ORIGINAL ARTICLE

Perceptions of injectable therapies with cardiovascular benefit: an ACNAP survey of healthcare professionals to explore facilitators and barriers

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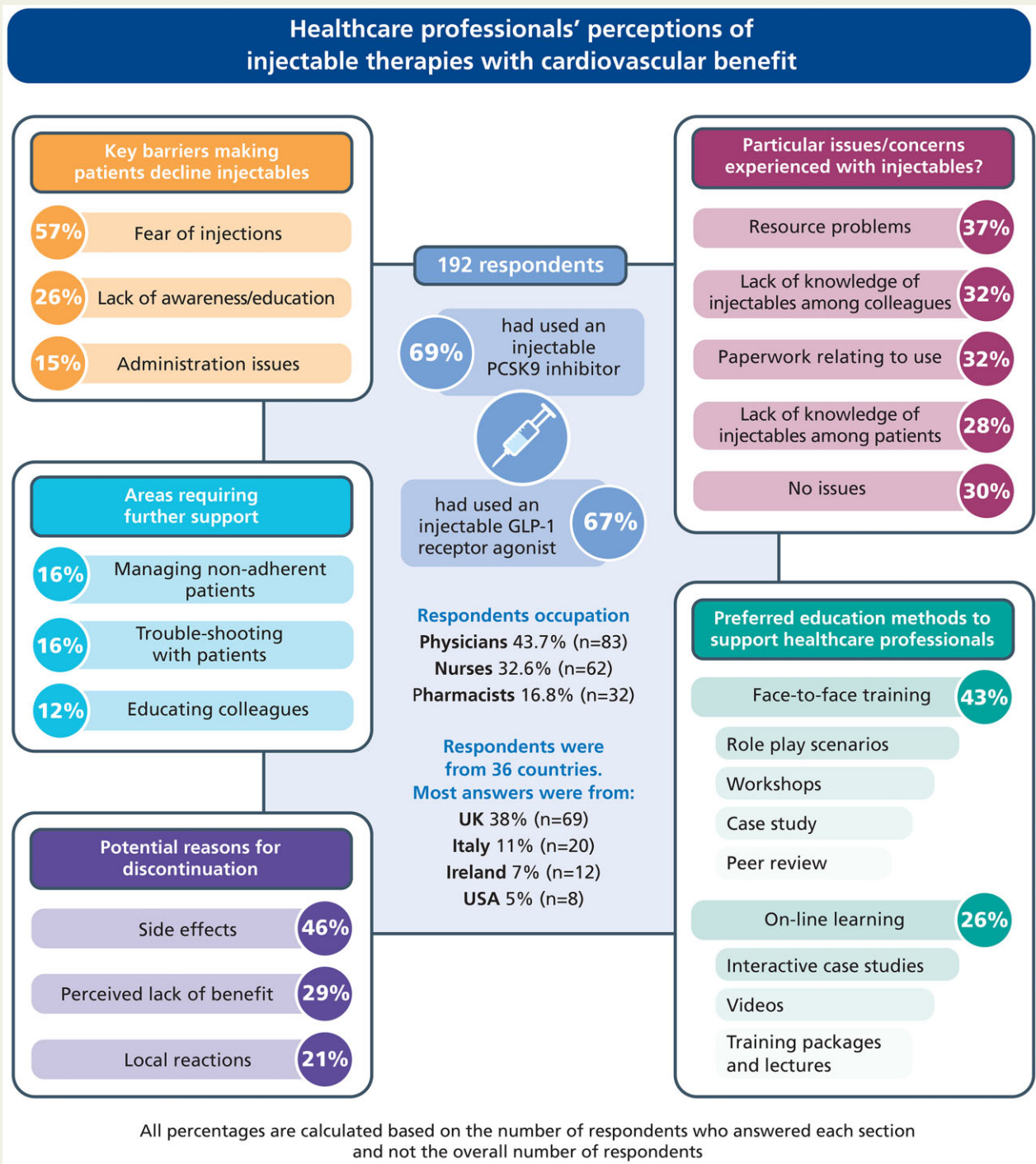|	
Aims	Injectable medicines are increasingly used to manage risk factors for cardiovascular (CV) events, such as dyslipidae-mia and diabetes. These include proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists. Little is known about perceptions of injectable therapies among CV health-care professionals (HCPs). This study explores their views to identify relevant facilitators and barriers to the use of injectables with CV benefit.
Methods and results	A 22-question survey was distributed internationally via online channels. In total, 192 anonymous responses were received (43.7% physicians, 32.6% nurses, 16.8% pharmacists, 6.8% others). Among respondents with experience of these medicines, 69.1% had used an injectable PCSK9 inhibitor and 67.0% had used an injectable GLP-1 receptor agonist. Commonly raised issues were resource problems (36.5%), lack of knowledge among colleagues (32.3%), paperwork (32.3%), and lack of patient knowledge (28.1%). Key barriers respondents felt made patients decline these treatments were fear of injection (56.6%), lack of awareness or education (26.4%), and administration issues (15.1%); potential reasons for discontinuation included side effects (46.4%), perceived lack of benefit (28.6%), and local reactions (21.4%). The main topics around injectables requiring further support included managing non-adherent patients (16.2%), troubleshooting with patients (16.2%), and educating colleagues about injectables (12.2%). Preferred educational methods to support HCPs were face-to-face training (43.5%) and online learning (26.1%); favoured formats were based on role playing and case studies.
Conclusion	Healthcare professionals highlighted various potential barriers to initiation, continuation, and adherence with inject-able therapies in CV medicine. Although some require healthcare system changes, many could be addressed through simple measures based primarily on enhanced training and support for patients and HCPs.

