reference case. Costs are presented in Euros

Variables	WLS Forte®		Standard multivitamin		Difference	
	Resource	*Cost*	*Resource*	*Cost*	*Resource*	*Cost*
Costs within the health sector						
Multivitamin supplement	74 patients	8.880	74 patients	6.216	0 patients	2.664
DTC's	10 patients	3.350	23 patients	7.705	13 patients	− 4.355
Drug costs per deficiency	28		29			
Iron	1 patient	82	8 patients	656	7 patients	− 574
Vitamin B11 (folic acid)	2 patients	34	5 patients	85	3 patients	− 51
Vitamin B12	1 patient	55	6 patients	330	5 patients	− 275
Zinc	6 patients	900	9 patients	1.620	3 patients	− 720
Vitamin B1	3 patients	48	2 patients	32	− 1 patient	16
Vitamin B6	1 patient	19	0 patients	0	− 1 patient	19
Costs outside the health sector						
Traveling costs	10	164	23	377	13	− 213
Parking costs	10	30	23	69	13	− 39
Costs due to absenteeism	10	2.400	23	5.520	13	− 3.120
Total costs		*€15.962*		*€22.610*		*€− 6.648*

DTC diagnose treatment combination

regularly and make sure their nutritional status is being checked at least every 12 months.

Furthermore, this paper only shows the results of 1-year follow-up based on the costs per patient for a 3-month treatment period. When extracting the results to a longer follow-up period, it is to be expected that the differences in nutritional deficiencies between WLS Forte® and sMVS will grow even further. This is partly because the human body is able to create stocks for certain vitamins or minerals. After metabolic surgery, the body will first reclaim these stocks before developing a deficiency. Some of these stocks are large enough to prevent patients from developing deficiencies in the first year after metabolic surgery.

Some possible limitations should also be discussed. First, the cost-effectiveness of the different multivitamin supplements have been retrospectively determined with only 1 year follow-up. Longer follow-up was however not possible to achieve from the RCT since the Medical Ethics Committee (MEC) decided after 1 year that it was unethical to exclude patients from taking WLS Forte® since the results of WLS Forte® were superior to that of a sMVS. At that point, the randomized component of the study was terminated, and it was impossible to perform a fair analysis of the following years. Furthermore, we have made some assumptions to perform a complete cost-effectiveness analysis. These assumptions may differ from reality. A third element is that this analysis is performed from the perspective of the Dutch health care system. Therefore, it is difficult to extrapolate the results to other countries. Before extrapolating, epidemiologic and cultural factors, availability and system of healthcare, differences in medical treatment, financing of health care, and absolute and relative price indexes should be taken in account. Finally, it would have been preferable if the improvement in quality of life had been used as an outcome parameter in this study.

However, with all these limitations in mind, this cost-effectiveness analysis is able to provide patients, physicians, health insurance companies, and the ministry of health an overview of the costs resulting from post-surgical deficiencies.

Table 5 Differences in costs between treatment with WLS Forte® and a sMVS

Variables	WLS Forte®	sMVS
Change on developing a deficiency	14%	30%
Costs within health sector per patient (€)	181	225
Costs outside health sector per patient (€)	35	81
Total costs per patient (€)	216	306
Incremental costs per patient (€)	*− 90*	*NA*

sMVS standard multivitamin supplement

Conclusion

The majority of costs for the evaluation and treatment of a vitamin or mineral deficiency after RYGB consists of personnel costs. Costs for the medication used for treating the deficiencies are relatively cheap. Use of WLS Forte® is more expensive compared to sMVS for the patient. However, treatment with WLS Forte® resulted in less vitamin or mineral

deficiencies which eventually resulted in significantly lesser overall costs from the perspective of the Dutch Health Care.

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Compliance with Ethical Standards

Conflict of Interest IMCJ, FJB, and EOA are consults for FitForMe™, Rotterdam, the Netherlands. All the other authors have nothing to declare.

Informed Consent Statement Informed consent was obtained from all individual participants included in the study.

Statement of Human and Animal Rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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