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About the cover:
A new time study examining tasks performed by home infusion pharmacists reveals patient calls is primary among the professional services essential to this care model. Home infusion pharmacists speak with patients to monitor their therapeutic progress, communicate changes in their care regimen, answer questions, and troubleshoot problems.

NHIF
National Home Infusion Foundation

From the Editor

Michelle Simpson, PharmD, BCSCP
Editor-in-Chief, *Infusion Journal*

The National Home Infusion Foundation (NHIF) is pleased to introduce *Infusion Journal* and welcome readers to the first issue of a peer-reviewed medical journal devoted to infusion therapy. NHIF established this scholarly publication to meet the need for communicating research specific to infused medications, related clinical pathways, and operating procedures.

This publication's mission is to share original research in infusion therapy conducted by a broad range of infusion specialists that will advance evidence-based practice and shape industry standards.

Infused medications are used to treat a wide range of conditions impacting all settings of care. Infusion continues to grow because of the reputation and enthusiasm of those who perform the services and make a difference in patients' lives. For *Infusion Journal* to succeed, our readers must share with others how they solved an infusion problem or filled a gap. Meeting patients where they are opens possibilities regarding administering infusion medications in the community. These notions direct the research of the future.

NHIF believes there is sufficient scientific content to support *Infusion Journal*. Infusion providers have access to extensive data and unique context, but they lacked a journal to foster the orderly communication of the information. Illustrating the unmet need for a journal specifically focused on infusion therapy, the three studies in this first issue of *Infusion Journal* concentrated on research in home infusion. Two of the studies were multi-center and showed that home infusion research is being performed on local and national levels.

Infusion Journal needs you to investigate your research ideas and innovative solutions and share your results and conclusions with your peers. It is how the industry can advance infusion within the medical literature. *Infusion Journal* provides an outlet for communicating research in a formal and validated way. Submissions undergo editorial review followed by a double-blind peer-review evaluation of the content. The journal follows procedures in compliance with the highest standards for ethical publishing and requires authors to provide documentation of co-authorship work allocation and disclose conflicts of interest.

As Editor-in-Chief, I am dedicated to publishing content that reflects the interest and needs of all professions and represents infusion research. In medicine, information is often exchanged through local meetings, conferences, small groups, and one-on-one conversations. *Infusion Journal* offers the opportunity to exchange ideas on a larger and more scientific scale. Maintaining rigorous standards of peer review, editorial review, selection, revision, appropriateness of cited works, publication reach, and author services is our commitment to authors and readers. I am honored to lead this initiative with a team of dedicated editors and advisors who support and encourage the mission of *Infusion Journal*.

To learn more about the journal and review information on manuscript submission, visit:

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A Multi-Center Time Study of Home Infusion Pharmacist Professional Services

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ABSTRACT

Introduction

Pharmacist professional services are paramount to the success of the home infusion process. Even though there is a general understanding of the type and scope of care that a pharmacist provides, the various tasks and how they differ between therapy types and drug administration method are unknown. Using home infusion pharmacist time utilization data collected in this study, the amount of time the home infusion pharmacist spends managing and caring for the patient was determined. The categories of professional services the pharmacist provides and the time and task differences between therapy types and methods of administration was also determined.

Methodology

This prospective time study analyzed pharmacist recall of time spent on a predetermined list of patient tasks using a formatted Excel® spreadsheet. Data was collected January-October 2021. The goal was to capture time data related to at least 2 dispensing cycles.

Results

The mean pharmacist time per patient per day was 35.85 minutes (SD=35.86). Based on this number, the direct salary costs associated with pharmacist services for the therapy categories described in this study is estimated to be $35.17 per patient per day. Over the course of the study, 400 pharmacist tasks were completed for 30 patients of which 49.30% involved drug preparation and compounding and 20.30% involved care coordination and communications. The mean tasks per patient was 13.33 (SD=7.03) and the mean tasks per patient per day was 1.33 (SD=.85). Anti-infective patients using an ambulatory pump required the most tasks per day (2.77, SD=1.20) and anti-infective patients using an IV push required the least (1.09, SD=.84). The mean time per task was 22.96 minutes (SD=28:29). Even though anti-infective patients who use a pump required the most time per day, they averaged the least number of study days (4.25) while anti-infective patients using an IV push averaged 14.39 study days.

Discussion

Patient assessments require the most time; 40:48 minutes per task. Assessments ensure that the patient's therapy is appropriate, evaluates patient safety, and ensures the home environment and caregiver support is sufficient. Sterile drug preparation and compounding comprises half of all pharmacists' services which is expected since compounding has grown increasingly complex.

Conclusions

This pharmacist time study illustrates the type of tasks and the amount of time dedicated to home infusion professional services. Pharmacist's average 35.85 minutes per day caring for each patient. Even though the data shows that patient care is highly customized, there are trends that can be applied to understanding a pharmacist's workflow.

Keywords: *Pharmacist services, time study, patient assessment, clinical monitoring, sterile compounding, plan of care, care coordination, infusion*

Introduction

As an active member of the home infusion team, the pharmacist provides a vast array of patient-focused professional services, which are paramount to the success of the infusion care process. A professional pharmacy service is defined as an action or set of actions undertaken in or organized by a pharmacy, delivered by a pharmacist, who applies their specialized health knowledge personally or via an intermediary, to optimize the process of care, with the aim to improve health outcomes and the value of health care.[1] The pharmacist actions referred to in the definition are multifaceted and when applied to the home infusion pharmacist begins with deeming the patient's appropriateness for home infusion.

Prior to admitting a patient to the home infusion service, the pharmacist is central to completing a sequence of tasks. Pharmacist tasks include performing assessments and consulting with the patient, physician, and nurse to determine a plan of care for the home infusion medications, which involves determining how the drug will be administered (i.e., IV push, elastomeric device, gravity, or mechanical pump). Concurrently, the pharmacist reviews and/or recommends an individualized medication monitoring plan and coordinates the preparation of the compounded sterile preparations, equipment, and supplies. Throughout therapy, the pharmacist or their designee speaks with the patient to assess the medication's effects and if the patient is not responding to the drug or developing an adverse effect, the pharmacist will evaluate the situation and notify the physician.[2]

There is a common understanding of the home infusion pharmacist's professional contributions to the care of patients. However, the pharmacist's time commitment to the various tasks and how they differ between therapy types and drug administration method is unknown. Since home infusion billing bundles pharmacist professional services with items used by the patient to administer the medication and maintain the intravenous access device (e.g., pumps, tubing, dressing change supplies) it is not possible to isolate and measure pharmacist work using billing data.

Studies that investigate tasks and quantify the amount of time to complete a given task are known as time utilization or time and motion studies and are common in health care because they assist in understanding the time requirements specific to a health care profession.[3] These studies were initially used to determine costs and inefficiencies in health care delivery and then expanded the focus toward patient safety and quality.[3] Time utilization studies offer a precise standard in quantifying health care workers' time expenditures on clinical activities and provide valuable insight into system specifications and workflow design.[4,5] In brief, time utilization data is valuable for understanding the typical work required to efficiently provide a high-quality health care service.

The literature reveals that studies tracking a pharmacist's time have been conducted. Unfortunately, the investigations did not include home infusion pharmacy as the work setting. The published studies included retail, clinical, hospital, ambulatory, academics, and a free clinic dispensary, with the primary goal to locate inefficiencies.[4,6] Research specific to home infusion pharmacist professional services and the time utilized has not been reported. The results from this investigation will assist in quantifying the home infusion pharmacist's time commitment to tasks that are involved with caring for the home infusion patient. Equally important, the results can be applied to pharmacist staffing decisions and inform policies that support appropriate reimbursement for home infusion services. The secondary purpose of this study is to gain insight and describe the home infusion pharmacist's workload.

Study Objectives

The objectives of using home infusion pharmacist time utilization data collected in this study are:

1) Determine the amount of time a home infusion pharmacist spends managing and caring for a home infusion patient;
2) Quantify the categories of professional services (tasks) the pharmacist provides; and
3) Determine the time and task differences between therapy types and methods of administration.

Methodology

A descriptive, multi-center, home infusion pharmacist time utilization study was administered by the National Home Infusion Foundation (NHIF). The NHIF web page invited all home infusion providers to participate in a study that involved pharmacists self-reporting time spent on clinical tasks related to patient care. The pharmacists at the participating provider locations received an orientation video, data entry guide, patient tracking Excel® spreadsheets, and when needed, individual telephonic support.

A home infusion pharmacist expert committee was utilized to determine the study therapy types to be included, dispensing cycles, pharmacist task categories, and examples of tasks within each category. Since it was hypothesized that the amount of pharmacist professional time varies according to the patient therapy type and administration method, time measures were delineated for the 8 therapies and administration types shown in Figure 1.

