

**FEASIBILITY PROJECT TO DETERMINE STRATEGIES FOR SELF-
ADMINISTRATION OF A SUBCUTANEOUS ORPHAN DRUG FOR TREATMENT OF
SHORT BOWEL SYNDROME: IMPACT ON ADHERENCE**

by

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BIO SKETCH

Ginny Strootman has been a nurse for over 25 years and an infusion nurse for 20 years. Her area of specialty is development and implementation of nurse/patient educational programs to enhance positive patient outcomes. Ginny's primary area of employment has been in alternate care settings and pharmaceutical operations in the biotech market. Her patient populations are those with rare and chronic disease states requiring orphan drugs.

KEY WORDS

Adherence; Chronic disease; Discontinuation rates; Feasibility project; GLP2 analog;

Medication refill; Orphan drug; Rare Disease; Parenteral Nutrition; Short Bowel Syndrome

ABSTRACT

Several strategies have been suggested to improve the nurse education provided to the nurses who educate the patients. The assumption is by providing evidence-based strategies to promote adherence to the nurses, prior to educating the patients, an increase in adherence rates can be demonstrated. Strategies discussed involve a feasibility project whereby an improved nurse educational model demonstrates improvement in medication adherence rates for adults with a rare and chronic disease states that self-administer an orphan drug for short bowel syndrome.

INTRODUCTION

Working within a Biotechnology (Biotech) pharmaceutical company is a challenge particularly when considering a patient population that falls into the category of having a rare and chronic disorder. Biotechnology is a term used to describe a process of manufacturing drugs involving the manipulation of microorganism, such as bacteria, or biological substances like enzymes to perform a specific process within the human body. The biotech companies focus on research and development of novel compounds that can treat rare and chronic disorders.¹ These novel drugs are referred to as orphan drugs.

The United States Rare Disease Act of 2002 defines a rare and chronic disorder “as one that affects a small patient population, typically populations smaller than 200,000 individuals in the United States.”² Patients with rare disease typically require orphan drugs to sustain a healthful, quality of life and are often times taught to self-administer their own orphan drugs either by injection or infusion. The rare disease that was the focus of this feasibility project is short bowel syndrome that affects about 20,000 adults in the United States.^{3,4}

Short bowel syndrome (SBS) is a serious and complex gastrointestinal disorder that may be life threatening. SBS is defined as “a combination of symptoms and signs that occur after extensive surgical resection of the intestine with less than 200 cm of functional small intestine remaining.”^{3,4,5} Short bowel syndrome is one of the major recognized causes of intestinal failure and results from resection of the intestine that is attributed to an underlying disease states or congenital defect. Regardless of underlying etiology the end result is the inability to maintain protein, energy, fluid, electrolyte or micronutrient balances while on a suitable oral diet.^{4,5,6} The body tries to compensate after intestinal resection by increasing the capacity of the remaining intestine with patients naturally adapting during the first six to eighteen months following

surgical resection.^{3,4,5} In most patients, within two years after resection 90%-95% of the adaptation potential is achieved.^{4,7} Reduced intestinal absorptive capacity may lead to malnourishment and dehydration which causes many of the complications of SBS. The most prominent complications include diarrhea, extreme weight loss and diminished overall health.^{3,4,7}

The body tries to adapt to the loss of intestine by enhancing the absorptive capacity of the remaining intestine in an effort to absorb as much fluids and nutrients as possible. A natural process for compensation is mediated by structural and functional changes by increasing villus height and crypt depth as well as increasing blood flow to the remaining intestine.^{3,4,6} This natural adaptation is believed to be the result of production of a naturally occurring gut hormone glucagon-like peptide-2 (GLP2) that enhances digestive and absorptive capacities.^{8,9,10} GLP2 is a 33 chain amino acid long peptide secreted by the enteroendocrine L cells in the distal small intestine and proximal large intestine.^{8,9,10} GLP2 has an important role in intestinal adaptation and several studies have shown that exogenously supplied GLP2 promotes structural and functional changes that increase the absorptive capacity of the intestine.^{8,9,10}

