Review Article

Parenteral Therapy in Domiciliary and Outpatient Setting: A Critical Review of the Literature

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Abstract

The clinical homecare sector is often associated with high-cost drug parenteral (injectable) therapy treatments and has been rapidly growing in the United Kingdom (UK) at a 20% annual rate. It was estimated that this could further rise to 60% if extended to all medicines that are considered to be suitable for care at home. The latest data shows that the homecare medicines services sector continues to grow in number and complexity, with over 500,000 patients and a spend of UK£3.2 billion in 2021. Given the extent of the National Health Service (NHS) expenditure and the number of patients involved, it is essential to understand and explore the patients' and HCPs' experiences, views, and perceptions of this therapy. As identified during this literature review, homecare provides opportunities for improved cost savings and improved patient experience, but several issues have already been reported worldwide. Patient education, training, support, and regular supervision, as well as the competency of HCPs to manage these patients, have all been identified as factors that contribute to the success or failure of self-administration of parenteral therapy at home, which might impact treatment outcomes and adherence. This is an area that needs urgent research.

Keywords: Home parenteral therapy, Healthcare at home, Homecare, Self-administration, Self-injection, Patient experience

Introduction

Over recent decades, the delivery of healthcare has increasingly moved from the hospital to a community setting. This has been driven by; technological improvements, changes in medical and wider healthcare culture, patient preferences, and efforts to lower the cost of care [1]. Gradually, patients are discharged from the hospital with parenteral (injectable) therapy to continue at home for a specified period, or life-long [2]. Patients with chronic diseases may receive the greatest benefits from home treatments [3]. The complexity of therapies delivered in a homecare setting ranges from subcutaneous (SC) injections to home parenteral nutrition (HPN). Such complex therapies require an aseptic technique, care of the central venous catheter (CVC), and the use of infusion control devices. Treatment in the home is considered convenient, comfortable, and flexible leading to greater independence compared to inpatient hospital treatment [4]. Home therapy can reduce unplanned hospital readmissions. Hospitalization may be hazardous for some patients (e.g., immunocompromised, children, and the elderly) because of the risk of acquiring hospital infections with multi-resistant organisms [5].

The clinical homecare sector is often associated with high-cost medications and has been growing in the UK, by over 20% annually. It was estimated that this could rise to 60% if extended to all medicines considered suitable for care at home [6]. In 2011 there were up to 200,000 people in England receiving homecare medicines services, costing around UK£1 billion expenditure annually [7]. In 2019, clinical homecare accounted for up to 25% of the secondary care medicines budget and 355,000 patients were receiving clinical and medication homecare services, accounting for UK£2.1 billion or 30% of the National Health Service (NHS) secondary care medicines budget [6]. The homecare medicines services sector continues to grow in number and complexity, with >500,000 patients costing UK £3.2 billion in 2021 [8]. However, Potera found that 84% of domiciliary patients used their autoinjectors incorrectly. More than half of those who made errors missed three or more steps during the administration process [9]. Additionally, applying the "forgetting curve theory" would suggest that recall and retention of information worsen progressively without

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practice and repetition. This could mean around half of the information given to patients during training for self-injecting may be forgotten within one hour, 80% in two days, and 90% within a week [10].

Materials and Methods

Aim

This review aimed to investigate HPT using qualitative methodology to gain an in-depth understanding and to further develop the work already done using quantitative methods. This could help improve how services are delivered in this specialist area and how service commissioners will measure the quality of service in the future.

Search Methods

Articles on HPT were searched using the PubMed/MEDLINE database with combinations of these:
home injectable therapy, injections, parenteral therapy, patient experience, biologic therapy, homecare, patient training, self-administration, self-injection, autoinjector.

Home Parenteral Nutrition (HPN) and Intravenous Fluid Therapy

Parenteral nutrition (PN) is an extremely complex intravenous (IV) admixture containing all the required nutrients mixed in the same plastic bag container [11]. Long-term PN is indicated for *"prolonged gastrointestinal tract failure that prevents the absorption of adequate nutrients to sustain life"* [12]. PN is used when oral feeding or enteral nutrition is not possible, or insufficient nutrition is absorbed. Chronic IF (CIF) can result from surgical resection of intestinal fistulae, obstructions and occlusions, dysmotility, intestinal obstruction/occlusion, or extensive disease of the small bowel mucosa. These can originate from either non-malignant or malignant diseases [13, 14]. For stable patients with chronic or irreversible intestinal failure, HPN is the primary and life-saving therapy that can be safely administered in the home environment, for months, years, or lifelong [12, 14].

HPN, in most cases, is supported by relatives and/or community-based professionals providing nutrition support outside the hospital. The rigorous and demanding HPN care regimen places significant demands on patients and carers. The regimen is challenging, and patients and their families often experience fatigue, low mood, sleep disturbances, social isolation, and inactivity. They may worry about potential life-threatening infections and side effects, or the cost of therapy. Patients on HPN and their carers must manage infusion procedures using a strict aseptic technique and must also use an electronic infusion-control device. HPN has a demanding schedule as the PN usually requires a daily 12-hour infusion, infused during the night-time which results in frequent awakenings from pump noises, alarms, and nocturia. The detrimental effects of insomnia on family and social life were found to reduce their quality of life (QoL) [15, 16].

