Mitigating the risk of COVID-19 exposure by transitioning from clinic-based to home-based immune globulin infusion

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Purpose. Intravenous immune globulin (IVIG) therapy is used in patients with hypogammaglobulinemia to lower the risk of infections. IVIG and subcutaneous IVIG (SCIG) therapy have been to shown to be safe and effective when administered as clinic-based infusions. Concern from both patients and providers for increased transmission of the coronavirus disease 2019 (COVID-19) virus to immunosuppressed patients with scheduled medical visits and procedures made it necessary for us to reassess our process of how we manage patient care in general and chronic clinic infusions in particular. Here we describe our experience of transitioning patients from clinic-based to home based IVIG and/or SCIG infusions to decrease the risk of COVID-19 exposure.

Methods. Criteria were developed to identify high-risk immunosuppressed patients who would be appropriate candidates for potential conversion to home based IVIG infusions. Data were collected via chart review, and cost analysis was performed using Medicare Part B reimbursement data. A patient outcome questionnaire was developed for administration through follow-up phone calls.

Results. From March to May 2020, 45 patients met criteria for home-based infusion, with 27 patients (60%) agreeing to home-based infusion. Posttransition patient outcomes assessment, conducted in 26 patients (96%), demonstrated good patient understanding of the home-based infusion process. No infusion-related complications were reported, and 24 patients (92%) had no concerns about receiving future IVIG and/or SCIG doses at home. No patient tested positive for COVID-19 during the study period. Clinic infusion visits decreased by 26.6 visits per month, resulting in a total of 106 hours of additional available infusion chair time per month and associated cost savings of $12,877.

Conclusion. Transition of clinic based to home based IVIG/SCIG infusion can be successfully done to decrease potential exposure during a pandemic in a high-risk immunosuppressed population, with no impact on patient satisfaction, adherence, or efficacy. The home-based infusion initiative was associated with a reduction in costs to patients and an increase in available chair time in the infusion clinic.

Keywords: COVID-19, immunosuppressed population, intravenous immune globulin, subcutaneous immune globulin

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the coronavirus disease 2019 (COVID-19) pandemic, which has not only impacted the general population but also presented unique challenges in the care of immunosuppressed patients, who may be at higher risk for developing severe disease. Concern for increased transmission of SARS-CoV-2 to immunosuppressed patients with scheduled in-person medical visits and procedures has necessitated reassessment of our institution's process for delivery of optimal patient care during the pandemic.[1]

Although there are limited pertinent data specific to the immunosuppressed population, reports from China demonstrated that patients with cancer who contracted COVID-19 were at 3.5 times higher risk for needing mechanical ventilation, for ICU admission, and for death compared to patients without cancer.[2,3] Home-based intravenous immune globulin (IVIG) therapy and subcutaneous IVIG (SCIG) therapy have been shown to be safe and effective, with reported clinical outcomes comparable to those with clinic-based IVIG infusions.[4] Additionally, studies have shown that patients receiving home-based vs clinic-based infusions had significantly lower rates of pneumonia ($P = 0.0071$) and bronchitis ($P < 0.0001$); the differences were significant in the first 3 weeks after the first infusion, suggesting that the infusion setting was a primary determinant of infection rates.[5] At our institution home-based infusion was identified as an acceptable strategy because it would allow patients to continue receiving treatment with minimal exposure to infusion clinics or hospital-based clinics, thereby decreasing the risk of acquiring COVID-19 in this high-risk patient population. This observation influenced our decision to develop an initiative to

transition patients to home-based IVIG therapy due to their high risk of acquiring infectious disease, particularly COVID-19.

The Smilow Cancer Center Hematology Clinic at Yale New Haven Health is a 340B Drug Pricing Program–eligible integrated hospital-based center, with the outpatient oncology/hematology clinics located in the same building as the inpatient oncology/hematology units, medical intensive care units, and units converted to COVID-19 units. The hematology clinic consists of a 32-chair infusion center with an attached physician clinic. By monthly volume, IVIG infusion visits constitute 3% of all infusion clinic visits.

The purpose of the initiative was to identify high-risk, immunosuppressed patients and safely convert them from receiving IVIG therapy in a hospital-based infusion clinic to home infusion therapy. Secondary endpoints included assessment of patients' experience with conversion to home infusion, the time between home infusion referral and first home infusion, time between last clinic infusion to first home infusion, COVID-19 positivity rates amongst these patients, and a cost analysis of the impact of conversion to home infusion on patients and our institution.

