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40 years of advances in Bariatric Surgery
40 años de avances en Bariatría

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Abstract

Introduction: Bariatric surgical practice changes in the community setting may be under-reported. We present the developments in a Spanish bariatric surgical practice in the community setting of Alcoy from 1977 through the present.

Methods: Bariatric surgical techniques employed in a country community setting over the course of nearly four decades were reviewed retrospectively and qualitatively.

Results: Surgeons and medical professionals from Alcoy, Spain were involved in the evolution of bariatric surgery patient management and surgical technique from 1977s through 2017. During the last 40 years, 1,495 patients were treated in our clinics. Spanish bariatric surgeons contributed to advances in gastric bypass (GBP) in the 1970s, vertical banded gastroplasty (VBG) in the 1980s, biliopancreatic diversion/duodenal switch (BPD/DS) in the 1990s, and innovations associated with laparoscopy from the 1990s onward. Outcomes and approaches to prevention and treatment of bariatric surgical complications are reviewed from a community perspective. Contributions to the bariatric surgical nomenclature and weight-loss reporting are noted.

Conclusions: The practice of bariatric surgery in the community hospital and private clinic must be updated continuously, as in any human and surgical endeavor. Medical professionals in community bariatric practices should contribute their experiences to the field through all avenues of scientific interaction and publication.

Keywords
Obesity surgery; Bariatric surgery; Community hospital; Bariatric tendencies

Resumen

Introducción: Los cambios en la práctica de cirugía bariátrica en un hospital comarcal han sido muy importantes. Presentamos la evolución en el Hospital Comarcal de Alcoy (HCA) desde su origen en 1977 hasta el presente.

Métodos: Se revisan retrospectivamente las técnicas quirúrgicas bariátricas empleadas en un entorno comarcal a lo largo en cuatro décadas.

Resultados: Los cirujanos Alcoy, han estado involucrados en la evolución de la gestión de los pacientes de cirugía bariátrica y las técnicas quirúrgicas desde 1977 hasta la actualidad. Durante los 40 años trascurridos, 1,495 pacientes fueron tratados en nuestras clínicas comenzando con la derivación gástrica (DG) en la década de 1970, la gastroplastia vertical anillada (GVA) en la década de 1980, el cruce duodenal (CD) biliopancreático en la década de 1990, y con el acceso por vía laparoscópica desde la década de 1990.

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Los resultados y los enfoques para la prevención y el tratamiento de las complicaciones de la cirugía bariátrica así como la contribución en la nomenclatura de cirugía bariátrica y la notificación de pérdida de peso son revisados desde una perspectiva comarcal.

**Conclusiones:** La práctica de la cirugía bariátrica en el entorno comarcal debe ser actualizada continuamente. Los cirujanos bariátricos pueden contribuir con sus experiencias en el ámbito comarcal con actualizaciones y publicaciones.

**Palabras clave**
Cirugía de la obesidad; La cirugía bariátrica; Hospital comarcal; Tendencias bariátricas

**Abbreviations**

1	extsuperscript{eu} in Europe  
1	extsuperscript{sp} in Spain  
1	extsuperscript{w} in the world  
AL Alimentary limb  
ABS Adolescent bariatric surgery  
ASBS Amer. Society for Bariatric Surgery  
ASMBS American Society for Metabolic And Bariatric Surgery  
AEC Asociación Española de Cirujanos  
BMI Body Mass Index = kg/m	extsuperscript{2}  
BS Bariatric surgery  
BOLD Bariatric Outcomes Longitudinal Data  
BPD Biliopancreatic diversion  
BPD/DS BPD/Duodenal switch  
BPL Biliopancreatic limb  
CC Common channel  
CPM Caloric-protein malnutrition  
DIA Duodenoileal anastomosis  
DS Duodenal switch  
ExBMI Expected BMI  
ECEP European Centers of Excellence Program  
EGJ Esophago-gastric junction  
FBMI Final BMI  
GBP Gastric bypass  
GERD Gastroesophageal reflux  
GGF Gastro-gastric fistula  
GT Gastric tube  
IFSO International Federation for the Surgery of Obesity and Metabolic Disorders  
IBMI Initial BMI  
JIB Jejunum ileal bypass  
JIA Jejunum-ileum anastomosis  
LDS Laparoscopic duodenal switch  
LGB Laparoscopic gastric band  
LGBP Laparoscopic gastric bypass
Introduction