FIGURE 1 | Therapy and Administration Type and Dispensing Cycle

Therapy Type	Administration Type	Data Collection Time Frame
1. Anti-infective	Ambulatory infusion pump	10 days with 2 dispenses
2. Anti-infective	IV push	10 days with 2 dispenses
3. Inotropic therapy	Ambulatory infusion pump	14 days with 2 dispenses
4. Anti-neoplastic chemotherapy	Ambulatory infusion pump	21 days with 2 dispenses
5. Parenteral nutrition patient	Ambulatory infusion pump	14 days with 2 dispenses
6. Monoclonal antibody	Any method	Starting with initial home dose through 2nd dispensing cycle
7. Subcutaneous immune globulin	Ambulatory infusion pump	45 days with 2 dispenses
8. Intravenous immune globulin	Ambulatory infusion pump	45 days with 2 dispenses

Data Collection

Data collection was conducted January through October 2021 and involved tracking pharmacist patient care time starting at the time of referral and continuing through the minimum number of days shown in Figure 1. The goal was to capture time data related to at least 2 dispensing cycles which included the initial dispense at the start of care and at least 1 subsequent dispense. Data collection then continued through the minimum number of days after 2 dispensing cycles were captured. The time for the second dispense to occur varied based on the therapy type. Patients were not followed through discharge for this study.

Pharmacists self-reported the amount of time (minutes) spent on each patient task using an Excel® file for each patient serviced. The tasks were classified according to predetermined categories (Figure 2). Using retrospective recall, pharmacists tracked the time spent on a task category for a given patient immediately after completing the task. For example, if the pharmacist was reviewing

FIGURE 2 | Pharmacist Professional Services Task Category

Task Category	Examples
1. Performing patient assessments and documenting the assessment results in the patient EMR	• Reviewing current illness • Reviewing past medical history • Reviewing current medication list • Reviewing prescribed infusion medication • Assessing home environment/ caregiver status • Assessing ambulatory status and other physical limitations that may interfere with self-administration • Assessing vascular access device compatibility with prescribed medication • Interventions to facilitate initiation of home infusion therapy
2. Developing, implementing, and documenting the plan of care	• Reviewing existing, and obtaining supplemental physician orders for prevention of acute infusion reactions, access device de-clotting agents, access device maintenance solutions, etc. • Developing a monitoring plan • Developing an access device maintenance plan • Patient education plan • Interventions performed • Documenting and updating the care plan in the EMR
3. Clinical monitoring and related intervention activities	• Obtaining, tracking, and trending lab results • Lab evaluations • Interventions performed • Recommendations made because of monitoring activities • Documentation of monitoring and interventions in the EMR
4. Drug preparation and compounding activities	• Dispensing • Determining appropriate beyond use dates • Compounding process oversight (patient specific) • Supply selection • Shipping • Documentation of compounding, dispensing, and delivery activities
5. Care Coordination and communication	• Telephonic interactions and the time spent performing the task • Patient communication • Prescriber communication • Internal communication (i.e., billing) • Only include if not able to fit into a category above
6. Other patient-related work tasks	• Case conferences • Work not covered above

the prescribed infusion medication, the task category was "1." After completing the task, the pharmacist noted the total task time directly related to their role in the task in the tracking form (Figure 3). Once a patient had completed 2 dispensing cycles and the minimum number of days, the data collection tracking form was submitted to NHIF via a data submission portal.

FIGURE 3 | Home Infusion Pharmacist Professional Services Excel® Tracking Form

NHIF HOME INFUSION PHARMACIST TRACKING FORM-CLINICAL SERVICES TIME STUDY					
Location DPC					Patient Therapy Type Codes
Patient ID #					1: Antiinfective using an ambulatory infusion pump 2: Antiinfective utilizing IV push administration 3: Inotropic using an ambulatory infusion pump 4: Anti-neoplastic chemotherapy (i.e.5-Fu) using ambulatory infusion pump 5: Parenteral nutrition patient 6: Monoclonal antibody administered intravenously with initial home dose 7: Subcutaneous immune globulin-pump administered 8: Intravenous immune globulin-pump administered
Patient Age					Care Activity Task Codes
Patient Data Start Date					1: Performing patient assessments and documentation 2: Developing, implementing, & documenting care plan 3: Clinical monitoring and intervention activities 4: Drug preparation and compounding activities 5: Care coordination and communications 6: Other patient related works tasks
Patient Data Stop Date					
Patient Therapy Type Code	Therapy	Medication	Date Added	Administration Method	
Secondary Therapies (IV)					
Data Entry					
Date	Task Code #	Start Time	End Time	Comments/Notes	

Using Excel®, researchers calculated the patient total days, total patient minutes for each task category, and total patient minutes for pharmacist professional services. Next, the data for all submitted forms was combined and compiled into a single Excel® file. This file was imported to IBM SPSS® (Statistical Product and Service Solutions) for additional analysis.

Analysis

The main objective of this study was to measure how much time home infusion pharmacists spent managing and caring for a patient per day and the time spent in each category of tasks that are completed. The time measurements collected during the study were used for the following calculations: The total pharmacist time spent on a single patient was divided by the number of study days to calculate the amount of time per day for 1 patient. This was calculated for all the patients in the study, and an average value was determined from the sum of time per day for all patients divided by the number of patients in the study. The resulting value is defined as the mean amount of time a pharmacist spends per patient per day. Time measurements of related tasks were collected during the study and the following calculation used to determine the mean value for pharmacist time per task: The sum total patient time for each task category was divided by the sum of the number of completed tasks within each of the 6 categories. The mean value for pharmacist time for each therapy type was calculated using the sum of the total time of tasks by therapy divided by the number of completed tasks. The mean value for pharmacist time for each method of administration was calculated using the sum of the total time for tasks divided by the number of completed tasks within each administration method.

IRB (Institutional Review Board) Status

The patient's plan of care was not impacted by this study. All patient care data was retrospectively recorded. No identifying patient data was provided by the participating provider locations. Furthermore, the provider location was deidentified using a data participation code (DPC) provided by a 3rd party consultant. This study was therefore exempted from IRB review. To ensure that both provider and patient were deidentified, the patient code was the provider's unique DPC followed by a 2-digit patient identifier, only known by the pharmacist.

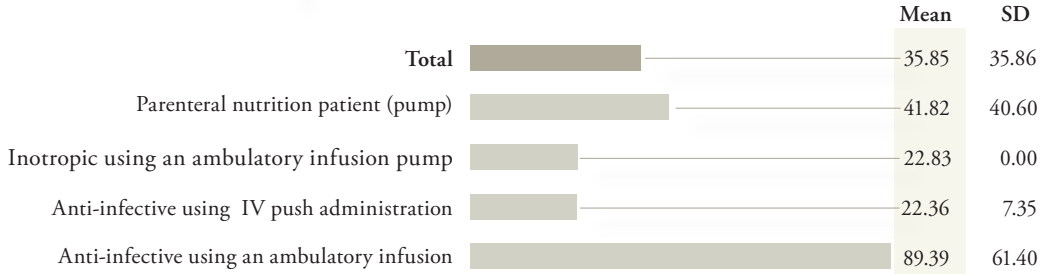
Results

This multi-center study included 367 cumulative study days representing 30 patients from 5 unique providers throughout the mid-west and east regions of the United States. The mean number of study days per patient was 12.23 (SD=7.06) which included at least 2 dispensing cycles. The mean patient age was 59.53 (SD=13.80) with a range of 27-77 years. As shown in Table 1, anti-

TABLE 1 | Patient Therapy Category and Study Days

Therapy Category	Patients (n)	Total Study Days	Mean Study Days	SD
Anti-infective using an ambulatory infusion pump	4	17	4.25	1.50
Anti-infective using IV push administration	18	259	14.39	7.20
Inotropic using an ambulatory infusion pump	1	18	18.00	0
Parenteral nutrition using ambulatory infusion pump	7	73	10.43	4.96
Total	30	367	12.23	7.06

FIGURE 4 | Mean Pharmacist Time (Minutes) Per Patient Per Day by Therapy Category



infectives administered by IV push were the predominate patient therapy category represented in the study followed by parenteral nutrition using an ambulatory infusion pump. No data was submitted for the chemotherapy, IGG, or monoclonal antibody therapy categories. The remaining study results align with the study objectives.

Home Infusion Pharmacist Patient Care Time and Workflow

Determining the average time spent by pharmacists caring for an individual home infusion patient was a primary objective of the study. As shown in Figure 4, the mean pharmacist professional services time per patient per day is 35.85 minutes (SD=35.86). A secondary objective was to analyze the impact of therapy type and administration method on pharmacist time. Figure 4 also illustrates the variation in time spent by patient category. Anti-infective patients using an ambulatory pump required the most time per day (89.39 minutes) while anti-infective patients using IV push administration required the least amount of time (22.36 minutes). While this metric provides a useful average for time spent per patient per day, actual pharmacist work is not evenly distributed and occurs at intervals throughout the patient episode of care. To illustrate this trend, pharmacist task data was analyzed and plotted by study day.