An accidental miss-programming of an HPN infusion pump by the carers, resulted in a rapid infusion of a pediatric IV lipid emulsion and fat overload syndrome, in a 2-year-old girl on HPN [17]. Venous catheter-related infections are a common, serious complication of HPN [18]. Dealing with the central venous line is demanding for patients and carers, and some feel dependent and worry about becoming a burden [15]. HPN is an invasive therapy where patients might have other major physical (e.g., high output fistula) or psychological problems such as anxiety and fear of serious complications including severe infections, thrombosis, and hepatic failure [19].

Baxter [18] reported impact on QoL is associated with the number of HPN infusion days per week and their need for "HPN-free days" and health professionals require tools to address medical and psychosocial issues [20], an area that has not yet been explored in-depth in the UK.

Immunoglobulin Replacement Therapy (IRT)

Immunoglobulin (Ig) replacement therapy is administered in patients with immunologic deficiency syndromes like primary and secondary immunodeficiency disease (PID and SID). PIDs represent a heterogeneous group of >200 congenital rare disorders characterized by reduced or absent function in single or multiple components of the immune system leading to increased susceptibility to recurrent infections, particularly bacterial respiratory tract infections. The most common PID is common variable immunodeficiency (CVID), a primary deficiency characterized by low levels of IgG, IgA, and/or IgM, with a failure to produce specific antibodies. SIDs may also be caused by viral or bacterial infections, malnutrition, or immunosuppressive medications [21].

IRT aims to raise the IgG levels in serum to normal concentrations, increase immune protection, reduce infections, improve QoL, and slowly reduce or arrest the progression of associated organ damage [22]. They can be administered either IV (IVIg) or SC (SCIg), and both can be performed in the home setting, although SCIg is more common in home care and IVIg is more common in hospitals [4, 22, 23]. SCIg is administered in smaller weekly doses, which results in lower peak and higher IgG trough levels compared to the higher doses of IVIg infusions with longer intervals between [21]. Home-based SCIg showed lower cost and greater efficiency compared to hospital-based IVIg for PID, providing better health outcomes [24].

Risso [3] showed patients and carers reported benefits of home treatment compared to hospital treatment with IVIg or SCIg therapy, such as reduced hospitalization and a greater sense of control. The advantages reported were, receiving treatment at home, no time or cost requirement in travel or hospital stay, reduced risk of hospital-acquired infections, freedom to determine administration times, and self-adjustment of the infusion rate according to personal preferences and at a comfortable room temperature. Home

patients reported greater autonomy in their daily life improving their overall well-being. However, patients and carers reported fewer positive experiences at the commencement of the home-based service, practice sessions, and the administration of parenteral Ig therapies, compared to HCPs and concluded that this was likely to be due to a lack of familiarity with the procedures [4].

Conversely, in a study of children aged 1-5 years hospital IVIg therapy was preferred by parents over SCIg at home because of once-monthly treatment, fear of giving injections to children, and perceived better control of the disease when visiting the hospital regularly [23]. Families receiving IVIg reported greater satisfaction and less anxiety, even though IVIg therapy was associated with some disadvantages for them (e.g., increased absence from school or work). Those who preferred the SCIg therapy reported fewer side effects using this route [23], while it is considered more effective and safer than IVIg for children with PID [25]. Another study, in parents and older children (5-15 years of age), showed that parents were more satisfied with home-based SCIg compared to hospital-based IVIg [26].

Outpatient Parenteral Antimicrobial (Antibiotic) Therapy (OPAT)

OPAT is an option for patients to receive parenteral antibiotics but is clinically well enough not to be in the hospital. It has become an option for the management of a range of infections and patients and involves the administration of IV antibiotics through venous catheters at home, by a trained patient, carer, or health professional [27, 28].

Keller *et al.* [28] studied the performance of OPAT-related medical tasks at home by patients and by caregivers. They showed that the required tasks are complex and potentially hazardous and that instructions given to patients and caregivers sometimes contained errors. Patients reported struggling to understand instructions provided in the patient instruction manuals, which they found difficult to use, and that different nurses gave inconsistent instructions. Patients did not understand how strictly they needed to follow medication administration schedules, how to perform handwashing, when to wear gloves, at what temperature to administer medication, and how to ensure the infusion was completed [28]. Moreover, they frequently forgot to flush all lumens of multiple lumen venous catheters, swab skin with alcohol, remove air, and clamp and/or unclamp their venous catheters. The authors concluded that patients and carers are required to master a range of tasks to achieve six overarching goals: *"learning about OPAT, receiving supplies and medications in a timely manner, administering the medication and maintaining the venous catheter, performing activities of daily living, troubleshooting, on-therapy monitoring"*. They concluded that HCPs caring for OPAT patients could better support patients and carers [28].