Morbid obesity is a pandemic condition that affects humans of all countries, races and continents. The cause is multifactorial and one the most influential factors are changes in environment and lifestyle that support consumption by humans of more calories than they utilize. When BS is employed to treat the disease of obesity, the stomach and small bowel, organs of the digestive pathway are healthy, and not the direct cause of disease. The term, BS, comes from the Greek "baros" meaning “weight,” and “iatrein” means “treatment”—treatment of the broad etiology of obesity through surgery. In order to influence the weight of a patient, a bariatric surgeon can operate on the stomach to reduce caloric intake (restriction), and/or on the small intestine, to cause malabsorption of nutrients by shortening the length of the intestine (without any bowel removal). In mixed techniques, restrictive and mal-absorptive components are combined. "Metabolic Surgery" (MS) represents an expansion of the concept of BS to reflect the management of metabolic conditions, such as hypercholesterolemia and/or diabetes.

When BS is used to treat obesity, the organs, the stomach and the small intestine, are healthy and are not the direct cause of the disease. The bariatric surgeon operates in the stomach to reduce caloric intake (restriction), and / or in the small intestine, to cause poor absorption of nutrients by shortening the length of the intestine useful for full absorption (bypassing a part). In mixed techniques, the restrictive and mal-absorbing components are combined.

1950s—origins of BS/MS

Henriksson (1) performed the first, isolated, JIB in Gothenburg, Sweden in 1952 but BS field was actually initiated in 1953 at the University of Minnesota by two groups, Varco and Buchwald and Kremen and Linner (2).

During the latter half of the 20th century, J. Howard Payne (3) and other surgeons were performing malabsorptive operations. In 1964, Buchwald inaugurated MS by diverting the distal one-third of the small bowel to treat hypercholesterolemia (4,5). Edward Mason initiated the technique of the GBP in 1965 (6).

Methods

The aim of this review special article of the surgical changes made in a 40 years period in the practice of bariatric surgery at the Virgen de los Lirios Hospital and Clínica San Jorge de Alcoy, Spain
Setting

Alcoy County is located in the Alicante province of Southeastern Spain, close to the Mediterranean Sea. The population of the city is 60,000, and the county community, 140,000. Alcoy has a 300-bed National Health Service (NHS) state of the art facility, the Virgen de los Lirios district hospital, which includes an intensive care unit and operating room with three-dimensional camera laparoscopic facilities, computerized tomography and radio magnetic scans, a blood bank, standard and interventional radiology, an explant transplantation center. San Jorge Clinic is a smaller private institution where private patients were treated. All patients were treated by the same primary surgical staff.

Results

Development of bariatric surgery in Alcoy, Spain

1970s—beginnings of BS in Alcoy

On June 19, 1977, we initiated the first GBP in Spain, performed as recommended by Dr. Mason (6) in 18 patients, an experience not published until 1980 (7). Much later, in 2013 (8), we learned that Prof. Garcia of Seville (already deceased) had performed the first malabsorptive JIB (9-12) in 1973 as recommended by Scott (13).

1980s and 1990s —vertical banded gastroplasty

Mason (14), in 1982, published his paper on the first VBG. In 1986, we published our first experiences with VBG using staplers (15). Dr. Andreo, our radiologist, published a description of the VBG “peanut deformity” (16).

Gastro-gastric fistula (GGF), a communication between the gastric pouch and the gastric fundus, was the main undesirable complication of the VBG. Five of our first 10 patients had this complication. While not life-threatening, the complication destroyed the intended restriction of the operation. Therefore, in 1988, our group devised the "vertical division with linear stapler and staple-line suture", separating both staple-lines with a continuous serosal suture (17). The technique was presented in Milan, Italy in the 1st World 1988 Surgical Week that won the Best Poster Award. We operated on 130 patients with this technique without a single GGF. McLean et al in 1993 published later the same technique (18).

We reported our high expectations of VBG (19) and reviewed the same patients 5 years later, commenting that “the VBG... was a frustrating experience” (20,21). And less than 2 years later, VBG disappeared from the bariatric armamentarium.