Figure 5 shows the number and category of pharmacist tasks performed each of the study days for 3 randomly selected patients. The anti-infective patient using an ambulatory infusion pump had 7 study days with 16 pharmacist tasks completed while the inotrope patient using an ambulatory infusion pump had 18 study days with 21 tasks. The anti-infective patient using the IV push administration method had 17 study days with 24 pharmacist tasks. As shown in Figure 5, the variety, and number of tasks at start of care are highest, while some

FIGURE 5 | Pharmacist Task Data for 3 Patients: Task Number & Category Per Study Day

Patient 1. Therapy Type:
Anti-infective using an ambulatory infusion pump

Study Day	1	2	3	4	5	6	7
Task Category	1	1,2,2,1,5,5,4,4	4			5,3,4	3,4,3

Patient 2. Therapy Type:
Inotrope using an ambulatory infusion pump

Study Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Task Category	5	2,5,4,4,4,1	3,5,1	4				3		5,4	4					3	5,4,4,4	4

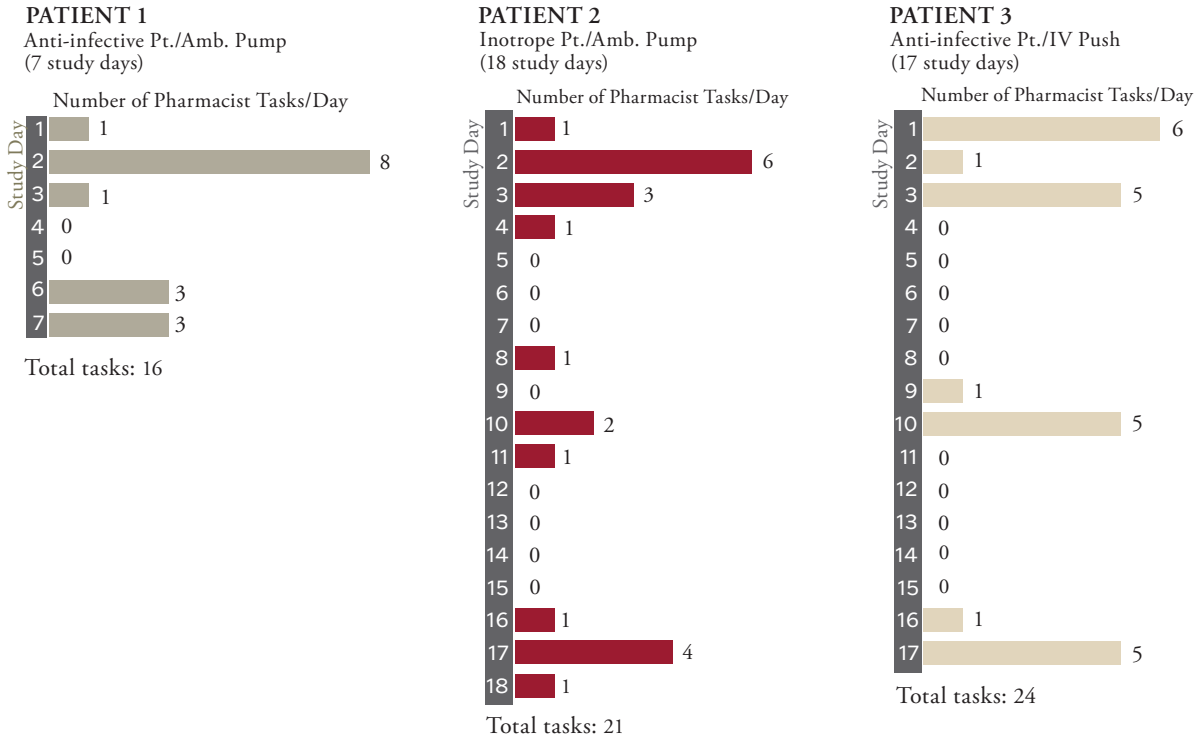
Patient 3. Therapy Type:
Anti-infective using IV Push Administration

Study Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Task Category	1,4,4,3,4,4	3	5,4,4,4,4						3	5,4,4,4,4						3	5,4,4,4,4

* Numbers are listed in order performed

Task 1 - patient assessment and documentation in EMR | **Task 2** - plan of care | **Task 3** - clinical monitoring and interventions | **Task 4** - drug prep and compounding | **Task 5** - care coordination and communication | **Task 6** - Other

FIGURE 6 | Number of Pharmacist Tasks Per Study Day: 3 Sample Patients



days do not require pharmacist time. This trend is more obvious when the data is observed in the graph shown in Figure 6.

Home Infusion Pharmacist Tasks

Pharmacist tasks were grouped into 6 categories as shown in Table 2. A total of 400 tasks were completed for the 30 patients. The data reveals that pharmacist time is nearly equally split between patient care (50.7%) and drug preparation activities (49.3%). The mean tasks per patient per day was 1.33 (SD=0.85). Anti-infective patients using an ambulatory infusion pump required the most tasks per day (2.77, SD=1.20) and anti-infective patients using IV push administration required the least (1.09, SD=0.84).

TABLE 2 | Frequency of Pharmacist Task and Percentage of Total Tasks

Task Category	Task (N)	% of Total N
1. Performing patient assessment and documentation	53	13.30%
2. Developing, implementing, and documenting care plan	29	7.20%
3. Clinical monitoring and intervention activities	36	9.00%
4. Drug preparation and compounding activities	197	49.30%
5. Care coordination and telephonic communications	81	20.30%
6. Other patient-related work tasks	4	1.00%
Total	400	100.00%

Pharmacist Time Per Task

The most time-consuming task category was patient assessments and documentation which averaged almost 41 minutes (SD=35.05) per task. Overall, the mean aggregate time per task was 22.96 minutes (SD=28.29). Drug preparation and compounding required a mean time of 25 minutes per task and comprised almost half of all tasks performed (Figures 7 and 8).

Discussion

Home infusion is associated with positive outcomes, low rates of adverse events, and high rates of patient satisfaction.[7] Of the home infusion patients (n=6,353) who responded to Patient Satisfaction Surveys in 2019 as part of an NHIF benchmarking

FIGURE 7 | Total Pharmacist Tasks Performed and Percentage by Category

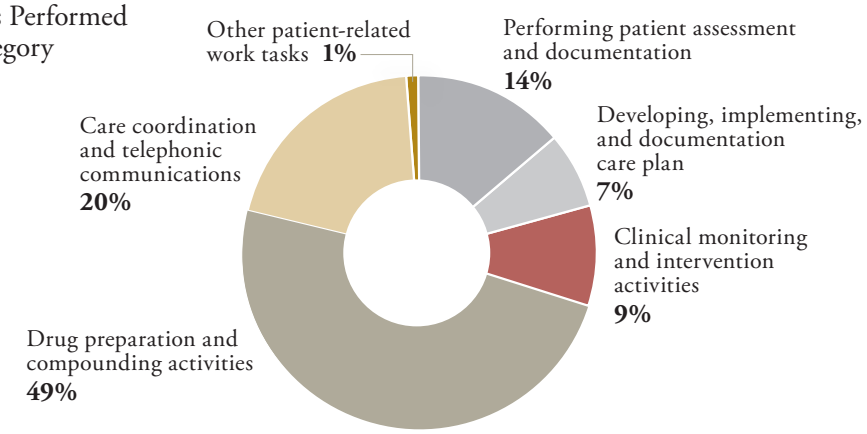


FIGURE 8 | Mean Pharmacist Time (minutes/seconds) Per Task

	Mean	SD
All tasks	22:57.3	28:29.6
Other patient-related work tasks	37:15.0	48:57.5
Care coordination and telephonic communications	11:43.7	14:30.0
Drug preparation and compounding activities	25:21.3	30:57.9
Clinical monitoring and intervention activities	08:16.7	05:49.4
Developing, implementing, and documenting care plan	21:37.2	18:48.0
Performing patient assessment and documentation	40:48.7	35:06.0

program, approximately 93% indicated that the pharmacy staff was always courteous and helpful.[8] The patient's satisfaction with the pharmacist is essential, given the amount of time pharmacists dedicate to assessing, planning, monitoring, and preparing the patient's infusion therapy.

Delivery of the home infusion service requires a multi-disciplinary clinical team of pharmacists, nurses, dietitians, physicians, and others, as well as support staff that process referrals, perform compounding tasks, manage deliveries, and submit claims for payment. The focus on the pharmacist should not diminish the contributions of the entire home infusion team, however home infusion pharmacist professional work is not well understood and therefore worthy of investigation.

Patient assessments are the most time-consuming tasks pharmacists perform, averaging slightly over 40 minutes per task. Assessments are used to document the patient's therapy is safe and appropriate for their diagnosis, and verify the home environment and caregiver support is sufficient for successful home therapy. The individual plan of care developed through the assessments, ensures proper monitoring and establishes the goals of therapy. To complete these tasks, pharmacists spend roughly 20% of their time coordinating and collaborating with patients and their health care providers.

Sterile drug preparation and compounding has grown increasingly complex over the past 2 decades; thus, it is expected that it comprises half of all pharmacists' services. Infusion pharmacists are responsible for dispensing sterile medications

that are safe, accurate, and free of contamination. Ensuring the stability and sterility of the types of home infusion medications included in this study requires expertise in evaluating drug stability studies and proficiency in sterile compounding procedures and facility operations. National standards for sterile compounding have become so complex that pharmacists with this expertise are now recognized through a Board of Pharmacy Specialties Certification designation.[10]

Therapy Type Impact on Pharmacist Time

The study demonstrates significant variability in the amount of pharmacist time spent across the different therapy categories. One interesting observation is that patients using ambulatory infusion pumps generally required more time per day than patients using the IV push method of administration. To better understand pharmacist time, the number of study days must be considered. For example, even though anti-infective patients who use an ambulatory infusion pump required the most time per day, they averaged the least number of study days (4.25) while anti-infective patients who used an IV push averaged 14.39 study days.