A small qualitative UK study [29] of parents' experiences of pediatric OPAT showed, despite periods of anxiety, parents, and children reported that home-based treatment provided a sense of comfort, security, and normality. This also helped the parents to recover from the stress of their child's illness even though this normality had been affected by the inconvenience of administering daily antimicrobial therapy. The parents did not feel pressured to accept OPAT. The knowledge that support from the hospital was available when required enhanced parents' satisfaction. However, the study found that most parents could not remember receiving information about possible adverse events (AEs). Some parents said that they were *"so focused on caring"* or *"too tired"* to concentrate that they did not look at the instruction manuals until the OPAT therapy was complete. They perceived most concerns about OPAT were "*minor and manageable*." However, one anxious parent perceived OPAT to be *"a scary experience"* while another parent said, *"it was like you're home now, you deal with it"* [29]. Glick reported that parents made errors and struggled with the management of complex discharge instructions [30].

Palliative Home Care Therapy

Management of complex symptoms in palliative care commonly depends on a range of SC-administered medications. Patients at the end of life are often unable to take medications orally due to the underlying disease, and symptoms such as nausea, vomiting, delirium, agitation, or dysphagia (difficulty swallowing) [31]. The condition of these patients can change rapidly, often outside normal working hours, when there is limited access to support [32]. In addition, community palliative care providers struggle with the demand increasing pressure on hospitals [33].

Studies have demonstrated that supporting carers with tailored education, can ensure confidence to safely and competently prepare and administer SC medications to relieve symptoms in their terminally ill family members at home [33]. The major issue surrounding this practice was a perception that it might generate additional and unnecessary stress and anxiety affecting bereavement, as well as legal issues for HCPs and carers [33, 34].

A recent systematic literature review [35] found that HCPs believed that anticipatory prescribing could deliver reassurance, and symptom control, and prevent hospital admissions. However, there was insufficient published evidence about patients' views, experiences, and attitudes towards such therapy, or its impact on symptom control, patient comfort, safety, and reduced hospital admissions.

Home Chemotherapy

Most chemotherapy is still administered in the hospital or a specialist oncology day treatment/outpatient setting. However, patient satisfaction was higher with home chemotherapy, when a trained nurse delivered the chemotherapy [36]. Patients reported advantages of home-based chemotherapy: better communication, availability, and personalized care and treatment, increased feelings of

independence and control, fewer problems and expenses related to travel, better involvement of family members, reduced disruption to home life, reduced anxiety, reduced waiting time, familiar environment, and privacy, and reduced financial worries. However, they also expressed concerns: fear of the infusion control device malfunctioning or extravasation, lack of supervision by professionals, the commitment of (unpaid) time of carers, wearing a portable infusion device that restricted daily activities, sports, and hobbies, and reduced networking and sharing experiences with other cancer patients, with no *"escape"* from the illness and/or treatment [37]. A UK study evaluated home chemotherapy experiences from highly trained nurses [38]. The study concluded that patients would need to agree to self-administration of cytotoxic therapy in their home and must be thoroughly trained by a competent chemotherapy-trained HCP. Patients need written and verbal information about the drug, storage, administration process, personal protective equipment, waste disposal (including laundry management of bed linen and clothing 72 hours after the therapy cycle), and cytotoxic spill management [39].

Allergen-Specific Immunotherapy (IT)

Allergen-specific IT is a disease-modifying treatment for allergic rhinitis which administers repetitive exposure to allergenic proteins into immunologically active tissues under the skin or oral mucosa (e.g. grass pollen immunotherapy in selected patients with immunoglobulin E (IgE)-mediated seasonal allergic rhinitis) [40]. Even though SC IT (SCIT) is the predominant form of IT, it is the least preferred IT delivery method reported by patients. However, patients who preferred SCIT liked that it does not require daily administration, does not have a bad taste, or causes mouth itching compared to oral IT. Common barriers to adherence identified include inconvenience and negative feelings about injections, concerns about efficacy, and treatment cost [41].

Heart Failure Home Inotropic Infusion Therapy

Heart failure (HF) or congestive heart failure (CHF) is a spectrum of cardiac conditions associated with hypertension and/or acute myocardial infarction. Additional factors, like coronary artery disease, ventricular hypertrophy, and cardiomyopathies, affect cardiac output, circulating fluid volume, respiration, peripheral resistance, and blood viscosity, resulting in insufficient blood flow and tissue perfusion. Over time this leads to decreased myocardial function [42]. Patients with advanced HF have treatment options limited by disease severity and comorbidities. For some patients, surgical interventions like cardiac transplantation or mechanical circulatory support (e.g., left ventricular assist device implantation, etc.) may prolong life and improve QoL or reduce symptom burden. Inotropes can be used in HF patients awaiting cardiac transplantation to maintain hemodynamic stability, until a donor's heart becomes available, or as a bridge to a decision of palliative care. After the patients are stabilized on inotropes in the hospital, they may be discharged to continue therapy at home which will be ceased when definitive surgery is performed. Inotropes commonly used are digoxin, dopamine, dobutamine, norepinephrine, milrinone, levosimendan, and omecamtiv mecarbil [43]. However, a proportion of patients with HF will ultimately progress to end-stage HF and will receive inotropes for palliation. Patients with HF favor quality over quantity of life and need to be well informed about the benefits and harm of inotropic agents so they can make informed decisions. The implementation of such therapy requires the infusion of inotropic agents through a long-term central venous catheter, continuously or intermittently, adequate patient and carer education, and organization of home-based care [42].