Before adequate adaptation is achieved, required nutrients and fluid must be supplied intravenously by administering fluids, electrolytes, vitamins, minerals, trace elements and fat emulsion to sustain nutritional stability.^{11,12,13} SBS patients initially need this intravenous parenteral nutrition (PN) with the goal to gradually decrease or discontinue parenteral nutrition once the intestine has achieved natural adaptation.^{7,11,12} Some patients may require lifelong parenteral nutrition if sufficient functional adaptation is not achieved.^{12,14} In the U.S. it is estimated that at least 20,000 adult patients with SBS receive parenteral nutrition.^{6,7,12}

Although lifelong PN keeps patients alive, the negative impact can be seen in a very high mortality and morbidity rate due to inherent risk and complications.^{11,14} Sepsis, liver failure and thrombosis account for 15%-20% of deaths.^{12,14} It is apparent that PN dependency affects quality of life: sleep is often interrupted because of the need for frequent urination caused by the high volumes of fluids infusing. Parenteral nutrition can have long term problems with the gallbladder, pancreas and liver.⁶ Given their many restrictions and potential complications patients have a difficult time maintaining employment. Moreover after the exclusion of the cost of hospitalizations and prescriber services, PN supplies alone may cost up to \$122,000 per year.^{4,11}

Realizing the complications and cost associated with long-term parenteral nutrition a goal of SBS treatment is to wean or eliminate its use through intestinal adaptation or use of novel orphan drug treatment options. One such orphan drug option is the subcutaneous administration of exogenous GLP2 . Administering a once daily subcutaneous injection and increasing the absorptive capacity of the intestine remaining can wean parenteral nutrition weaned to less infusion days and volume per week or completely discontinued.^{7,9}

Administration of this subcutaneous injection was developed to provide a self-administered orphan drug option for the SBS patient. The orphan drug comes as a lyophilized powder that requires several steps to reconstitute prior to administration, necessitating a nurse to provide reconstitution training to the patient.

The impact for patients in learning to self-administer their orphan drug is in providing a sense of control around their disease state allowing them to choose when and where to self-administer. Being in charge of their own self-administration leads to a reduction or elimination of visits to an outpatient or clinic setting and a reduction in the cost of care such as co-pays

associated with clinic type visits. In the current healthcare arena reimbursement for daily office visits or clinic visit to receive a daily subcutaneous injection are generally not reimbursable not to mention the quality of life surrounding daily visit to an office or clinic. A home environment was an approved location of care for self-administration of such a therapy therefore patient education was required to ensure competency prior to considering the patient independent with subcutaneous self-administration.

For self-administration of an orphan drug to be successful, biotech companies have dedicated themselves to making available a team of nurse educators who can provide instructions to the patient on disease state management, drug administration, storage, adverse events and to promote adherence.

This feasibility project demonstrated that prior to educating a patient to self-administer a subcutaneous orphan drug, an evidence-based approach to support adherence was essential. These strategies were integrated into the existing patient and nurse educational materials and re-introduced to the patient during their initial injection training visits.

SIGNIFICANCE OF ADHERENCE

With increasing numbers of efficacious self-administered treatments, the need is apparent for better understanding and management of non-adherence.¹⁵ Current statistics regarding the negative effects of decrease adherence rates provide support of interventions to promote adherence to prescribed therapy. Typically adherence rates for prescribed medications are about 50% with a range from 0% to over 100%.^{16,17} According to a recent study by the Center for Disease Control (2013) data demonstrated medication prescriptions never filled at 20% to 30%; rates of medication adherence drop after first six months; and medication not continued as prescribed are found in about 50% of cases.^{16,17} The World Health Organization estimated that

by 2020, adults affected by at least one chronic condition requiring medication therapy will grow to \$157 million. It is estimated that the annual cost of medication treatment will grow to at least \$100 billion to \$289 billion and costs \$2000 per patient in physician visits annually.¹⁷

ASSESSMENT OF PROBLEM

Within one biotech company it was noted a decrease in adherence rates of 5%-10% beginning in January 2014. This was deemed unacceptable by the biotech company as decrease in adherence rates resulted in an increase in symptoms and lack of benefit to therapy resulting in patients remaining on PN. As result of declining adherence rates a discontinuation task force was formed by the stakeholders of the biotech company assessing gaps impacting adherence. One gap realized was the nurse education model in place and the lack of strategies to support adherence by the patient.