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Graphical Abstract

Healthcare professionals' perceptions of injectable therapies with cardiovascular benefit

Key barriers making patients decline injectables

- 57% Fear of injections
- 26% Lack of awareness/education
- 15% Administration issues

Areas requiring further support

- 16% Managing non-adherent patients
- 16% Trouble-shooting with patients
- 12% Educating colleagues

Potential reasons for discontinuation

- Side effects 46%
- Perceived lack of benefit 29%
- Local reactions 21%

192 respondents

69% had used an injectable PCSK9 inhibitor

67% had used an injectable GLP-1 receptor agonist

Respondents occupation
Physicians 43.7% (n=83)
Nurses 32.6% (n=62)
Pharmacists 16.8% (n=32)

Respondents were from 36 countries. Most answers were from:
UK 38% (n=69)
Italy 11% (n=20)
Ireland 7% (n=12)
USA 5% (n=8)

Particular issues/concerns experienced with injectables?

- Resource problems 37%
- Lack of knowledge of injectables among colleagues 32%
- Paperwork relating to use 32%
- Lack of knowledge of injectables among patients 28%
- No issues 30%

Preferred education methods to support healthcare professionals

- Face-to-face training 43%
- Role play scenarios
- Workshops
- Case study
- Peer review
- On-line learning 26%
- Interactive case studies
- Videos
- Training packages and lectures

All percentages are calculated based on the number of respondents who answered each section and not the overall number of respondents

Introduction

Cardiovascular disease (CVD) remains one of the leading causes of mortality and morbidity worldwide.[1,2] Traditional strategies for managing risk factors are largely based around lifestyle changes and oral medications such as statins and blood pressure-lowering agents. However, where these approaches are ineffective or insufficient, novel strategies using injectable medicines are increasingly being

Implications for practice

- Many barriers to injectable therapy use in cardiovascular medicine could be addressed through enhanced training and support for patients and healthcare professionals (HCPs).
- Practical prescribing guidelines would help HCPs to identify eligible patients.
- Patient and caregiver starter packs may enhance acceptance and adherence with these treatments.

used. Currently, licenced options include proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors and inclisiran for lipid lowering, and glucagon-like peptide-1 (GLP-1) receptor agonists for treating diabetes.

With regard to dyslipidaemia, oral statins remain the mainstay of treatment. However, not all patients achieve their targets,[3] particularly those with comorbidities such as obesity or diabetes.[4] Injectable PCSK9 inhibitors offer an important alternative, and can be used for the primary prevention of cardiovascular (CV) events in patients with familial hypercholesterolaemia, or for secondary prevention in patients with established atherosclerotic CVD who are likely to benefit from further cholesterol lowering while on maximum dose statin/ezetimibe therapy or who are statin intolerant.[3,5] Furthermore, a new injectable therapy for lowering cholesterol, inclisiran, has recently entered a large-scale trial in the UK.[6]

In type 2 diabetes, GLP-1 receptor agonists—most of which are administered by injection—can significantly reduce the risk of major adverse cardiovascular events (MACE) in addition to their glucose-lowering properties.[7] They are now a recommended first- or second-line treatment option in patients with type 2 diabetes and elevated CV risk.[8]

Thus, increasing numbers of CV patients are likely to be prescribed injectable therapies. In most instances, these will be self-administered; in others, a healthcare professional (HCP) may perform the injections. Either way, this will inevitably create new challenges, as demonstrated in other diseases with high use of injectables, such as diabetes.[9–11] Across 20 studies of injectable therapies in chronic conditions, key facilitators of their use included health improvement, prevention of disease complications, patient control of their own disease, medication effectiveness, and convenience in management.[12] Barriers tend to fall into three main areas: patient-related factors (e.g. fear of injection), HCP factors (e.g. lack of knowledge and skills), and system issues (e.g. lack of time).[10,12] However, regular injection for primary prevention is a relative unexplored paradigm in CV medicine.