Hereditary Angioedema (HAE) Home Infusion Therapy

HAE is a rare autosomal dominant genetic disease affecting approximately 1 in 50,000 people. It is characterized by recurrent and unpredictable non-itchy swelling attacks affecting parts of the body, like subcutaneous and submucosal tissues of the extremities, urogenital region, abdomen, upper respiratory tract, oropharynx, face, and gastrointestinal tract [44-46].

The attacks can be painful (e.g., abdominal attacks), disruptive, disfiguring, and potentially life-threatening, especially if they involve the larynx. They impair daily function and affect QoL [46]. The incidence of swelling varies from >1 per week to <1 per year. The symptoms occur without urticaria/wheels and fail to respond to antihistamines, glucocorticoids, and adrenaline (epinephrine). Abdominal swellings can peak for 24 hours before spontaneously resolving within 2-4 days, whilst intraoral swellings start slowly but then progress over several hours and need emergency treatment. Triggering factors are mechanical trauma, medical, dental, and surgical procedures, estrogen-containing contraceptives, angiotensin-converting enzyme (ACE) inhibitors, psychological stress, fatigue, and strenuous physical activity [44].

The most common form of HAE (C1-INH-HAE) is caused by C1 esterase inhibitor (C1-INH) deficiency due to mutations in the SERPING1 gene, leading to inappropriate kallikrein-kinin system activation and bradykinin release, resulting in excess production of bradykinin, bradykinin B2 receptor activation, increasing vascular permeability and edema/angioedema [44, 46, 47]. The majority of patients can be categorized into two conditions; Type I (HAE-1) accounts for 80-85% of cases and is characterized by low production of functionally active C1-INH protein whilst Type II (HAE-2) affects 15-20% of cases, with normal or elevated levels of non-functional C1-INH protein [44, 45].

Treatment consists either of on-demand treatment to manage HAE attacks or short- or long-term prophylaxis to reduce the frequency and severity of attacks but cannot eliminate acute attacks. Plasma-derived C1-INH (pdC1-INH), recombinant human C1-INH (rhC1-INH), icatibant, and ecallantide are all

effective for the acute treatment of HAE-1 and HAE-2. IV pdC1-INH is indicated for short-term prophylaxis (pre-procedural), whereas for long-term prophylaxis SC C1-INH or lanadelumab should be used as first-line therapy [48].

Current guidelines recommend home therapy in HAE management where feasible, which results in significantly reduced HAE-related number and duration of hospitalizations, reduced androgen-derivative usage, reduced frequency of attacks, and the number of days missed from school or work, resulting in greater patient satisfaction and improved QoL [48, 49]. Patient selection for domiciliary HAE treatment depends on the nature of HAE, severity, and frequency of attacks, the efficacy or tolerability of prophylactic therapies, and the current effect of HAE on QoL. Also, the patient's expectations, mental or physical capacity, patient compliance or reliability, the ability to maintain infusion skill set, patient consent, awareness of risk, partner or carer availability, local primary care support, communication access, venous access quality and availability, plan of action if the administration is difficult and physician's risk-benefit judgment [49]. For the on-demand therapy of acute attacks, besides IV plasma-derived C1-INH concentrates, two SC products can be used, icatibant and ecallantide. Ecallantide is not suitable for self/home administration due to the risk of an anaphylactic reaction [50].

Rheumatoid Arthritis (RA) Therapy

RA is a common chronic systemic autoimmune disease. It has an unclear etiology, is more frequent in females, and is predominantly found in elderly patients. It is characterized by the infiltration of inflammatory cells such as T-cells, B-cells, macrophages, and plasma cells, into joints. These release cytokines that cause the synovium to release proteolytic enzymes, destroying bone and cartilage. Key cytokines involved in RA are tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), interleukin-6 (IL-6), and granulocyte-macrophage colony-stimulating factor (GM-CSF), which all play a role in the pro-inflammatory reaction [51].

RA affects synovial joint linings causing progressive disability, socioeconomic burden, and ultimately, premature death. It has symmetrical joint involvement which includes clinical symptoms like arthralgia, swelling, redness, and limited range of motion. Early diagnosis is essential to reduce joint destruction and functional disability. The optimal time to start treatment is within the first 12 weeks after symptoms occur [51, 52].