Recognition of a gap in the current nurse education model was first identified by analyzing the data from January 2013 through October 2014 (Figure 1) evaluating the variable of adherence rates noting a decrease of medication refills of 5% -10% per month.

There was an initial spike in adherence rates averaging 100% to 80 % with a few peaks and valleys through-out the months best explained by patients refilling medications at or around time insurance coverage was changing at the end of the year. Patients tended to refill medications to carry them for several months in the event new insurance coverage denied or delayed approval for refill.

By January 2104 the adherence rate began a steady downward trajectory from 80% to 66% again with a few peaks and valleys at or around time insurance coverage was changing. The desired adherence rates the stakeholders of this biotech company deemed acceptable was 80%-90%. Based on assessment and findings a practice change was presented to stakeholders

that promoted the development and implementation of a nurse education model focusing on improvement of adherence rates. Emphasis was on incorporating evidence-based strategies promoting adherence into the new nurse educational model.

THEORETICAL FRAMEWORK

When developing strategies to promote adherence with self-administration several nurse theories supported a nurse model of care to teach self-administration of a subcutaneous orphan drug. Dorothea Orem's Self Care Deficit Theory (SCDT) cites one major assumptions of her theory as "people should be self-reliant and responsible for their care"¹⁸. According to Orem self-care activities are those an individual initiates and performs independently to maintain life, health and wellbeing.¹⁸

According to Virginia Henderson's Needs Theory, the definition of nursing states: "the nurse does for others what they would do for themselves if they had the strength, the will and the knowledge...the nurse makes the patient independent of him or her as soon as possible."¹⁹ Furthermore in Henderson's *The Nature of Nursing* (1964), the role of the nurse is "to get inside of the patient's skin and supplement his strength, will or knowledge according to his needs, and provide an environment in which the patient can perform activity unaided."¹⁹ (pg. 64) Both Orem and Henderson's theories promote self-care and self-behaviors that promote independence from the nurse. Developing and implementing a nurse education model that fostered behaviors that promoted self-administration identified the theoretical framework of Orem and Henderson identified as the models that promoted self-reliance and patient responsibility for their care.

SUMMARY OF LITERATURE

When developing the new nurse model a literature review was conducted to identify evidence-based strategies that promoted adherence. Table 1 summarizes five peer-reviewed articles citing interventions that were included in the new nurse model. [Insert Table 1]

All five peer reviewed articles provided resounding similarities on strategies to increase adherence which included: patient education and health literacy, increase communication with healthcare professionals, providing written materials, cueing/taking medication with routine, telephonic follow up, clinical case management/counseling and ongoing discussion on misconceptions and fear.^{21,22,23,24,25} Although this list is not inclusive of all variables it does summarize those that appeared consistently throughout each article as well as correlate to the findings the biotech company had postulated.

IMPLEMENTATION OF STRATEGIES

Evidence-based strategies were integrated into the existing patient training materials that are provided by the nurse to the patient during first two home injection trainings. Additionally, the nurse training power point presentation was updated to include discussion points around setting expectations, communication expectations with prescriber and increased communication with nurse and internal case manager.

Patient education materials enhanced to include interventions identified as those promoting adherence are outlined in table Table 2. [Insert Table 2]

Enhancements included patient friendly descriptions around disease state, setting goals, and how to increase lines of communication with their healthcare team. Upon completion of enhanced patient and nurse education materials re-education was provided to the nurse educator prior to training patients on self-administration to ensure comprehension of new materials.