Review of the standard deviation, minimum, and maximum amount of time per task category shows considerable variance which is to be expected due to the wide range of complexity associated with individual patient therapy, home environment circumstances, payer mix, and acuity level. As a multi-center study, proprietary staffing models and business practices may also be a factor.

Cost of Pharmacist Services

Providers are reimbursed by commercial payers for pharmacist services as part of a bundled "per diem" that also pays for items such as IV tubing, IV catheter supplies, and pumps in addition to administrative costs. Medicare does not recognize pharmacists as health care providers and only pays for services offered by nurses in the home. As a result, the costs associated with pharmacist services are obscured and not well understood. To estimate the daily per patient salary costs for pharmacist professional services, the median annual salary ($126,110) for pharmacists from the U.S. Bureau of Labor Statistics 2018 report can be extrapolated based on the time spent per patient per day.[9] The direct salary costs (not including benefits) associated with pharmacist services for the therapy categories described in this study are estimated to be $35.17 per patient per day. This is based on the mean time spent per patient per day multiplied by the median hourly rate of $60.63. Traditional therapies such as anti-infectives, inotropes, and parenteral nutrition comprise 90.5% of all home infusion patients, therefore the cost estimate determined here is applicable to most patients receiving home infusion.[9]

Study Limitations

The study results were limited to the following types of infusion patients: anti-infectives using an ambulatory infusion pump, anti-infectives using IV push administration, inotropics using an ambulatory infusion pump, and parenteral nutrition using ambulatory infusion pump. Due to the differences observed in the therapy type data, future studies will include data from chronic therapies such as monoclonal antibodies and immune globulin. The most common limitation of this self-report time study is the potential for pharmacists to be more productive since their tasks and time were tracked. This phenomenon is noted as the Hawthorne effect and is common in self-report research.[11] Even so, self-report is commonly used to collect time utilization data. A final limitation is that the data was only collected for 2 dispensing cycles (an average of 12 days) starting with the beginning of therapy and not collected through discharge. It is not known whether the mean time per patient per day would remain consistent throughout the entire length of the therapy.

Conclusions

This home infusion pharmacist time utilization study illustrates the type of tasks and the amount of time dedicated to home infusion professional services. Pharmacists completed 400 tasks over 367 study days for the 30 patients in the study. Of the 6 categories of tasks, half (50.7%) of all pharmacist work is dedicated to patient care activities, while the remaining 49.3% involved drug preparation and compounding activities. The data shows that

pharmacists average 35.85 minutes per patient per day of professional work to provide patient care. Based on this number, the direct salary costs associated with pharmacist services for the therapy categories described in this study is estimated to be $35.17 per patient per day.

This is the first study to quantify and describe the amount and type of pharmacist professional work performed when caring for patients who infuse medications in the home setting. Time and task differences between therapy and administration methods were noted, and graphs illustrate the intensity of pharmacist services at the start and at various intervals during care. Even though patient care is highly customized, the data shows trends that can be applied to understanding a pharmacist's workflow.

Disclosures

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Commentary: When reviewing a manuscript submitted by one of *Infusion Journal*'s editors or staff, the author/editor is deliberately excluded from all aspects of the review process. The Editor-in-Chief or alternate editor is responsible for handling the peer review process independently of the author/editor. The author/editor is not aware of the choice of peer reviewers, and the author/editor is not present when discussing the manuscript at editorial meetings.

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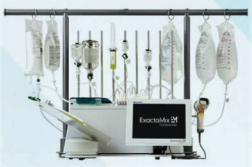

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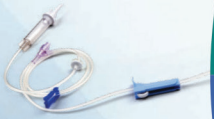

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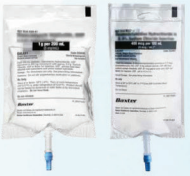

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A 10-Year Retrospective Pilot Study of Parenteral Diphenhydramine Use in Home Infusion Patients

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ABSTRACT

Introduction

Patients who administer chronic parenteral diphenhydramine are at risk of developing behavioral issues that may represent misuse or abuse. The purpose of this study was to assess potential risk factors and comorbidities for medication noncompliance in the home infusion patient population prescribed parenteral diphenhydramine.

Methods

The study was a retrospective review of the patient population prescribed parenteral diphenhydramine from 2010 to 2020. Data collected from the electronic health record included age, gender, race, indication, type of specialty practice prescribing, duration of therapy, prior history of oral diphenhydramine use, reason for discontinuation, comorbidities, and concomitant medications. Comorbidities assessed included chronic pain, tobacco use, alcohol use, psychiatric disorders, venous access device infections, history of venous thromboembolism, documented overdoses, and history of drug abuse.

Results

Between 2010 and 2020, 101 patients were prescribed scheduled parenteral diphenhydramine. After exclusions, the study group contained 76 patients who met the inclusion criteria. Noncompliance was documented in 27 patients (35.5%). Noncompliance was associated with a diagnosis of mast cell disorder (25.9%) and nausea and vomiting (44.4%). Comorbidities associated with noncompliance included chronic pain (88.9%) and psychiatric disorders. The age range for the compliant group was 20-69 and the noncompliant group was 20-49. Noncompliance was more common in females than males in the study.

Conclusion: The analysis of this patient population supports patients showing signs of parenteral diphenhydramine misuse tend to have higher rate of comorbidities associated with substance use disorders when the duration of therapy was 3 months or longer.

Keywords: *Diphenhyrdramine, abuse, noncompliance, infusion, intravenous, Benadryl®*

Introduction

The abuse of prescription drugs in the United States has reached an epidemic level.[1] In 2012, the National Survey on Drug Use and Health found that more than 16.7 million people (12 years and older) in the U.S. abused prescription drugs and concluded that approximately 2.1 million people met the criteria for a Substance Use Disorder related to prescription drugs. This represented a 250% increase in prescription drug abuse over the previous 20 years.

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines drug abuse as a Substance Use Disorder (SUD) when a patient presents with at least 2 of 11 predefined criteria (see Table 1).[2]

There are many case studies of diphenhydramine abuse and withdrawal in literature searches.[3,4,5] Most case studies involve the abuse of over-the-counter (oral) diphenhydramine. Surveys of pharmacists conducted in Great Britain showed that half or more suspected that diphenhydramine and other sedating antihistamines are subject to misuse.[6,7] There is little clinical information available about the diagnosis, prevention, and treatment of diphenhydramine abuse. In general, patients with a SUD are at a higher risk of being diagnosed with depression, bipolar disorder, anxiety, post-traumatic stress disorder (PTSD), eating disorders, schizophrenia, and attention deficit hyperactivity disorder (ADHD).[8] Risk factors specific to sedative-hypnotic prescription drug abuse include white race, female sex, being uninsured, being unemployed, panic symptoms, other psychiatric symptoms, alcohol abuse, or dependence, cigarette use, illicit drug use, and history of intravenous drug use.[9]

Diphenhydramine is an antihistamine with anticholinergic and sedative side effects. It competes with histamine for H1-receptor sites in the gastrointestinal tract, blood vessels, and respiratory tract. Side effects of diphenhydramine include tachycardia, blurred vision, urinary retention, constipation, anorexia, diaphoresis, xerostomia, central nervous system depression, sedation, dizziness, agitation, confusion, and psychosis. The potential for misuse appears to be related to elevating mood, increasing energy levels, and euphoria.[3,4] There may also be increases in dopaminergic neurotransmission along pathways that affect the reward system.[3] Patients with schizophrenia or other psychiatric conditions may experience a reversal of secondary negative symptoms associated with antipsychotic medications (such as lack of motivation, flattened affect, and social withdrawal) when taking diphenhydramine due to its anticholinergic effects, further enhancing the risk of abuse.[3]

A small subset of patients who are prescribed diphenhydramine infuse the drug parenterally. For patients that require ongoing administration of parenteral (primarily intravenous, IV) diphenhydramine, home infusion companies can provide patients with the medication and supplies needed to infuse in the home setting. Because this applies to a small number of patients, there is a scarcity of information for dosing and managing them. The risk of SUD related to

TABLE 1 | DSM-5 diagnostic criteria for Substance Use Disorder (SUD)[2]

A problematic pattern of use leading to clinically significant impairment or distress is manifested by 2 or more of the following within a 12-month period:

1. Often taken in larger amounts or over a longer period than was intended
2. A persistent desire or unsuccessful efforts to cut down or control use
3. A great deal of time is spent in activities necessary to obtain, use, or recover from the substance's effects
4. Craving or a strong desire or urge to use the substance
5. Recurrent use resulting in a failure to fulfill major role obligations at work, school, or home
6. Continued use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by its effects
7. Important social, occupational, or recreational activities are given up or reduced because of use
8. Recurrent use in situations in which it is physically hazardous
9. Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance
10. Tolerance
11. Withdrawal

diphenhydramine has the potential to be especially problematic in the home infusion population when the IV route is utilized, given that this route results in rapid drug bioavailability and is the most efficient route to produce euphoria for many drugs.