All but one of the 'biologic' medications used for the treatment of RA are administered parenterally. Self-injection devices have been developed to reduce the impact of parenteral self-administration on patients' lives, however, several issues have been identified; needle phobia, anxiety, injection site reactions including pain and stinging, lack of confidence, incorrect administration, non-adherence to treatment and problems with using the self-injecting devices due to arthritic deformity of the hands [53, 54].

A study, found that patients were not feeling empowered (perceived lack of personal input, information, and decision about the treatment options), and HCPs were focused on disease treatment, not patients' experience [54]. Patients received minimal and varied one-to-one training on self-injection resulting in anxiety, mistakes, fear of injecting, lack of confidence, and negative social stigma about injections. Also, HCPs often failed to explain the management of fear and anxiety, and patients felt not confident, which also influenced patient expectations and their perception of treatment outcomes. HCPs blamed their workload for suboptimal communication. The study highlighted the patients' desire to be informed and play an active role in the decisions and treatment plans about their disease [54]. Another study found that therapy with more user-friendly devices, with fewer injection-site reactions, improves patients' overall treatment experience [55]. One UK-based study reported that younger patients (<61 years) were more confident about self-injecting their therapy, preferring SC over IV administration. On the other hand, older patients demonstrated a preference for IV infliximab administered by HCPs. They also wanted more *"contact with other patients/meeting others"* and *"staff availability if problems arise"* [56].

Multiple Sclerosis (MS) Therapies

MS is the most common chronic inflammatory autoimmune disabling disease affecting young adults, where activated lymphocytes and other inflammatory immune cells progressively infiltrate the central nervous system (CNS) causing inflammation, demyelination, neurodegeneration, and axonal damage [57, 58]. The pathological hallmark of MS is the presence of multiple focal areas of myelin loss within the CNS called demyelinated plaques or lesions, characterized by loss of motor and sensory function [59].

The underlying cause of MS is still uncertain, but the evidence implicates the involvement of genetic, infectious (Epstein–Barr virus infection), and environmental factors (vitamin D deficiency), smoking and obesity. The inflammatory infiltrates contain predominantly T-lymphocytes, while B-cells and plasma cells are also present but in much lower numbers [57, 60, 61].

Around 90% of MS patients show a relapsing-remitting disease pattern initially, which is characterized by regular clinical attacks. However, with time, attacks become less frequent with incomplete recovery, and most gradually develop increasing disability with progressive axonal loss and secondary progression of the disease. Most relapses leave residual deficits which accumulate leading to sustained disability. Secondary progressive MS generally appears 10-15 years after relapsing-remitting illness has begun. Half of MS patients are unable to work 10 years after illness onset, and 30% are wheelchair-bound. Life expectancy is reduced by 5-10 years on average. Approximately 10% of individuals

experience progressive disease development from the outset, with no relapses 9primary progressive MS), and there is currently no disease-modifying medication available. MS patients may have a variety of symptoms depending to the anatomical location of localized inflammation within the Brain. MS treatment comprises of MS-specific disease-modifying medicines as well as therapy to alleviate symptoms caused by neurological dysfunction (i.e. fatigue, depression, neuropathic pain, spasticity, bladder disturbance, erectile dysfunction, tremor, walking) [57, 62]. Interferons are natural regulatory cytokines that bind to specific interferon-alpha/beta receptors on the surface of immune cells and inhibit inflammatory cytokine synthesis while increasing the production of anti-inflammatory cytokines. In addition, interferon reduces T-cell activation and lymphocyte migration across the blood-brain barrier. Glatiramer acetate is a heterogeneous mixture of synthetic polymers of random sequences of four amino acids, has a complex and yet not fully understood mechanism of action, presumed to involve modulation of immune processes. It acts on innate monocytes, dendritic cells, and B cells, modulating the adaptive functions of B and T cells and inducing anti-inflammatory and regulatory cytokine secretion. It participates in the generation of glatiramer acetate-specific T-cells changing their function from pro-inflammatory to anti-inflammatory. In addition, glatiramer acetate-specific T-cells migrate through the blood-brain barrier inducing local secretion of anti-inflammatory cytokines at the site of the lesions [58].

Observed adherence rates were as low as 30-40% two years after starting treatment. The frequency of administration of a specific DMD (once a week, three times a week, daily) and a patient's perceived lack of immediate treatment benefit compared to the side-effect profile, are assumed to play a role in poor adherence [63]. In addition, cognitive impairment may cause forgetfulness and reduced fine motor skills due to MS progression may complicate self-injections and promote non-adherence. Other factors that influence adherence are injection anxiety, becoming tired of self-injecting, low efficacy, and depression [64]. Various autoinjectors have been developed to improve convenience, reduce discomfort, provide reminders, and improve adherence [65, 66].

Inflammatory Bowel Disease (IBD) Therapy

IBD describes two distinct chronic relapsing and remitting disorders that cause inflammation of the mucosa in the gastrointestinal tract. Crohn's disease (CD) can affect the whole gastrointestinal tract whilst ulcerative colitis (UC) involves the colon only. There are no curative medicinal therapies for CD or UC, and the treatment is intended to reduce inflammation, promote healing of the mucosa, prevent the development of colorectal cancer, and induce and maintain remission [67]. The use of monoclonal antibody (mAb) biological therapy has revolutionized management.