PROJECT DESIGN AND DESCRIPTION

Methods to evaluate the outcome of this practice change included analysis of aggregated medication refill data found within the organizational internal database for SBS patients. Medication refill rates were used to determine if a patient was adherent to the prescribed subcutaneous self-administration of an orphan drug (V. Gopalakrishnan, personal communication 2013) & (M. Theves, 2014).

Patient adherence rates were calculated on monthly basis and compared to previous months adherence rates. Patient information was aggregated and de-identified by assignment of a unique identification number to patients at time of referral by healthcare provider. Approval was obtained by Capella University Internal Review Board (IRB) to protect patients' identity.

ANALYSIS OF IMPACT

Baseline adherence rates in January 2015 were 74.2% and have shown a steady upward trajectory over the five months of the evidence based project implementation. Figure 2 illustrates the impact of the project implementation on adherence rates for patients self-administering a subcutaneous orphan drug.

As of May 2015 an adherence rate of 83.2% was achieved, which is within the acceptable adherence rates identified by the biotech company's stakeholders. Stakeholders considered any incremental increase in adherence rates above the initial baseline of January 2015 a significant achievement in providing a therapy option for the SBS patient population.

A comparison of pre-implementation of new nurse model with post-implementation of new nurse model is illustrated in Figure 3 which supports the positive impact evidence-based strategies on adherence had during the project initiative.

The upward trajectory seen in adherence rates over the five months of the implementation phase demonstrated that the evidenced-based strategies developed and implemented had a positive effect on adherence. With the positive impact on adherence rates obtained the biotech company has decided to implement the evidence-based strategies in other self-administered orphan drug therapies provided.

LIMITATIONS OF PROJECT

A weakness of this project was the limited time for data collection to reasonably demonstrate a statistical significance in outcomes of adherence rates. Although the adherence data did not validate long-term statistical significance the clinical significance cannot be underestimated in terms of patient outcomes. Clinical significance demonstrates a practical or applied value of a treatment effect. The real world effect of SBS treatment and benefit to the patient related to decrease in PN as well as complications, sleep disruptions, hours of infusion and cost cannot be overlooked. Long-term studies and data collection in the area of self-administration of orphan drugs certainly can add to the existing findings and expand nursing knowledge on strategies that impact adherence.

CONCLUSION

The biotech industry increasingly serves patients with rare and chronic disorders who require administration of orphan drugs. In order to promote a positive patient experience and ensure adherence to prescribed medications a nurse education model incorporating evidence-based strategies is one practice change initiative to be considered.

By developing and implementing a new nurse model, patient adherence rates were positively affected which translated to patients receiving benefit from the orphan drug. Such benefits were noted with decrease utilization of PN as measured in number of days and volume

infused per week. Patient outcomes as a result of changes in PN utilization impact the quality of life around daily infusions, interrupted sleep and high cost of supplies. Additionally long term complications of PN related to sepsis, gallbladder, pancreas and thrombosis were decreased as a result of reduction in PN.

Although SBS patients require PN and those who have not achieved intestinal adaptation will require long term PN, the goal is to gradually decrease or discontinue PN once intestinal adaptation has been achieved. Having an incremental increase in adherence provided the SBS patient a novel treatment option that contributed to improved quality of life.

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FIGURES:

Figure 1: Adherence rates identifying a gap in current nurse educational model

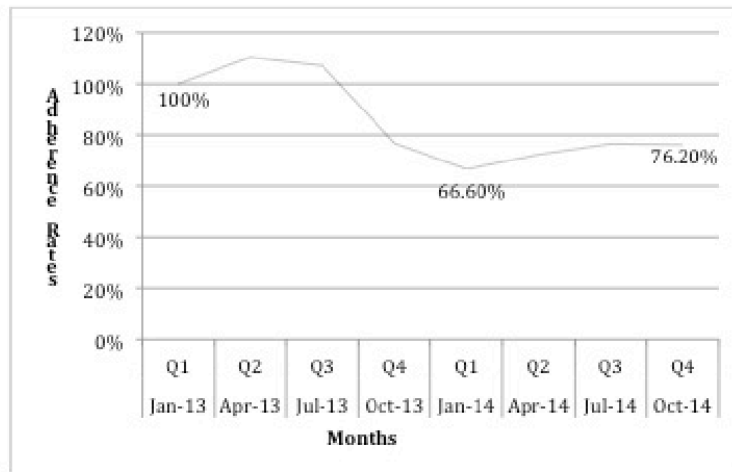
**Figure 1** Adherence rates identifying gap in current nurse education model