An example of an indication that may require chronic parenteral diphenhydramine treatment is Mast Cell Activation Syndrome (MCAS). MCAS includes a heterogeneous group of disorders characterized by the release of mast cell mediators. The disorders are generally considered incurable. Mast cells contain more than 200 mediators, including histamine and tryptase, which contribute to their immune-related and non-immune functioning.[10] When activated, mast cells release these mediators, which can result in the signs and symptoms of an allergic reaction which are present in many mast cell disorders. First-line therapies for MCAS include avoidance of triggers and treatment of symptoms. Patients who experience anaphylactic reactions may require epinephrine, steroids, and antihistamines to control symptoms.[10]

One study of patients with MCAS found that infusing diphenhydramine continuously at 10-14.5 mg/hr appeared safe and effective, and reduced disease flares.[11] The study was performed in 10 patients with life-threatening MCAS (aged 18-49; 9 were women) who experienced continuous anaphylactoid or severely dysautonomic flares. At baseline they were treated with subcutaneous epinephrine, H2-Blockers, and intermittent diphenhydramine. Baseline dosing of diphenhydramine among patients was 600-800 mg per day in divided doses (an average of 25-33 mg/hr) administered via IV, intramuscular, or oral routes. All were hospitalized for essentially continuous anaphylaxis and were started on continuous diphenhydramine infusion (CDI) while inpatient. CDI was initially started at 5 mg/hr IV. A rescue dose of diphenhydramine 25-50 mg IV was given with each disease flare, along with an increase of CDI by 1-2 mg/hr. One patient stopped CDI due to reaching 17 mg/hr without effect. Other patients were stabilized on 10-14.5 mg/hr, with a reduction in flare severity and a reduction of flare frequency to 1-4 times per month. Stabilized patients ceased continuous flares within 24 hours and were discharged home on CDI with ambulatory pumps within 48 hours. In the home setting they had diphenhydramine 10-25 mg IV available as needed for flares. Patients were followed for 0.5-21 months with continued reduction in flares (1-4 times per month). The author of the study reported no evidence of tolerance or waning of effect during follow up.[11]

It is the experience of pharmacists at a regional home infusion provider that the patient population is at risk of developing behavioral issues with chronic parenteral diphenhydramine that may represent misuse or abuse. Aside from the MCAS study above, there is little information available to guide clinicians on the optimal dosing of outpatient chronic parenteral diphenhydramine. In addition, there is a lack of clinical information and guidance of the risk factors for and treatment of diphenhydramine abuse. Therefore it was decided to conduct a retrospective analysis of our patient population to determine next steps.

Purpose

To review the patient population who were prescribed parenteral diphenhydramine from 2010 to 2020 in order to assess potential risk factors or comorbidities associated with noncompliance. To assess the direction of future research in the area of SUD related to chronic parenteral diphenhydramine use.

The purpose of this study was not to diagnose drug abuse or SUD.

Methods

In the first quarter of 2021, the pharmacists conducted a retrospective review of patients who had been prescribed scheduled parenteral diphenhydramine (predominantly intravenous) from 2010 to 2020. Patients of all ages were included if any doses were dispensed to them during that time period. Patients were excluded if they only received oral diphenhydramine, if diphenhydramine was prescribed as a premedication for an intermittent specialty medication (ex: prior to intermittent infliximab infusions), or if it was dispensed as part of an anaphylaxis kit.

Data collected included age at start of treatment with parenteral diphenhydramine, gender, race, indication, type of specialty practice prescribing, duration of therapy, prior history of taking oral diphenhydramine, and reason for discontinuation. Comorbidities assessed included chronic pain, tobacco use, alcohol abuse, various psychiatric disorders, history of line infections, history of venous thromboembolism, documented overdoses, and history or family history of drug abuse. Concomitant medication drug classes were also assessed.

Because of the retrospective nature of this study and the limited diagnostic information available, few criteria

used in the diagnosis of SUDs could be evaluated (see Table 1).[2] Rather than trying to diagnose abuse or a SUD, the pharmacists collected information about patient noncompliance that indicated misuse for this pilot study.

For the purpose of our study, noncompliance was defined as meeting at least one of the following criteria: documentation in the patient electronic medical record of more than 1 early refill request; the documented intervention of a home infusion clinician related to problems with diphenhydramine therapy; necessity of a compliance contract related to diphenhydramine noncompliance; documentation in an alerts field of noncompliance or early refills; other documentation in the electronic medical record stating the prescriber was aware of noncompliance. For this study, patients will be referred to as "noncompliant" if they met any of the criteria above, and will be labeled as "compliant" if they did not have documentation of noncompliance as above.

Institutional Review Board (IRB) Status

The research involved secondary data analysis where the data set was deidentified before analysis and recorded in a manner where the resulting data contained no information that could be linked directly or indirectly to the identity of the subjects.

Results

Between 2010 and 2020, 101 patients were prescribed scheduled parenteral diphenhydramine. After excluding patients as described above, 76 met inclusion criteria (see Table 2). After data collection and analysis, 49 patients (64.5%) were determined to be compliant and 27 (35.5%) patients had documentation of noncompliance. Of the 76 total patients, 58 (76.3%) were female, 17 (22.4%) were male, and 1 (1.3%) was transgender. Of the patients who had documentation of noncompliance, 24 (88.9%) were female and 3 (11.1%) were male. The majority of compliant patients

TABLE 2 | Patient Demographics

	All Patients, n=76	Compliant, n=49	Noncompliant, n=27
	n(%)	n(%)	n(%)
Total Patients	76 (100%)	49 (64.5%)	27 (35.5%)
Sex			
Male	17 (22.4%)	14 (28.6%)	3 (11.1%)
Female	58 (76.3%)	34 (69.4%)	24 (88.9%)
Transgender (F to M)	1 (1.3%)	1 (2.0%)	0
Age*			
0-9	4 (5.3%)	4 (8.2%)	0
10-19	3 (3.9%)	3 (6.1%)	0
20-29	15 (19.7%)	8 (16.3%)	7 (25.9%)
30-39	16 (21.1%)	8 (16.3%)	8 (29.6%)
40-49	17 (22.4%)	9 (18.4%)	8 (29.6%)
50-59	11 (14.5%)	8 (16.3%)	3 (11.1%)
60-69	8 (10.5%)	7 (14.3%)	1 (3.7%)
70-79	1 (1.3%)	1 (2.0%)	0
80-89	0	0	0
90-99	1 (1.3%)	1 (2.0%)	0
Race			
Native American	1 (1.3%)	0	1 (3.7%)
Black/African American	1 (1.3%)	1 (2.0%)	0
Hispanic or Latino	2 (2.6%)	1 (2.0%)	1 (3.7%)
White (Non-Hispanic, Non-Latino)	64 (84.2%)	40 (81.6%)	24 (88.9%)
Unknown	8 (10.5%)	7 (14.3%)	1 (3.7%)

*Age at start of treatment with parenteral diphenhydramine

FIGURE 1 | Percentage of Noncompliant Patients by Age Range (n=27)

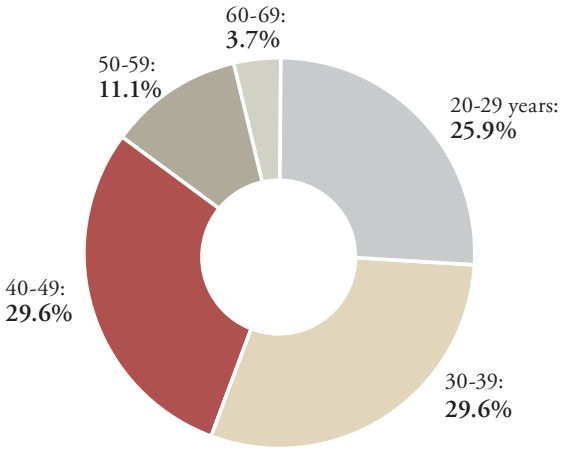


TABLE 3 | Indication for Parenteral Diphenhydramine Therapy

	All Patients, n = 76	Compliant, n = 49	Noncompliant, n = 27
Abdominal pain, n (%)	1 (1.3%)	0	1 (3.7%)
Anti-infective premedication, n (%)	27 (35.5%)	23 (46.9%)	4 (14.8%)
End of Life Care and Comfort, n (%)	8 (10.5%)	7 (14.3%)	1 (3.7%)
Idiosyncratic anaphylactoid events, n (%)	1 (1.3%)	0	1 (3.7%)
Itching, n (%)	2 (2.6%)	2 (4.1%)	0
Mast Cell Disorder, n (%)	9 (11.8%)	2 (4.1%)	7 (25.9%)
Nausea/vomiting (+/- itching), n (%)	27 (35.5%)	15 (30.6%)	12 (44.4%)
Rash, n (%)	1 (1.3%)	0	1 (3.7%)

fell into a wide range of age groups from age 20 to 69, while noncompliant patients were mostly concentrated between the ages of 20 and 49 (see Figure 1). Given the small numbers of patients who were non-white, we were unable to assess trends based on race.