Methods

A multidisciplinary team of hematology physicians, advanced practitioners, nurses, care management personnel, and pharmacists was assembled to oversee the initiative. Criteria were established for use in identifying immunosuppressed patients at high risk for COVID-19 transmission who had scheduled infusion visits in a hospital setting for potential conversion to home-based immune globulin therapy. The criteria were as follows: clinic visits for IVIG only, with no additional appointments between infusions; not receiving concurrent intravenous chemotherapy; transfusion independent; not residing in a nursing

home or skilled nursing facility; insurance coverage for home infusion; and patient in agreement with receiving home infusion. An electronically generated list of patients receiving IVIG in the hematology clinic was reviewed, and each patient was reviewed by a pharmacist to determine eligibility based on the above criteria. The patients meeting the eligibility criteria were discussed with the primary physician for final approval to initiate transition to home-based IVIG therapy. Either the physician or an advanced practitioner then discussed the home infusion opportunity and documented the patient's approval to start the process. Care management personnel referred the patient to the home infusion company and the pharmacy providing the medication orders. IVIG formulation was decided on the basis of insurer preference. Currently, our health system does not provide home-based infusion services, which are provided by a contracted infusion company. This contracted home infusion company notified our institutional representatives of insurance denials and unacceptable out-of-pocket costs, which resulted in patients continuing their IVIG infusion in the hospital-based clinic. Practice nurses further provided support with addressing patient's questions during the process in addition to follow-up assessment after the first completed home infusion. Follow-up assessment questions (Figure 1) were asked of each patient after the first home IVIG dose. Days between home infusion referral and the first home infusion and days between original clinic infusion and first home infusion were calculated. COVID-19 testing was done in symptomatic patients and those with a known positive contact. COVID-19 positivity was defined as a positive nasal polymerase chain reaction swab along with signs and symptoms of COVID-19.

Reimbursement for the infusion chair time was calculated according to the Medicare Part B fee schedule for outpatient infusion of a complex biologic agent.[6] Assessment of clinic infusion appointments and chair time infusion allotment was performed over 1 month and

over a 4-month time period (April through July 2020) or at a patient's earliest clinic appointment if it occurred prior to the end of July. These time points allowed us to appropriately conduct a monthly financial analysis along with a financial analysis during the early months of the COVID-19 pandemic.

This initiative was established as a quality improvement project and was exempt from institutional review board approval. Baseline data on patient characteristics along with information on duration of time for conversion were collected via electronic medical record chart review. Collected data included patients' age and gender, oncologic diagnosis, whether or not they were hematopoietic stem cell recipients, reason for IVIG use, brand of IVIG, and insurance coverage.

Results

From March to May 2020, a total of 45 patients met criteria for home-based IVIG infusion. Eighteen patients were excluded due to declining home infusion or inability to self-administer SCIG at home. Twenty-seven patients (60%) agreed to home-based immune globulin infusion and received at least 1 dose of home-based immune globulin therapy. The most common disease state among patients receiving IVIG therapy for hypogammaglobulinemia was lymphoma (52%). Sixty percent of patients had received a hematopoietic stem cell transplant. Baseline demographics can be found in Table 1. The median duration of time between the referral to home care company and the first home infusion was 15 days (range, 6-49 days). The median duration of time from a patient's original IVIG clinic infusion date to the first home infusion, accounting for missed infusion dates and early administration dates, was 22 days (range, –3 to 80 days; negative number denotes early administration). Based on insurance coverage, 23 patients (85%) continued to

receive the same IVIG formulation during home-based infusion therapy, and 4 patients (15%) were converted to an SCIG formulation. Twenty-one patients (77%) continued to receive home-based immune globulin infusions after their first dose, 2 patients (7%) preferred to transfer back to clinic-based IVIG infusions after improvement in pandemic conditions, and 5 patients (16%) transferred back to clinic after the first dose. The reasons for transferring back to clinic-based IVIG infusion consisted of reinitiation of chemotherapy (*n* = 2), patient preference (*n* = 2), and home setting did not meet home infusion company criteria (*n* = 1). No patient developed symptoms or had a documented exposure warranting a COVID-19 test.