There are multiple biologic agents, from different classes, available to treat moderate to severe CD or UC [68]. For CD they include infliximab, adalimumab, vedolizumab, and ustekinumab, whilst infliximab, adalimumab, golimumab, vedolizumab, and ustekinumab are used in the treatment of UC [68]. Infliximab and adalimumab are used to treat severe active CD in patients whose disease has not responded to conventional therapies such as immunosuppressants and/or corticosteroids [69]. Vedolizumab is used as second-line therapy when the anti-TNF drugs infliximab or adalimumab did not control the symptoms. Ustekinumab may be used where immunosuppressants or steroids did not control the symptoms, or when an anti-TNF drug has not been effective or started to fail to control the symptoms. In UC, vedolizumab can be used if other treatments did not improve the condition, or if anti-TNF drugs do not control the symptoms [70]. Vedolizumab has shown gut selectivity as it selectively prevents the infiltration of leukocytes into the gastrointestinal submucosa which is contributing to its favorable benefit-risk profile, although some skin-related side effects (e.g. psoriasis, acne) have been reported [71, 72]. Evidence suggests little difference in efficacy between infliximab and adalimumab in the treatment of CD [73]. Infliximab can be administered every 4-8 weeks by IV infusion, mainly in the hospital setting. Adalimumab, and recently also infliximab, can be given by an SC self-injection, fortnightly, at home. The decision mainly depends on the patient's preference [68, 74].

Allen [75] reported a patient preference for hospital infliximab IV treatment over SC self-injecting of adalimumab at home, which the authors attributed to the frequency of administration and mode of administration. Patients did not like the idea of self-injecting, even though they liked the idea of the convenience of injecting at home.

Low-Molecular-Weight Heparin (LMWH) Therapy

Venous thromboembolism (VTE) includes deep venous thrombosis (DVT) and pulmonary embolism (PE). They are common preventable causes of morbidity and mortality in hospitalized patients. DVT occurs when a blood clot forms in the deep veins and blocks the blood flow. This can happen after surgery, trauma, or when a person has been immobile for a long time. PE is a potentially fatal complication occurring when a clot detaches and travels to the lungs causing a blockage of pulmonary blood flow. Hospital-associated thrombosis (HAT) can occur up to 90 days after surgery and discharge from the hospital and patients are at high risk of VTE [76]. Studies report up to 42% of medical inpatients have moderate to high risk for developing VTE, while around 10-20% may develop VTE during their hospital stay. Also, VTE contributes to >10% of deaths in medical inpatients [77]. HAT accounts for 50–60% of all VTE occurrences [78]. Clinical trials [79, 80] have shown a DVT risk reduction of 50-65% with the appropriate use of thromboprophylaxis.

The National Institute for Health and Care Excellence (NICE) VTE guideline [78] indicates that SC injection of LMWH is the first-line pharmacological VTE prophylaxis, and recommends extended post-discharge VTE prophylaxis with

LMWH in certain patient groups for ≥35 days.

NICE recommends ensuring that people who are discharged with pharmacological VTE prophylaxis can use it correctly, or have arrangements made for someone to be available to help them [78]. However, studies have confirmed that the existence of guidelines for pharmacological VTE thromboprophylaxis does not ensure outpatient LMWH adherence. Reported non-adherence rates ranged between 13% and 21% and non-adherent patients missed between 38% and 53% of their outpatient LMWH injections after hip and knee arthroplasties. Almost 13% of patients reported that they decided not to inject themselves or had forgotten at least one LMWH injection [81]. It was found that patients might refuse injectable VTE prophylaxis because of fear, anxiety, discomfort, inconvenience, a lack of understanding about the risk factors of VTE, and the purpose of pharmacological prophylaxis [82]. A study of patients' perceptions and experiences with VTE prophylaxis found that patients described different levels of guidance provided during training. "*Some received training by a nurse that included a demonstration and observation while others recalled being handed the injection set on discharge and instructed to maintain the course of injections"* [76]. This study also reported patients' lack of knowledge and understanding of VTE symptoms and lack of awareness of potentially fatal PE risks.

Enzyme Replacement Therapy (ERT) in Fabry Disease (FD)

FD is a progressive, X-linked inherited lysosomal storage disorder arising from a deficiency of the lysosomal enzyme alpha-galactosidase A. This results in the progressive accumulation of globotriaosylceramide and related glycosphingolipids within lysosomes in a range of cell types (endothelial, renal, cardiac, and nerve cells). The lysosomal storage and cellular dysfunction in FD, trigger a cascade of events including cellular death, compromised energy metabolism, small vessel injury, oxidative stress, impaired autophagosome maturation, tissue ischemia, and the development of irreversible cardiac and renal tissue fibrosis. The disease starts in infancy, and the damage to organ systems develops with age leading to organ failure and reduced life expectancy [83]. The recombinant human alpha-galactosidase-A enzyme replacement therapy became available in 2002.