Baltasar et al (22) published in 1987 the first surgery for hypercholesterolemia done in Spain by diversion of the distal one-third of the small bowel and this is also the first Spanish publication on MS. The operation has been abandoned with the use of statins.

In 1984 RTVE (National Spanish TV) aired “JJ Soriano, más moral que el Alcoyano”, in the prestigious series "Vivir cada día". It was the first broadcast operation of obesity surgery in Spain. It dealt with the life of a super-obese of 148 kg and IMC-52 treated by VBG at Alcoy Hospital. And it should be noted that the hospital’s phones were blocked.

https://www.youtube.com/watch?v=pQIw3H9B_kg

On September 25, 1995, we assisted Dr. Favretti (23) of Italy in performing the first LGB in Spain at the Hospital La Paz, in Madrid. Carbajo (24) publicó la first experience. However, early on we abandoned use of the technique. LGB became less and less popular, first in Europe and then in the world.

1990s—duodenal switch

On March 17, 1994, we performed the first open DS in Spain. Our open DS series has 527 patients (5 deaths, 0.9% mortality) (25-27). At the ASBS meeting in Seattle in June 1995, we presented a video (28) depicting the full division vertical
gastrectomy and suturing of the staple line. Dr. Hess (29), saw the video and began using the continuous suture, noting that, "after seeing a video of Baltasar at the annual meeting of the ASBS, we modified our procedure for the subsequent 188 cases and had only a leak". A continuous running serosal suture of the staple line prevents leaks that may occur after SG (the first part of the DS). Dr. Hess performed the 1st DS in 1988 and Dr. Marceau (30) started on June 1990 and made the 1st DS publication in 1993 and both ought to be considered the "fathers of DS".

A second contribution of our DS video was the use of the transverse supraumbilical abdominal incision (Fig. 1a). This approach resulted in fewer incisional hernias, 10%, compared with the midline laparotomy incision (hernia rates of 31% to 39%). The transverse incision has 2 other advantages. One is a cosmetic: When patients lose weight, the size of the abdominal scar is reduced to less than one-third of that achieved with the laparotomic approach (Fig. 1b). The second benefit is that the transverse incision facilitates post-bariatric plastic surgery, as transpositions of the navel are readily performed with a single scar just above the pubis (Fig. 1c). Our group later published: a) Gastric emptying (31) an intermediate study on the DS (32,33) followed by comparative studies of VBG and DS (34,35).

Fig. 1. Transverse laparotomy and scars.

In 1990, the ASBS started Obesity Surgery (OS), as their official medium for reporting scholarly research and was included into the Index Medicus in 1995. This is a major accomplishment and recognition, and then became the journal of IFSO. AB entered into ASBS membership as the 1st member in 1997 and 1st IFSO in 1998 and served on the ASBS Standards Committee under the chair of George Cowan 1998-2004.

In addition to their contribution to BS by directing OS, Drs. Mervyn Deitel and George Cowan published three books and were very influential as surgeons and book publishers (36-39). Deitel’s acclaimed 1989 book inspired AB to specialize in bariatric surgery field (36).
Mid-1990s—laparoscopic BS and SECO

Wittgrove and Clark (40-42) lead the transition from laparotomic to laparoscopic BS. We were impressed by their 1993 1st RNY LGBP experience. In early 1996, they published their second paper. In the summer of 1996, AB was asked to review their third (42) paper for Obesity Surgery, which summarized outcomes in 75 patients (42). AB while making two presentations at the ACS meeting in San Francisco (43,44) visited them in San Diego and they told him that he was the 1st visiting surgeon to do so.

Our group in Alcoy performed the 1st LGBP on January 14, 1997, and reported it in the second SECO meeting in December, 1998, and then published the results of 16 cases (45). At the 1998-IFSO Bruges, Belgium meeting, there were only 2 surgical films on LGBP, one from Sweden by Gustavsson (46), and our own (47); these perhaps represented the 1st 2 reports on LGBP outside of the US. We concluded somewhat presciently that it was “a beautifully designed operation, with a very difficult learning curve but that probably will become the gold standard of bariatric surgery.”

Serra (48), in 1999, reported the 1st case of internal hernia after LGBP, which was cited by Higa et al in 2003 (49). Baltasar (50) reported the 1st 27 LGBP cases and received the REEAD 2000 Spanish National Surgical Award.