Out of the 27 patients who received at least 1 dose of immune globulin via home-based infusion, 26 (96%) had a follow-up phone call outcomes assessment. The follow-up questionnaire was not completed for 1 patient because he elected IVIG infusion at the home care company's on-site infusion clinic instead of home-based infusion. All patients had an understanding of the process prior to their home infusion. Only 3 of the 23 patients who received IVIG (13%) had issues with line access, but this did not impede patients from receiving their IVIG infusion. No patient receiving home IVIG therapy had any infusion-related complications, but 1 patient (4%) developed nausea and vomiting during home infusion. Ninety-six percent of the patients felt that their questions were appropriately answered (if they had any) by the home infusion nurse. With regard to future IVIG doses, 21 patients (91%) had no concerns about receiving doses at home, and 3 of 4 patients receiving SCIG (75%) had no concerns with receiving future SCIG doses at home (Figure 2).

The home-based IVIG therapy initiative decreased the number of clinic infusions by 26.6 visits per month. As each IVIG infusion appointment involves 4 hours of infusion chair time, the initiative reduced clinic chair time by a total of 106.4 hours per month, yielding

calculated cost savings of $12,877. During the period of April through July, an estimated total of 56 clinic infusions for IVIG were transitioned to home infusion visits. The total number of hours of infusion chair time during the April-July period (or until the next clinic appointment prior to July) was 228 hours (cost, $28,000). During that period only 1 patient was hospitalized (for 7 days), and that admission was not for IVIG-related or infectious disease–related reasons. The median number of additional clinic visits was 0 visits (range, 0-3 visits).

Discussion

Prior studies have shown that shifting to IVIG administration in the home-based setting, as well as shifting patients from IVIG to SCIG therapy, can result in similar therapeutic effectiveness, minimal adverse effects, and cost savings for patients.[4,7-9] Out of 45 patients evaluated, we were able to transition 27 patients (60%) to home IVIG or SCIG infusion therapy with no adverse effects. The median interval from referral to a home care company and the first home infusion was only 15 days, demonstrating a quick implementation time. The median interval from a patient's originally scheduled IVIG clinic infusion date to the first home infusion was 22 days, indicating an average delay in the first monthly dose of a couple of weeks. However, the range of days' delay (–3 to 80) was wide, with some patients receiving IVIG infusions several days earlier than their scheduled dose and other patients having a longer time to their next IVIG dose due to declined clinic visits in February and March, before the home-based IVIG infusion initiative was implemented.

Among the patients who were transitioned to home infusion of immune globulin, no patient acquired COVID-19. We recognize that IVIG therapy is not effective in the prevention of COVID-19, but the lack of COVID-19–positive patients could be attributed to the decrease

in potential exposure resulting from home-based infusion. With the transition to home-based infusion the median number of visits per patient per month decreased from 1 to 0 visits (in addition, the median number of additional clinic visits was decreased to 0), therefore decreasing exposure risks. One patient was hospitalized, but the admission was not associated with IVIG infusion or an infection.

Patient satisfaction was noted to be similar with the change to home-based infusions. Additionally, patients were noted to prefer home-based infusion due to a gain in independence along with increased patient adherence.[10] Out of the 45 patients evaluated, we successfully converted 23 patients to home-based IVIG infusion. Responses to the follow-up assessment questionnaire demonstrated that the majority of patients were educated appropriately by both the clinic infusion staff and home infusion company about their home infusion conversion and that additional questions were appropriately answered by the home infusion company. The one patient who did not feel as if questions were appropriately answered did not specify what those questions were in the follow-up assessment. Additionally, 13% of patients had issues with line access, but those issues did not affect patients' satisfaction with continuation of home IVIG infusion. A small proportion of patients (9%) had concerns with receiving future doses of IVIG, with 1 patient declining any future home-based IVIG infusions due to having experienced multiple interruptions of an infusion and concern over questions not being answered to their comfort level. The other patient who transferred back to clinic care cited a non–medication-related reason (ie, positive relationships the patient had developed with nurses at the infusion clinic).

There was also a significant difference in patient satisfaction in patients receiving SCIG compared to IVIG due to the ability to self-administer, being able to fit treatment into their schedule, and reducing amount of time taken to administer treatment ($P < 0.05$)[11,12]

During this home conversion initiative, a small number of patients (n = 4) were converted to a subcutaneous formulation. Follow-up assessments of those patients were favorable, but all patients voiced concern about being able to self-administer SCIG once the allotted time of nurse training was completed. One patient was unsure if she would be able to self-administer SCIG and, after the set training time with the home infusion nurse was completed, transferred back to the clinic to receive IVIG in the clinic setting