The most common indications for parenteral diphenhydramine therapy for all patients were anti-infective premedication and nausea/vomiting (see Table 3). A higher percentage of compliant patients had an indication of anti-infective premedication vs. noncompliant patients ([n=23, 46.9%] vs. [n=4, 14.8%]). A higher percentage of noncompliant patients vs. compliant patients had an indication of mast cell disorder ([n=7, 25.9%] vs. [n=2, 4.1%]) and nausea/vomiting ([n=12, 44.4%] vs. [n=15, 30.6%]).

When analyzing comorbidities (see Table 4), noncompliant patients tended to have chronic pain more frequently than compliant patients ([n=24,

TABLE 4 | Comorbidities

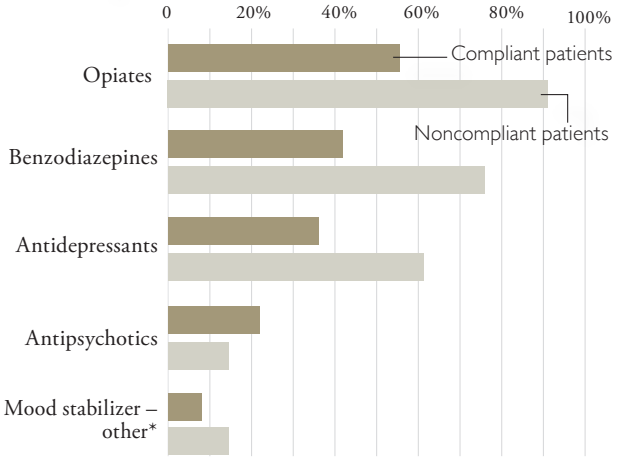
	All Patients, n=76	Compliant, n=49	Noncompliant, n=27
	n(%)†	n(%)†	n(%)†
Chronic Pain	50 (65.8%)	26 (53.1%)	24 (88.9%)
Tobacco Use (Past or Present)	18 (23.7%)	11 (22.4%)	7 (25.9%)
Alcohol Abuse	3 (3.9%)	2 (4.1%)	1 (3.7%)
Anxiety	30 (39.5%)	15 (30.6%)	15 (55.6%)
Depression	33 (43.4%)	17 (34.7%)	16 (59.3%)
Bipolar Disorder	4 (5.3%)	3 (6.1%)	1 (3.7%)
ADHD	6 (7.9%)	2 (4.1%)	4 (14.8%)
Eating Disorder	3 (3.9%)	1 (2.0%)	2 (7.4%)
PTSD	9 (11.8%)	4 (8.2%)	5 (18.5%)
Schizophrenia	2 (2.6%)	1 (2.0%)	1 (3.7%)
History Line Infections	10 (13.2%)	3 (6.1%)	7 (25.9%)
History VTE	29 (38.2%)	16 (32.7%)	12 (44.4%)
Documented Overdoses	1 (1.3%)	1 (2.0%)	0
History of Drug Abuse*	4 (5.3%)	2 (4.1%)	2 (7.4%)

ADHD = Attention Deficit Hyperactivity Disorder, PTSD = Post-traumatic Stress Disorder, VTE = Venous Thromboembolism

*History of Drug Abuse = self-history or family history

† Patients may have more than 1 comorbidity

FIGURE 2 | Concomitant Medications: Compliant vs. Noncompliant Patients (n=76)



* clonidine, divalproex, lamotrigine, lisdexamfetamine, and topiramate

88.9%] vs. [n=26, 53.1%]). Noncompliant patients had higher rates of psychiatric disorders except for bipolar disorder ([n=1, 3.7% for noncompliant] vs. [n=3, 6.1% for compliant]). Noncompliant patients had rates of anxiety and depression that were more than 20% higher than compliant patients ([n=15, 55.6%] vs. [n=15, 30.6%] for anxiety, and [n=16, 59.3%] vs. [n=17, 34.7%] for depression). A history of PTSD was identified in 18.5% (n=5) of noncompliant patients vs. 8.2% (n=4) of compliant patients. Noncompliant patients tended to have higher rates of history of venous thromboembolism (VTE) compared to compliant patients ([n=12, 44.4%] vs. [n=16, 32.7%]). There was a history of line infections in 25.9% (n=7) of noncompliant patients, compared to 6.1% (n=3) of compliant patients. Due to low incidences, it was not feasible to see trends in documented overdoses or history of drug abuse.

Patients were evaluated for the concomitant use of opiates, benzodiazepines, antidepressants, antipsychotics, and other mood stabilizers during parenteral diphenhydramine therapy (see Figure 2). The difference in prescribing of opiates for noncompliant vs. compliant patients was 35.5% ([n=25, 92.6%] vs. [n=28, 57.1%]), for benzodiazepines 34.9% ([n=21, 77.8%] vs. [n=21, 42.9%]), and for antidepressants 26.3% ([n=17, 63.0%] vs. [n=18, 36.7%]). Despite literature stating that patients taking antipsychotics may have an increased risk of diphenhydramine abuse due to the reversal of symptoms associated with antipsychotic medications, our patient population showed a decreased rate of antipsychotic use in noncompliant patients; this may be confounded by the small patient population studied (compliant [n=11, 22.4%], noncompliant [n=4, 14.8%]).[2] Patients were additionally evaluated for taking medications associated with SUD, such as buprenorphine, naloxone, and buprenorphine/naloxone. It was not feasible to assess differences in the use of these medications in this patient population due to low numbers (2 compliant patients, 2 noncompliant patients), and the concern that this information may not be useful due to prescribing practices in some specialties such as the practice of prescribing naloxone to patients taking opiates regardless of assessed risk of overdose.

There appears to be a strong correlation between duration of parenteral diphenhydramine therapy and compliance, as defined in this study (see Table 5). The majority of compliant patients had a duration of therapy of less than 2 weeks (n=20, 40.8%), while the majority of noncompliant patients were on parenteral diphenhydramine for greater than 3 months (n=23, 85.2%).

TABLE 5 | Duration of Parenteral Diphenhydramine Therapy

	All Patients, n=76	Compliant, n=49	Noncompliant, n=27
	n(%)	n(%)	n(%)
< 2 weeks	21 (27.6%)	20 (40.8%)	1 (3.7%)
2 weeks to 1 month	10 (13.2%)	9 (18.4%)	1 (3.7%)
1 - 2 months	3 (3.9%)	3 (6.1%)	0
2 - 3 months	5 (6.6%)	3 (6.1%)	2 (7.4%)
> 3 months	37 (48.7%)	14 (28.6%)	23 (85.2%)

Discussion

The results of this study reveal trends in the patient population, but based on the small sample size, significance differences can not be calculated. Furthermore, the correlations presented do not prove causation. Without further analysis and formal diagnosis, it is not possible to determine whether the noncompliance seen in these patients represents a SUD, or if the patients are exhibiting drug seeking behavior due to inadequate treatment of their underlying disease.

Unfortunately, there are no guidelines for the management of patients prescribed chronic diphenhydramine therapy. Other drug therapies, such as opiates, have guidelines available to direct prescribers on baseline patient evaluations (including benefit-to-harm analysis), obtaining informed consent (including education about goals, expectations, risks and alternatives), guidance on dosing and titration, patient monitoring, protocols for patients with history of drug abuse or psychiatric issues, managing adverse events, potential adjunctive therapies, driving and work safety, implications in pregnancy, the need for an identified managing provider, and guidance on when a specialist consult is needed.[12] General practices to reduce the risk of drug misuse include starting with the lowest possible dose, titrating doses slowly, and limiting the duration of therapy if possible. Early refills should be avoided.[12]

Despite having risk factors for SUD, some patients require treatment with medications that have abuse potential. Treatment with diphenhydramine is often necessary for the treatment of intractable vomiting or mast cell disorders. Guidelines are needed to direct clinicians on how to best manage these patients.

Limitations of this study include a small patient population and limited clinical documentation. Because of the lack of understanding about the potential for the misuse of parenteral diphenhydramine, these patients were not evaluated for diphenhydramine-related SUD by their providers in almost all cases. The retrospective nature of this study excluded patient interviews or requests for additional documentation from referring providers. The authors of this study acknowledge that based on the established definitions of compliant and noncompliant and the clinical information available, it cannot be concluded that noncompliant patients misused or abused diphenhydramine therapy.

Conclusions

The analysis of this patient population supports that patients showing signs of parenteral diphenhydramine misuse tend to have higher rates of many of the comorbidities associated with SUD (depression, anxiety, PTSD, eating disorders, schizophrenia, and ADHD).[8] They also had higher rates of multiple risk factors for sedative-hypnotic prescription drug abuse (especially female sex and psychiatric symptoms).[9] In addition, patients tended to be younger adults (aged 20 to 49); they had higher rates of chronic pain; and they had higher rates of line infections. Medication assessment revealed higher rates of opiate, benzodiazepine, and antidepressant use. The most common indications for parenteral diphenhydramine in this patient subset were mast cell disorders and nausea/vomiting, and the duration of therapy was greater than 3 months in most cases.