ERT for Fabry disease requires life-long therapy with IV infusions every 2 weeks, which can represent a considerable burden for patients, interfering with daily life activities and reducing QoL [84]. Home infusions of ERT may increase patient satisfaction, reduce costs and improve QoL, although it is not suitable for all patients [85]. Usually, the treatment is initiated in the hospital and then moved to the home setting, performed by specially trained nurses. The patients must be clinically stable, tolerate the infusions, have no evidence of adverse reaction to ERT, and have a suitable home environment [83, 84].

Injectable Therapy for Hypercholesterolemia

Therapy to reduce low-density lipoprotein cholesterol (LDL-C) reduces cardiovascular risk in both primary and secondary prevention, and oral statin therapy is the standard of care. However, some patients experience unacceptable side effects (e.g., myalgia and muscle weakness) or do not achieve the desired LDL-C-lowering effect, even with high-intensity statin therapy (e.g., familial dyslipidemia), remaining at high risk of atherosclerosis and cardiovascular events [86].

Around half of the cholesterol in the human body is biosynthesized *de novo* in the liver and intestines by the 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) enzyme. After biosynthesis and absorption, cholesterol is transported in the blood primarily by LDL proteins. LDL-C is then cleared from the circulation by binding to the hepatic transmembrane low-density lipoprotein receptors (LDLRs). LDL-C binds to the LDLR on the liver cell surface forming an LDLR–LDL complex which is then internalized into the hepatocyte, where LDLR can be either enzymatically degraded in the lysosome or recycled to the cell surface. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is an important regulator of circulating LDL-C levels as it inhibits the recycling of the LDLR. PCSK9 bound to LDLR makes it more susceptible to enzymatic degradation, leading to a reduced number of LDLRs on the cell surface. On the other hand, PCSK9-unbounded LDLR is more likely to be recycled to the surface of the cell. Therefore, the inhibition of PCSK9 will increase the number of available LDLRs on the cell surface and increase LDL-C uptake/clearance resulting in lower plasma LDL-C levels [87, 88]. mAbs that inhibit PCSK9 is a relatively new class of cholesterol-lowering medications providing significant reductions in LDL-C.

NICE recommends PCSK9 inhibitors for treating primary hypercholesterolemia or mixed dyslipidemia in patients who have a high risk of cardiovascular diseases (CVD), with LDL-C persistently >4.0 mmol/l, and with elevated CVD risk and LDL-C persistently >3.5 mmol/l. In primary heterozygous-familial hypercholesterolemia without CVD, evolocumab and alirocumab are recommended if LDL-C is persistent >5.0 mmol/l, or in patients with CVD risk where LDL-C is persistent >3.4 mmol/l, despite maximal tolerated lipid-lowering therapy [89, 90]. Patients can safely and effectively administer SC evolocumab at home without HCPs supervision, with the appropriate device training from an HCP [91]. The choice of a monthly or twice-weekly dosing regimen was not associated with any significant differences in adherence, acceptability, or patients' preferences [86].

Psoriasis (Ps) and Psoriatic Arthritis (PsA) Therapies

Ps is a chronic, systemic, genetic, autoimmune, inflammatory skin disease that typically follows a relapsing and remitting course and may be associated with other inflammatory conditions and comorbidities such as psoriatic arthritis, inflammatory bowel disease, and coronary artery disease [92-

94].

Ps have substantial negative physical, emotional, and psychosocial implications [94] and are associated with a decrease in QoL, lost productivity, and absence from work [95]. The most common form of Ps, affecting about 90% of patients with Ps, and characterized by sharply demarcated red, erythematous, pruritic scaly silvery plaques that can be localized in a few patches to generalized merged plaques covering large areas of the skin. The epidermis is thickened (acanthosis) with a thickened upper layer (hyperkeratosis) resulting in thick, scaly skin [51]. Other types of Ps include inverse Ps, guttate Ps, and pustular Ps (i.e. localized or generalized) [92, 93].

Inflammatory cells are present in all layers of psoriatic skin with inflammatory infiltrates composed of dermal dendritic cells, macrophages, T-cells, and neutrophils. Cytokines such as TNFα and interleukins (IL-12, IL-17, and IL-23) all contribute to the pathogenesis [51, 93]. Approximately 20% of people with Ps may also have PsA which is characterized by stiffness, pain, swelling, and tenderness of the joints and surrounding ligaments and tendons (i.e. dactylitis and enthesitis).

The management of patients who have a combination of severe Ps and PsA can be challenging and require close collaboration between a dermatologist and a rheumatologist. The severity of skin disease and arthritis are not usually correlated [96].

The severity of Ps can be calculated and expressed by the Psoriasis Area Severity Index (PASI) which combines the plaque appearance and severity (i.e. erythema, induration, and scaling) and percentage of the affected area of the skin [96]. The QoL of adult patients with Ps is measured through the Dermatology Life Quality Index (DLQI) which is a validated simple patient questionnaire, used to assess the impact of any type of Ps on physical, psychological, and social well-being [92].