Although less than 1% of our institution's patient population receives IVIG, it accounts for the third-highest drug cost in commercial plans and fourth-highest drug cost under Medicare.[10] For patients with commercial insurance, outpatient hospital settings are the most expensive site for IVIG infusion, with physician offices and non–hospital-owned clinics being the second most expensive site category for IVIG infusion and home infusion being the lowest-cost option. Compared to outpatient infusions in hospital settings, home-based infusions have been demonstrated to decrease the cost per infusion per patient by 31% due to the elimination of overage markup of medication and administration fees (P < 0.001).[13] Commercial plans and Medicaid provide coverage of IVIG without any out-of-pocket expenses. Commercial insurance companies have used data on the cost-effectiveness of home IVIG therapy by developing site-of-care programs, with 89% of the developed programs including an IVIG home infusion plan.[5] Alternatively, Medicare provides full coverage for SCIG therapy, but there is an out-of-pocket expense for home IVIG infusion. Medicare has expanded a bundled payment for in-home IVIG therapy for primary immunodeficiences, but that payment has not been expanded to include hypogammaglobulinemia. Based on their insurance coverage, we converted 19 patients with commercial plans to home IVIG infusion, 4 Medicare patients to home IVIG infusion, and 4 Medicare patients to SCIG therapy. Additionally, the gain of 106.4 hours of infusion

chair time per month optimized space for other departments to establish additional COVID-19 treatment areas and increase outpatient infusions of EPOCH (a chemotherapy regimen consisting of etoposide, prednisone, doxorubicin, cyclophosphamide, and vincristine). Seven patients receiving dose-adjusted EPOCH were able to transition from the inpatient to the outpatient setting. Staffing numbers were not affected with transitions to IVIG home infusion, and clinic staff were deployed to accommodate other treatments and chemotherapy infusions.

There were limitations of the study pertaining to COVID-19 exposure. Additional documentation of non–clinic-based travel (which potentially could have increased their exposure risk) was not obtained in these patients, although COVID-19 positivity was nil in this patient population. Unfortunately, our health system does not have a home infusion agency, and patients were referred to a contracting referral service for their home infusions. While home infusion is a service that is in the pipeline for our health system, it was not yet established at the time of the conversion initiative described here. While the loss of revenue from clinic-administered IVIG was compensated for by chair time gained, there are limitations in our ability to estimate the cost savings associated with clinic-based infusions, home-based infusions, and infusion chair time. In our health system, confounding factors in estimating such cost savings include payment of medication through private and state insurance coverage, the specifics of purchasing contracts within the system (along with 340B program eligibility), and contract referrals to the home infusion company along with additional home infusion costs for the infusion of the medication. Medicare Part B reimbursement pricing data were used to calculate the chair time to represent the lower end of reimbursement, which would be applicable to other hospitals. The majority of these

patients involved in the program had commercial insurance, which might have affected the range of reimbursement pricing.

Conclusion

Transition of clinic-based IVIG infusion to home-based IVIG or SCIG infusion can be successfully done to decrease potential infectious disease exposure during a pandemic in a high-risk, immunosuppressed population. Home-based IVIG and/or SCIG therapy may improve patient satisfaction in addition to improving patient adherence, with no decrease in effectiveness. Transitioning to home-based infusions was associated with a reduction in cost to patients and increased chair time in the infusion clinic.

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Figure 1. Implementation of home-based intravenous immune globulin (IVIG) therapy initiative. SCIG indicates subcutaneous immune globulin.

Figure 2. Responses to follow-up assessment questionnaire. IVIG indicates intravenous immune globulin; SCIG, subcutaneous immune globulin.

Key Points

- The coronavirus disease 2019 (COVID-19) pandemic has presented concerns among both patients and providers for increased risk of transmission with scheduled hospital-based clinic appointments, making it necessary to reassess patient care processes.
- At our institution, transitioning patients from clinic-based to home-based intravenous immune globulin (IVIG) infusion and/or subcutaneous IVIG infusion was demonstrated to decrease potential COVID-19 exposure during the early months of the pandemic, with no impact on patient satisfaction, adherence, or therapy effectiveness.
- Pharmacists played a major role in developing criteria to identify appropriate candidates for home-based infusion, transitioning medication orders, and follow-up assessment.