Further research and guidance regarding chronic parenteral diphenhydramine use in the home setting is needed. Research and guidance should include analysis of larger patient populations, risk factors for diphenhydramine misuse, benefit-to-harm analysis, optimal dosing and titration, patient monitoring, protocols for patients at risk of diphenhydramine abuse, management of adverse events, and potential alternative and adjunctive therapies. In the meantime, patients requiring chronic parenteral diphenhydramine should be maintained at the lowest possible dose, and the selection of method of administration should include considerations of abuse potential. Pharmacists and patient providers should work collaboratively to optimize treatment regimens in these patients to prevent the misuse or abuse of diphenhydramine.

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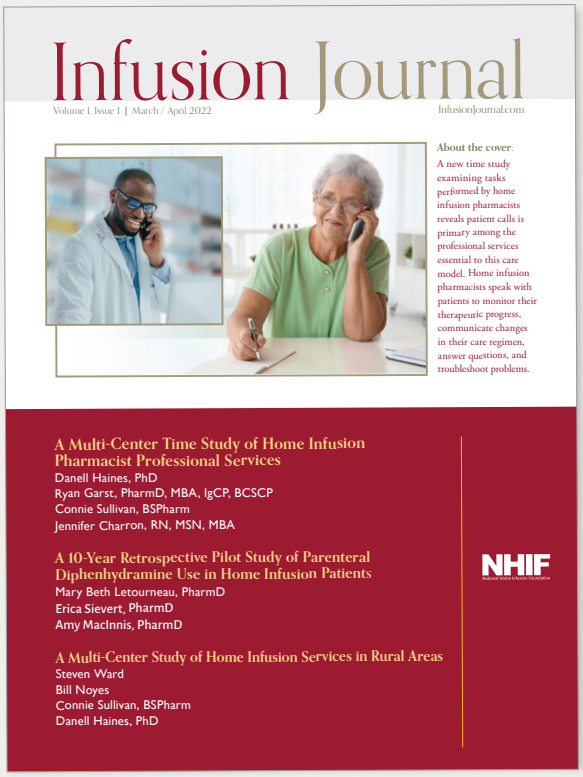

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ABSTRACT

Introduction

Approximately 15% of the U.S. population lives in rural areas. It is recognized that rural Americans have fewer health care opportunities when compared to metropolitan residents. One area of health care is home infusion with approximately 1,000 providers in the U.S. What is not understood is the availability of home infusion to rural patients. This study aimed to determine the annual percentage of home infusion patients living and receiving home infusion services in rural areas.

Methodology

This retrospective, multi-center study analyzed patient rural/non-rural status data collected from home infusion providers who utilize the CPR+® and CareTend® platforms for electronic health records. Patients were classified as rural if their zip code fell within the rural designation defined by the Centers for Medicare and Medicaid Services (CMS) DMEPOS Competitive Bidding Program. The analyzed data was from 2018, 2019, and 2020, and included calculating the total number of unique patients and those who were considered rural. From this information, the overall percentage of rural patients was determined. The rural percentage for each provider was coded into 1 of 4 categories (0-10%, 11-25%, 26-49%, and 50% or greater). The frequency and percentage of providers who fell into each category was calculated so that trends could be observed, and data summaries more easily determined.

Results

Rural/Non-rural data from 200 individual pharmacy locations was submitted for analysis. For the 3-year period, there were 545,280 unique home infusion patients of which 71,278 were considered rural. Overall, 13.1% of patients served by these home infusion providers lived in rural areas. The number and percentage of rural patients served increased over the 3-year analysis period.

Discussion

This is the first study to quantify the use of home infusion in rural populations. It is known that patients in rural areas experience challenges with health care, including increased travel time for physician visits and chronic disease management. Unquestionably, home infusion alleviates patient travel barriers. The study data shows that most home infusion providers are serving patients living in rural areas and the percentage of rural patients has increased from 2018 to 2020.

Conclusions

Home infusion use in rural areas is well-established. Home infusion may offer advanced, infusion-based treatments more accessible to patients with limited health care options due to lack of proximity to urban centers.

Keywords: *Rural population, infusion, health care disparity, access to care, travel barrier*

Introduction

The Centers for Disease Control and Prevention (CDC) estimates that more than 46 million Americans, approximately 15% of the population, live in rural areas.[1] According to the U.S. Census Bureau, a rural region is an area that falls outside of a metropolitan area while a metropolitan area has an urban core and a population of 50,000 or more.[2] Rural Americans are more likely to die from chronic diseases, are often under-insured, and have less access to health care compared to urban populations. Furthermore, a report published by The National Rural Health Association determined that the low patient-to-physician ratio for rural Americans contributes to poor health outcomes.[3] Another disparity is the patient-to-primary-care physician ratio which is 39.8 physicians per 100,000 people in rural areas compared to 53.3 physicians per 100,000 in urban areas.[3] Differences in access to physician specialists in rural areas is more pronounced with only 30 specialists for every 100,000 patients. By contrast, the ratio of specialists to patients in urban areas is 263 per 100,000.[3] Home infusion of parenteral medications for a range of diseases is routine in the United States. Even though a 2020 National Home Infusion Association (NHIA) report estimates there are 974 licensed home infusion providers caring for approximately 3.1 million Americans annually, no studies have been conducted that report the utilization of home infusion in rural areas.[4]

Study Objective

This study aims to determine the annual percentage of home infusion patients living and receiving services in rural areas of the United States.

Methods

This retrospective, multi-center study analyzed data from home infusion providers who utilize the CPR+® and CareTend® (WellSky®) prescription management platform and electronic health record (EHR) software products. Participation in the study was voluntary and open to all eligible client companies using the applicable software. Participation in the study was promoted to members of NHIA through postings on the association website and in e-newsletters. Data collection occurred from July 1, 2021, to August 31, 2021.

For this study, patients were classified as rural if their zip code fell within the rural designation defined by the Centers for Medicare and Medicaid Services (CMS) DMEPOS Competitive Bidding Program. Within the DMEPOS program, there are 4 categories of zip codes: Competitive Bidding Area, Non-Rural, Rural, and Non-contiguous. While this is a more constricted characterization of rural compared to the U.S. Census Bureau definition, it provides a reasonable method for classifying infusion patient data.

Participating providers were asked to generate a de-identified report that categorizes each unique patient as non-rural or rural. The report also filtered infused drug therapies based on the order type and excluded non-IV drug therapies (i.e., enteral, oral). Data was grouped by the number of unique patients who received an infusion therapy in each calendar year based on whether their zip code falls into a rural area as defined (see Figure 1 for a sample report). Sites were instructed to submit

FIGURE 1 | Sample Provider Report

Year	Unique Rural Patients	Unique Non-Rural Patients	% Rural Patients
Location 1	530	3,170	14.32%
2016	100	500	16.67%
2017	95	650	12.75%
2018	115	675	14.56%
2019	120	645	15.69%
2020	100	700	12.50%
Location 2	1,305	6,725	16.25%
2016	250	1,300	16.13%
2017	275	1,350	16.92%
2018	280	1,375	16.92%
2019	230	1,300	15.03%
2020	270	1,400	16.17%

data for a 5-year look-back period (2016 to 2020). The data was exported to Excel® files and submitted to NHIA either by email or through an anonymous data portal. The data was aggregated to a single Excel® file and imported to IBM SPSS® (Statistical Product and Service Solutions) for analysis.

Analysis

Determining the number of providers submitting data for each of the 5 years was the first step in the analysis. Next, the total number of unique patients per year was determined and the percent of those considered rural patients. Additionally, each provider's rural patient percent was calculated. Due to possible outlier data, the median provider rural percentage was determined. The rural percentage for each provider was also coded into 1 of 4 categories (0-10%, 11-25%, 26-49%, and 50% or greater). The frequency and percentage of providers in each category was calculated so that trends could be observed, and data summaries more easily determined.

IRB (Institutional Review Board) Status

The patients' care plan was not impacted by this study. All patient's rural/non-rural data was retrospectively recorded. No identifying patient data was provided by the participating provider locations. Therefore, this study was exempted from IRB review.

Results

Rural/Non-rural data was submitted for analysis from 200 individual pharmacy locations and represents 20.5% of all home infusion provider locations. The home infusion software implementation not being fully deployed for the full calendar year may have resulted in under-reporting in 2016 and 2017 from some providers, therefore, to minimize the risk of incomplete submissions, the data for 2016 and 2017 was removed from the analysis. Data submitted for 2018, 2019, and 2020 was used for the analysis.

For the 3-year period, there were 545,280 unique home infusion patients of which 71,278 were considered rural. Overall, 13.1% of patients served by these home infusion providers lived in rural areas as defined by Centers for Medicare and Medicaid Services (CMS) for the DMEPOS competitive bidding program. As noted in Table 1 and Figure 2, the number and percentage of rural patients served increased slightly over the 3-year analysis period.