Figure 2: Impact on adherence rates post project implementation

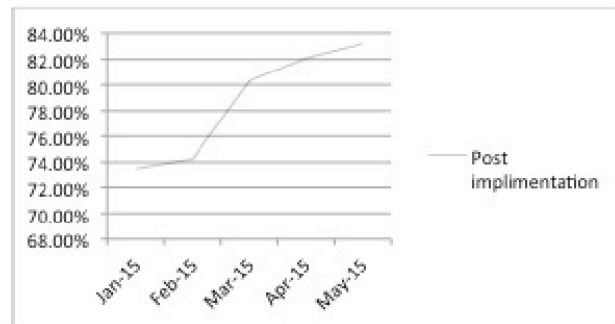


Figure 2 Impact on adherence rates post project implementation

Figure 3: Comparison of adherence rates pre and post implementation

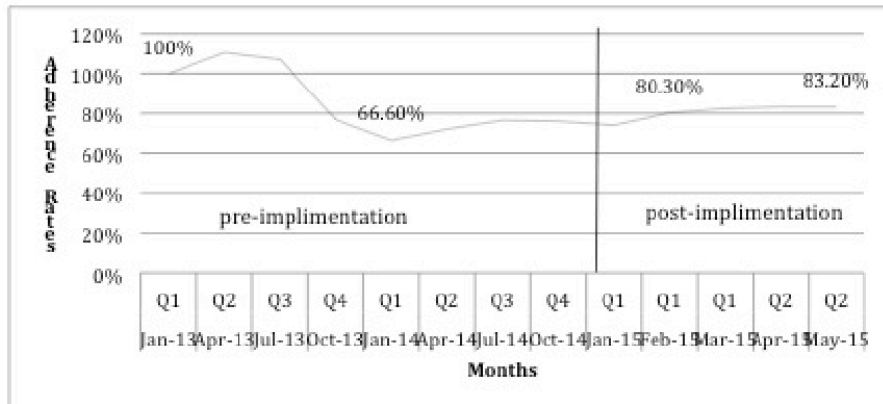


Figure 3 Comparison of adherence rates pre and post implementation

TABLES:**Table 1**

TABLE 1 Strategies to Promote Adherence						
Interventions	Study	A	B	C	D	E
Patient education and literacy		X	X	X	X	X
Open lines of communication		X	X	X	X	X
Telephone follow up with healthcare team		X	X	X	X	
Case Management			X	X	X	X
Training patients		X	X	X	X	X
Providing written materials		X	X		X	
Cueing/linking taking medication with a routine		X	X			X
Discussing misconceptions regarding efficacy and adverse events		X	X	X	X	X

Note. From: ²⁰Appendix E: Templates for evaluation and synthesis tables for conducting an evidence review, pg. 521.

Studies: **A.**²¹ **B.**²² **C.**²³ **D.**²⁴ **E.**²⁵

Table 2

TABLE 2 Educational Material Provided to Patient	
<u>Sent by Manufacture at time approval</u>	<u>Provided by nurse during injection training</u>
Welcome letter	How GLP2 analog works
Meet you care manager	Patient tracker
Patient stories	Getting the most from your therapy
Getting started with GLP2 analog	Home training feedback form

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I attest that this dissertation or capstone project is my own work. Where I have used the ideas or words of others, I have paraphrased, summarized, or used direct quotes following the guidelines set forth in the *APA Publication Manual*.

Learner name
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Ginny Strootman, RN, MS, CRNI, IgCN August 21, 2015

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