Table 1. Baseline Characteristics of Patients Transitioned to Home IVIG Infusion (*n* = 27)

Characteristic	**No. (%)**[a]
Age, median (range), y	65 (38-93)
Male	18 (66)
Primary diagnosis	
Lymphoma	14 (52)
Chronic lymphocytic leukemia	3 (12)
Acute lymphocytic leukemia	2 (7)
Acute myeloid leukemia	2 (7)
Posttransplant lymphoproliferative disorder	2 (7)
Waldenstrom's macroglobulinemia	2 (7)
Antiphospholipid syndrome	1 (4)
Myelofibrosis	1 (4)
Received hematopoietic stem cell transplant	16 (60)
Reason for IVIG	
Hypogammaglobulinemia	26 (96)
Antiphospholipid syndrome	1 (4)
IVIG brand	
Privigen	16 (59)
Gamunex	11 (41)
Insurance coverage	
Private or Medicaid	19 (70)
Medicare	8 (30)

Abbreviation: IVIG, intravenous immune globulin.

[a]All data are number (percentage) of patients unless otherwise indicated.

Figure 1

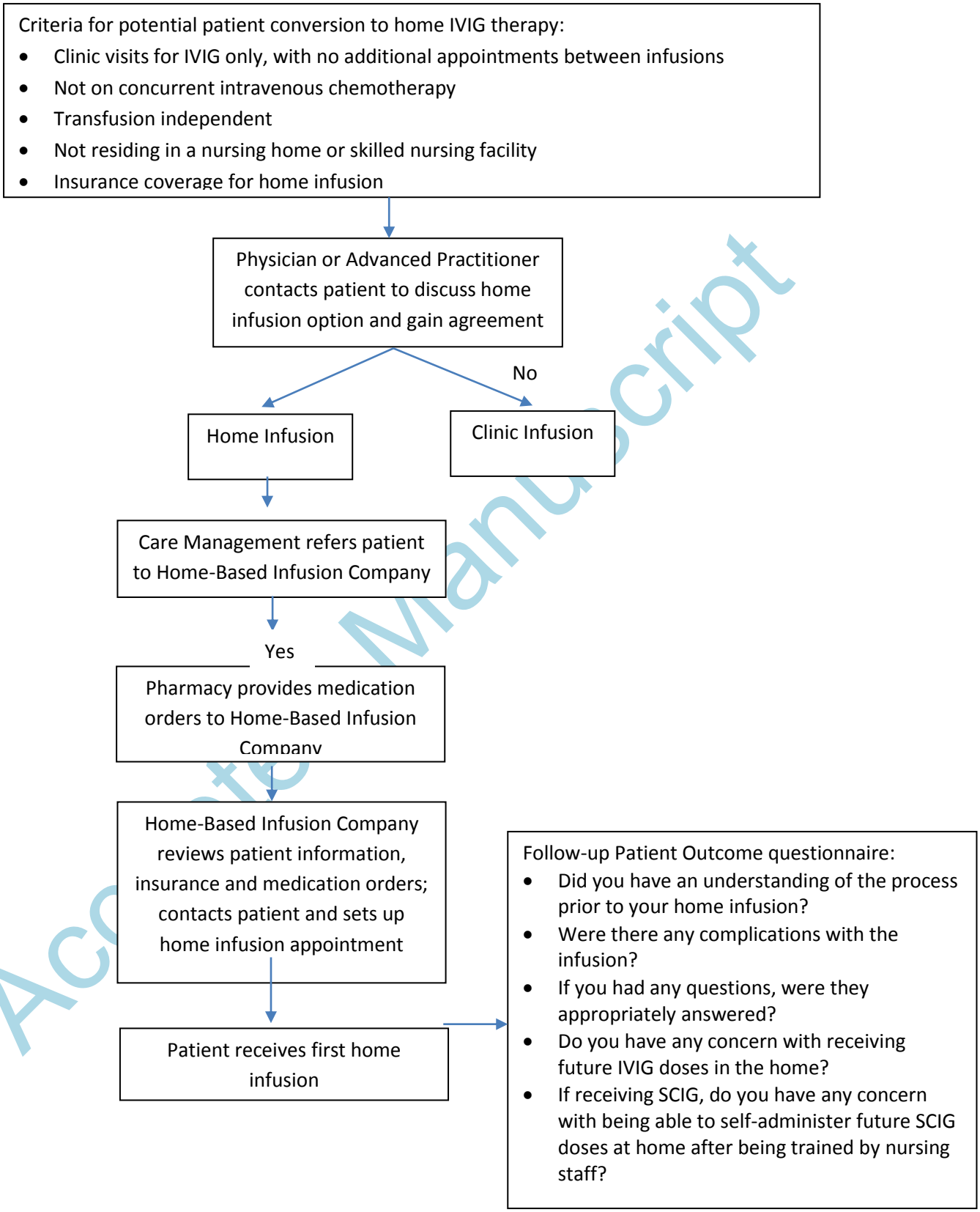

Figure 2