Whereas, in the initial Wittgrove technique, a #33 port was used to introduce the stem of the circular stapler, AB suggested using the stapler without a port (Fig.2). Later, Dr. Wittgrove (51) acknowledged that this was a feasible and practical approach and became the accepted standard technique (Fig.3).

Spanish Society for the Surgery of Obesity (SECO)

Our group founded SECO with 26 members in Alicante, Spain (Fig. 3) in December 1997. During the inaugural meeting, AB became the 1st President. The second meeting was held in Granada in 1998 with Drs. Capella and Álvarez Cordero as our first honorary members. In the following year, SECO became the 13th IFSO member society. SECO was accepted into the Spanish Surgical Society (AEC) in 2002, and AB was made SECO Honorary President. While AB was President of IFSO and SECO, we organized the VIII World Congress of IFSO-2003 and the 1st Ibero-American meetings in Salamanca. By 2004, SECO had the second highest number of publications in OS after the US, and continued to hold that position in 2005, 2006, and 2007, and held the third position in 2009 (52).

SECO has been proved to employ an effective operational structure. It has had 7 presidents, with that role changing every 2 years. SECO has created sub-brands, e.g., Fun-SECO, Campus-SECO, and Multidisciplinary-SECO. Each of these groups’ respective activities and information are readily accessed through its website (http://www.seco.org/). SECO now has 420 members and several honorary members who rank among the most distinguished bariatric surgeons in the world.
Spanish bariatric surgeons are well-considered and two of them have developed techniques that are worldwide used today. Dr. Miguel Carbajo of Valladolid on 2002 developed the OAGB (one anastomosis gastric bypass - BAGUA in Spanish) and Drs. Andrés Sánchez Pernaute and Antonio Torres at Madrid Clinic Hospital the SADI (Single anastomosis duodeno-ileal).

IFSO has recently appointed Dr. Antonio Torres, a past President of SECO, as Organizer, and Dr. Baltasar, as Honorary President, of the upcoming Annual IFSO-2019 Congress in Madrid. Spain is the third country (after Austria and Brazil) to organize 2 world conferences, and the second country with 2 IFSO presidents.

Our group’s members have operated as invited surgeons in Portugal (1997, 1st VBG; 2001, 1st DS; 2005, 1st SG); in Brazil (1998, Sao Paulo, 1st DS; 2004, Itajai, 2nd LDS); in Buenos Aires, Argentina (2002, 1st LGBP), in Ahmedabad, India (2005, 2nd LDS), in Jerusalem, Israel (2008, 1st LDS), and in Norway (2002, Forde, 1st LDS; 2002, Tonsberg, 2nd LSG). We have also been guest surgeons in several national hospitals and a guest speaker in 2003 at the 1st Spring ACS Meeting, the 1st ASBS Meeting in New York, and the 1st Fall meeting of ACS-ASBS in Chicago and at the Palace of
Medical Sciences of Moscow in 2009. We have also had the privilege of hosting 71 visiting guest surgeons who have traveled to Alcoy, Spain to learn LDS and LSG. AB is Honorary Member of Brazil, Argentina and Portugal bariatric societies.

**Early 2000s—laparoscopic duodenal switch**

Our group was present in 1999 when Gagner performed the 1st LDS in Terrassa, Spain, even before he and Ren (55) described it in 2000 as the most complex BS technique. We performed our 1st LDS on October 5, 2000 (56-59); Weiner et al (60) considered it to be the 1st LDS performed in Europe. We have done 413 LDS cases (2 deaths, 0.48%). Our LDS is performed by 3 surgeons using 6 ports (one “#12 single working port” in the right upper quadrant, one #10 port for the camera, and four 5-mm working ports). All bowel divisions are accomplished with staplers and all four anastomosis are hand sewn.

In 2000, we published the 1st Spanish book in BS, “Obesidad y Cirugía” (Obesity and Surgery) with 2 editions (61). The book was intended for the general public but was also widely read by Spanish medical professionals.