FIGURE 2 | Rural and Non-Rural Patients

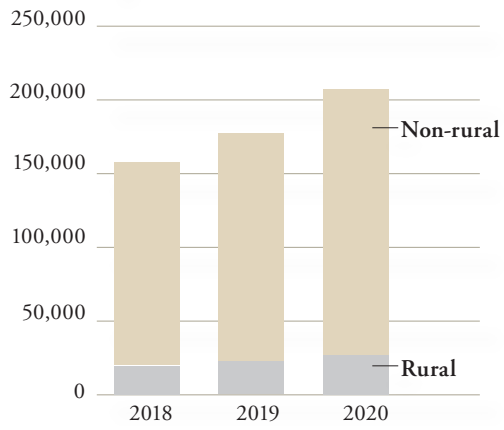


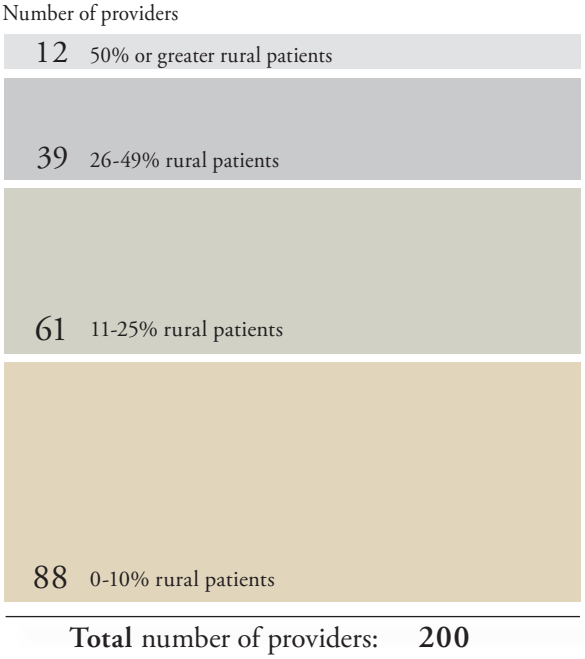
TABLE 1 | Comparison of Rural and Non-Rural Patients by Year

Year	N (sites)	Rural Patients	%	Non-Rural Patients	%	Total
2018	191	20,177	12.8%	137,791	87.2%	157,968
2019	191	23,219	13.0%	155,646	87.0%	178,865
2020	183	27,882	13.4%	180,565	86.6%	208,447
Total		71,278	13.1%	474,002	86.9%	545,280

TABLE 2 | Rural Percent Category

	Frequency	Percent
0-10% Rural Patients	88	44.0
11-25% Rural Patients	61	30.5
26-49% Rural Patients	39	19.5
50% or Greater Rural Patients	12	6.0
Total	200	100

FIGURE 3 | Location Groupings by Overall Percentage of Rural Patients



Further analysis revealed wide variation in the rural populations served by certain home infusion locations. It is surmised that providers with high percentages of rural patients may have been located nearer to the edge of, or outside a metropolitan area. Grouping the locations by their overall percentage of rural patients allows for closer examination of home infusion use in rural areas. Table 2 and Figure 3 illustrate that 25.5% of home infusion locations had rural populations of 26% or more, while 12 locations (6%) had rural populations greater than 50% of all patients served over the 3-year period. When the individual provider location's rural percentage is compared, the median (50th percentile) is 11.60% for 2018-2020. The median was slightly lower than the mean for each study year due to 12 providers who reported no rural patients. The medians for each year were: 2018 = 10.58%, 2019 = 11.80%, and 2020 = 12.26%.

Discussion

This is the first study to quantify the use of home infusion in rural populations. It is known that patients in rural areas experience challenges with health care, including increased travel time for physician visits and chronic disease management. Unquestionably, home infusion alleviates patient travel barriers. The study data shows that most home infusion providers serve patients living in rural areas, and the percentage of rural patients has slightly increased from 2018 to 2020. This study likely under-estimates the utilization of home infusion in rural populations due to the narrow definition of rural that was used to classify patients. Future research is needed to deepen understanding of rural home infusion and describe how rural patients gain entry to home infusion services, the therapies being provided, clinical outcomes, and financial impacts on providers serving rural patient populations.

Limitations

The primary limitation to the generalization of these results is data limited to a single software product for EHR data. Even though various client companies use the software, the study data does not include providers using other software products for electronic medical records. A secondary limitation of the study was not collecting demographic data from the pharmacies, which would allow for visibility of where the pharmacies are geographically, and the service areas covered. Future research should include variables contributing to the percentage of rural patients in the overall census.

Conclusions

The typical home infusion provider census is approximately 13.1% rural and 86.9% non-rural. There is broad variation among providers. Home infusion use in rural areas is well-established. It may offer advanced, infusion-based treatments that are more accessible to patients with limited health care options due to lack of proximity to urban centers.

Disclosures

WellSky is a member of the National Home Infusion Association Future of Infusion Advisory Council. This work for this study was independently funded by WellSky and NHIA.

Commentary: When reviewing a manuscript submitted by one of Infusion Journal's editors or staff, the author/editor is deliberately excluded from all aspects of the review process. The Editor-in-Chief or alternate editor is responsible for handling the peer review process independently of the author/editor. The author/editor is not aware of the choice of peer reviewers, and the author/editor is not present when discussing the manuscript at editorial meetings.

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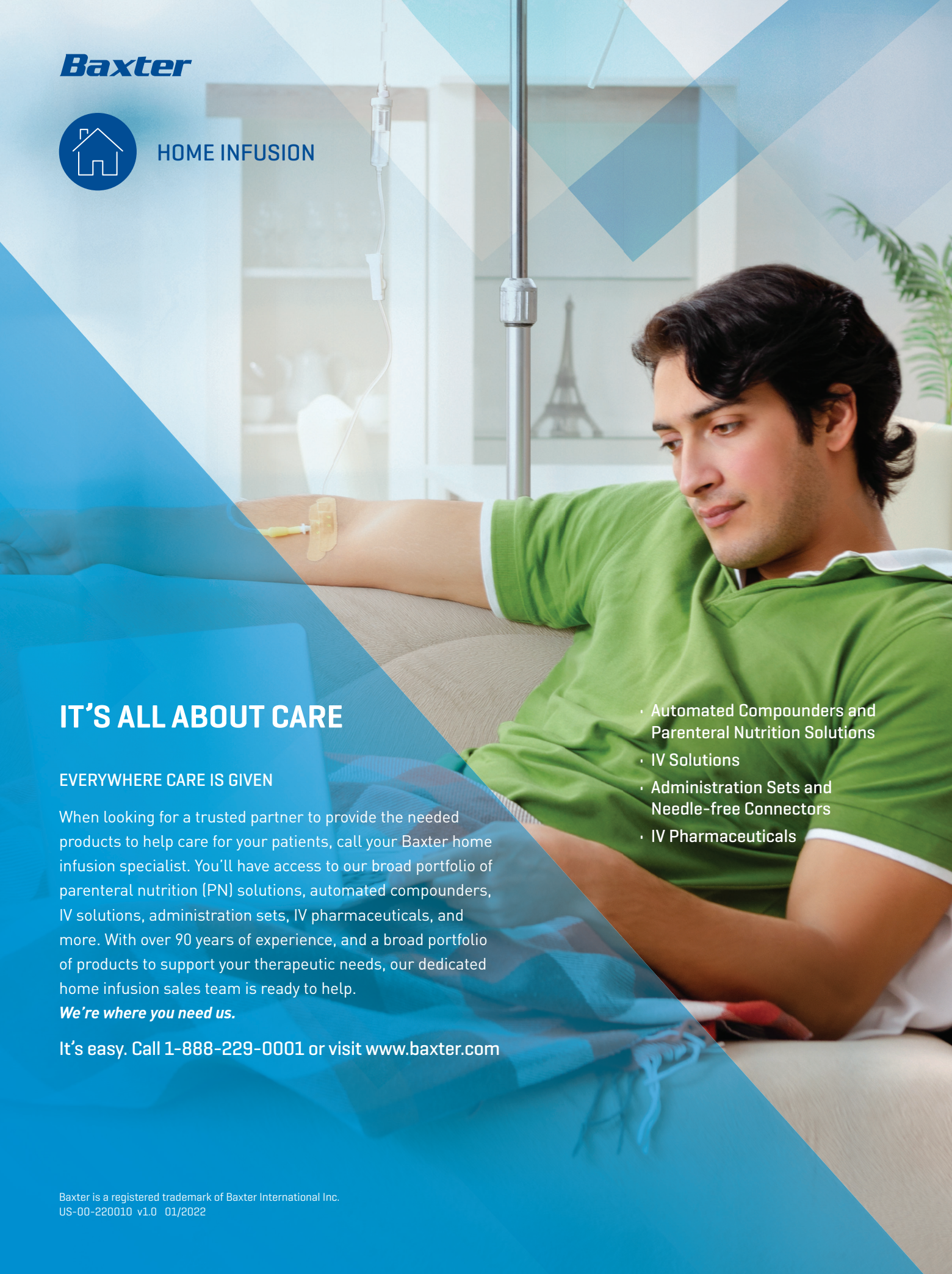

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