PASI and DLQI are routinely used to measure disease severity and its impact on QoL and to assess the need for systemic therapy and treatment response in patients with Ps. Mild Ps is defined as DLQI ≤5 and would usually be managed in primary care, while severe Ps is defined as PASI ≥10 and DLQI ≥10, for which specialist referral may be needed and systemic or biological therapy may be indicated [92, 96].

Mild to moderate Ps can be treated topically with emollients, corticosteroid creams, vitamin D analogues (e.g., calcipotriol), dithranol, tar preparations, and phototherapy, whilst moderate to severe disease often requires the use of systemic therapy with small-molecule non-biological agents (e.g., methotrexate, ciclosporin, acitretin, fumaric acid esters, apremilast, sulfasalazine) or biologic agents (e.g., etanercept, infliximab, adalimumab, certolizumab, ustekinumab, tildrakizumab, guselkumab, risankizumab, secukinumab, ixekizumab, brodalumab) [93].

Topical therapies are the first-line therapy according to NICE guidelines [92], while phototherapies and systemic non-biological agents are regarded as second-line therapy. Third-line therapy will include biological therapies with biological agents.

In the UK, biological therapy in Ps is indicated "*if the disease is severe (PASI≥10 and DLQI>10), and has not responded to standard systemic therapies (including ciclosporin, methotrexate, and psoralen and long-wave ultraviolet radiation - PUVA), or the person is intolerant of or has a contraindication to, these treatments."* Biologic agents target specific inflammatory pathways and are administered SC or IV on different weekly schedules. These agents target two pathways crucial in the development of the psoriatic plaque: the IL-23/Th17 axis and TNF-α-signalling [93].

A recent study explored patients' perspectives of their Ps, medication, and its management, where patients reported that *"adhering to recommended treatment regimens conflicted with the management of the physical and psychological demands of living with psoriasis"* [97]. Medication use was perceived as a source of emotional distress which resulted in self-reported poor adherence, including both medication overuse and underuse and rejection of prescribed therapy. The study showed that patients' adherence to parenteral biologic therapy can be poor because of treatment concerns (dislike of injections, worry to become dependent on medication), uncertain treatment efficacy (worry about adverse effects, worry about stopping the medication, no perceived benefit short-term). Patients complained about not being able to be prescribed their preferred biologic due to the absence of shared decision-making by HCPs [97]. Biologic agents offer the convenience of less frequent dosing than other topical or systemic medications [98]. A Japanese study, comparing patient and physician preferences to biological therapy for Ps, showed a preference in both groups for injection administration at a clinic by an HCP rather than self-injection at home [95].

Parenteral Therapy at Home (HPT)

The infusion day-center model for administering parenteral therapy has advantages for efficient care delivery, keeping staff and services in one place, and serving several patients simultaneously. When patients are treated at home, significant decisions are delegated to non-medical individuals. New homecare patients frequently find the first few days after discharge overwhelming [99]. Patients experienced changes in social, psychological, and physical functioning negatively impacting their perceived QoL.

Patients' and carers' education is vital to safely providing parenteral therapy at home. HPT training should be formal and comprehensive ensuring patients and carers achieve competence and can manage both routine situations at home. However, the most important is how to deal with the

unexpected and when to seek professional help [100]. Patient education should fully establish independence with care and self-management. This freedom should help them to adhere to their parenteral therapy in a safe manner, giving them more autonomy in their everyday lives at home and enhancing their capacity to manage with the stress and problems that come with this complex therapy. Reducing the stress and uncertainty caused by insufficient planning should help to a reduction in problems and an improvement in QoL [99]. One study [100] found that nurses, who play a central role in facilitating home infusion education, might lack the knowledge and confidence to teach home infusion to patients and their families, especially the novice. In addition, the lack of national guidelines might suggest that not all patients are learning the same information in the same manner.

Conclusion

As identified during the literature review, homecare provides opportunities for improved cost savings and improved patient experience, but several issues have already been reported worldwide. Patient education, training, support, and regular supervision, as well as the competency of HCPs to manage these patients, have all been identified as factors that contribute to the success or failure of self-administration of parenteral therapy at home, which might impact treatment outcomes and adherence.

A limited number of studies explored the patients' experience with HPT in the UK.

Little is still known about patients' experiences and perceptions about their training and education on self-administering HPT in the UK. Training is increasingly being outsourced to clinical homecare providers, and HCPs who initiated patients on long-term self-administration of HPT, might not always be directly involved in patients' training, supervision, or assessment of competence for self-injecting. It is very important to understand how patients are being trained, educated, and supported for this task, what is their experience and perception with received training and support, and to compare this with the views of HCPs who are involved with HPT.

It is clear from the literature reviewed, that while there is considerable literature on the use of injectable medications out of the hospital setting, there are few studies that have investigated the patients' preparation and training for such tasks and its impact on their experience with therapy and their health outcomes.

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