In 2005, SOARD, a journal on par with OS in the BS field, published its first volume. During these years, our publications described gastric emptying after DS (62), as well as pancreato-cutaneous fistula (63), cardiac tamponade by central catheter (64), hepatic impairment (65,66), liver failure and transplant (67), total gastrectomy (68), and different types of DS reversal (69). Thirty patients (3.2%) of the 923 DS patients studied underwent bowel lengthening for malnutrition. We also described (70) the 1st occurrence of mucosal jejunal wall hernias through the thin muscular bowel wall of patients with malnutrition and suggested that, in malnutrition, laparotomy may be safer than laparoscopy. We performed laparoscopic conversions from RNY to BPD as a successful and fairly easy therapy (71).

**Mid-2000s—laparoscopic sleeve gastrectomy and other innovations**

We completed our 1st LSG on December 12, 2002 and reported it 2005 (72). Ahmad et al (73) recently ranked this paper’s citation index 61st within BS. We published additional papers on LSG (74-75) and the performance of one of the 1st re-sleeves gastrectomies (76,77).

We operated LSG on 342 patients. Three of them experienced bleeding, 3 required an emergency intra-operative tracheotomy due to impossible intubation (78), and there were 3 EGJ leaks, and 2 deaths (0.6%) (one due to bleeding on the abdominal port and the second for EGJ leak). The entire LSG group had 93% EWL at 2 years, probably due to the systematic use of the very narrow sleeves and antrectomy, and to beginning the gastric stapling right at the pylorus (79).

Prevention, detection, and management of LSG leaks and fistulas at the EGJ have been a main concern for our group. At the IFSO-2000 meeting in Genoa, Italy we presented our use of the 1st non-removable stent (80). At that time removable-ones were not available, and so we used a non-removable Wall-stent that saved the patient’s life and that lasted 6 months until esophageal hypertrophy of the mucosa caused obstruction of the esophagus requiring a total gastrectomy with intra-thoracic anastomosis (68). In 2007 Serra published our experience in self-expanding stents (81).

**Salvage surgery for chronic EGJ fistulas**

In 2007 we used the 1st RNY diversion to correct chronic EGJ fistulas (82-84) and presented it for discussion at the 2nd and 3rd world LSG summits organized by Gagner et al and Deitel et al (85-86). This technique has become the standard management of this serious condition (Fig. 4).
Fig. 4. RNY-diversion to treat chronic leaks by end-to-side or side-to-side.

**Diabetes surgery**

On February 10, 2004 we performed the 1st diabetes surgery in Spain in a non-morbidly obese individual (BMI of 33 kg/m$^2$) using the DS without gastrectomy; this technique was later reported in 2014 by Marceau et al. Bou et al published our technique of SG with duodenal-jejunal diversion (SG+DJ) for diabetes (89).

In 2006, we published a report of our 1,000 bariatric operations (91), which won the Spanish National Surgical Award.

**Adolescent BS (ABS)**

A 10-year-old wheelchair-bound boy with a BMI of 42 kg/m$^2$, Blount’s disease, and knee fractures underwent LSG in 2008 (92). The patient was the 1st ABS done in Spain, and one of the world youngest BS patients at the time. He is doing very well nine years later (93), and has no impairment in his growth with a BMI of 26 Kg/m$^2$.

**European centers of excellence program**

In 2009, Drs. Scopinaro, Melissas, Fried, and Baltasar created the IFSO European Chapter of the Centers of Excellence (COE) Program (94). Multiple European centers and surgeons utilize this program currently.

**2010s—Publications and technical improvements**

*BMI-Latina* (Bariatric and Metabolic Ibero-Americana) was founded by us in 2011 as online journal published in Spanish, English, and Portuguese. The magazine was adopted by SECO in 2015 as the Spanish society’s magazine and we believe it will play a valuable role in BS in the Spanish and Portuguese speaking societies but since from 2015 only the abstracts of the English edition are published currently (95–98).

Recently, Serra et al (99) recommended 2 new technical improvements in SG, including our 1st publication on “sliding self-locking stitch” and the Aberdeen knot. Baltasar (100) described its use and he recommends the antrectomy starting at the pylorus plus an omental patch to cover the staple line and prevent rotation of the sleeve. We also called attention to the need to prevent stapling of the bougie (101) as well as a simple Whaps up bariatric telemedicine solution to detect early complications after hospital discharge (102,103).

By 2013, Spain was the country with the fifth most publications in SOARD. Now, in 2017, our group has 119 BS publications; we have reviewed >74 papers for Obesity Surgery, and >14 for SOARD, and other national and international journals. At the IFSO 2009 meeting in Paris, AB received the IFSO Lifetime Membership Award. On June 2011, at the ASMBS meeting in Orlando, Florida, AB (104) was second as a finalist for the prestigious ASMBS Outstanding Achievement Award (this is the “Oscar” of BS).
Discussion

In addition to participating in the aforementioned technical changes in the BS field, our Alcoy practice has contributed commentary on key concepts in the BS nomenclature and on reporting weight loss.

Nomenclature

BS is a relatively new specialty. We have long been interested in the development of BS nomenclature; our group, under the direction of the Royal Spanish Academy of Medicine, agreed that the correct name in Spanish for the SG technique is "vertical laparoscopic gastrectomy" (VLG), and also, that the end result of the VLG is the formation of a "gastric tube," or "sleeve"—and so it was approved in the General Assembly of the 2010 SECO meeting in Valencia.

We also published that the English term, "SG is an inappropriate, a misnomer term" as the meaning of "gastrectomy" is "amputation and elimination" of any part of the stomach. As right colectomy means the elimination of the right colon, not the left, and a left nephrectomy is the removal of the left and not the right kidney, the use of the term SG should more precisely mean "withdrawal of the sleeve," although, in fact, the sleeve is not removed, it is the sleeve portion of the stomach that remains. Therefore, we have suggested that the SG name is a misnomer and the correct term might be "sleeve-forming gastrectomy" (SFG), meaning more precisely a gastrectomy that forms a sleeve. We recognize that the term SG is so ingrained in common usage that it will likely prevail. Surgeons, besides performing excellent procedures, should also aim to speak and write correctly.

Weight-loss reporting

Weight-loss reporting is also controversial in BS. We have suggested that BMI measurement is much better than using WL measurement since it takes into account a patient’s height. We should not expect all patients with such different IBMs to reach an FBMI close to the ideal BMI of 25 kg/m$^2$. This is even more the case for high BMI patients. Dr. Borrás, our group’s mathematician, devised a mathematical system to measure the “expected BMI” = ExBMI = goal BMI, by using 7,410 real patients from multiple centers. The ExBMI mathematical formula for each patient is FBMI= IBMI X 0.4 +12. By using the BOLD system with a large patient sample, it will be possible to apply a better final mathematical formula using the concept of ExBMI. Using the ideal %ExBMI of 100%, any FBMI above that may be considered a success, and that below, a failure. Grading of the results depends on the extent of the deviation. A preliminary report of WL in our DS cases shows that at 5, 10, and 15 years, BMI of 85%, and an ExBMI of 96% suggest that almost all patients had an FBMI close to the goal results. Molina has recently confirmed these results.

BMI should be the standard measurement of obesity. DS is the most effective BS operation because it combines reduction on the intake and malabsorption as shown in the Fig. 5. A patient if with a BMI-100 the largest ever operated in Spain that dropped to BMI-34.

In total, 1494 patients with obesity were treated. The duodenal switch was used in 987 (515 ODS 472 LDS) with 0.7 mortality, one of the largest series in the world (of which 376 were from USA and Canada, 73 from Norway and 25 from England were operated on at the San Jorge Clinic).

Our videos about obesity can be seen at www.youtube.com/channel/UCEpwVhQEohunxKOhNqC71zg/videos?view=0&sort=dd&shelf_id=0
Conclusion

For the past 4 decades, from our community practice setting, we have followed the changes in the practice of BS throughout the world and participated in the evolution of the field. It has been extremely important and satisfying to continuously share and discuss evidence with our peers through the scientific literature, and in person, in local, national, and international interactions and meetings. We believe that small institutions can provide high-quality bariatric surgical care to patients and make significant scientific contributions to the field.

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We would like to thank the editors and all the cited colleagues in this paper for their enormous help, and for the pleasure we have received in meeting and coming to know them all, and also to learn from their excellent teachings.

Ethical Approval

All procedures involving human participants were performed in the studies cited herein in accordance with the ethical standards of the institutional and national research committees and with the Helsinki Declaration and amendments.

Informed Consent

Informed consent was obtained from all individual participants included in the studies cited.

Conflict of Interest

None of the authors has any conflicts of interest to disclose. J. N. Buchwald, Medwrite Medical Communications, WI, USA, received a fee for substantive manuscript revision.

References