A 2015 survey on injectable PCSK9 inhibitors found that most physicians and patients were willing to use them but highlighted a need for demonstration and testing.[13] However, the study was narrowly focused on general willingness; there remains a paucity of data on the broader perceptions of CV HCPs around injectable therapies and the barriers and facilitators of optimal use.

In clinical practice, individualized assessment of barriers to injectable medication use may help to facilitate their introduction,[1] and assist patients to adhere to treatment.[14] Various HCPs including nurses and pharmacists have a vital role in informing, educating, and coordinating patient care,[15,16] and hence it is essential that their perspectives are examined.

Using an online survey, the primary objectives of the present study were (i) to determine the views of HCPs involved in initiating injectable therapies and (ii) to identify the facilitators and barriers to providing injectable therapies.

Methods

Survey design and development

This research was undertaken by the European Society of Cardiology (ESC) Association of Cardiovascular Nurses and Allied Professionals (ACNAP). The survey was developed based on a literature review[12] and refined through consensus discussions. It was piloted on five HCPs to identify ambiguities and ensure that there were no issues with its use. The survey included 22 questions: 9 on respondent demographics and professional profile; 4 on usage of injectables with CV benefits; 5 on specific issues with injectables; and 4 questions on current knowledge and training needs. Seventeen questions were multiple choice. However, there were four questions that enabled comments in the free text; responses were analysed thematically based on an inductive approach[17] to provide quantitative as well as qualitative data.

A sub-analysis was also made using responses to the question 'Which injectables are currently in use in your workplace?' This analysis compared responses to other survey questions between those from centres using only PCSK9 inhibitors and those using only GLP-1 receptor agonists.

Only individuals involved in the delivery of services relating to injectables with CV benefit were asked to complete the entire questionnaire; those with no such experience answered questions on their demographics and professional profile but were not eligible to complete the remainder of the survey.

Survey administration and analysis

The survey was distributed as an online tool. Invitations to participate and a relevant weblink were sent to ACNAP members and other HCPs via national societies. The researchers also used their social media platforms and email to distribute the survey. The survey was provided in English via the ESC on 11 November 2019 and was sent to 36 019 recipients; it was therefore a convenience sample.

As injectables are not commonly used in CV practice, the aim was to disseminate the survey as widely as possible, with the expectation that only a small number would have relevant experience.

Data were collected anonymously and within the EU General Data Protection Regulation policy. The present analysis includes all responses submitted between 11 November and 20 December 2019.

Results

A total of 192 responses were received (completion rate: 73%; average time spent: 3 min). Of these, 180 identified the country in which

Table 1 Characteristics of respondents to online survey

Characteristic	Respondents, n (%)
Age (years) (N = 191)	
21–30	15 (7.9)
31–40	60 (31.4)
41–50	49 (25.7)
51–60	55 (28.8)
61–70	12 (6.3)
Gender (N = 192)	
Male	94 (49.0)
Female	98 (51.0)
Profession (N = 190)	
Physician	83 (43.7)
Nurse	62 (32.6)
Pharmacist	32 (16.8)
Other	13 (6.8)
Highest qualification (N = 191)	
Doctorate (PhD or equivalent)	61 (31.9)
Masters (MSc, MPharm)	59 (30.9)
Bachelor's (BSc, MBBS)	22 (11.5)
Certificate/diploma	30 (15.7)
Other	19 (9.9)
Years of qualification (N = 191)	
1–5	26 (13.6)
6–10	30 (15.7)
>10	135 (70.7)

they work; the majority were from the UK (n = 69), Italy (n = 20), Ireland (n = 12), or the USA (n = 8). Ninety-eight were female (51.0%) and most were aged 31–60 years (n = 164; 85.9%) (Table 1). Physicians accounted for the largest number of respondents (n = 83; 43.7%), followed by nurses (n = 62; 32.6%) and pharmacists (n = 32; 16.8%). The majority were qualified to PhD (n = 61; 31.9%) or MSc/MPharm level (n = 59; 30.9%), and most had >10 years of experience since qualification (n = 135; 70.7%).

Usage of injectables

In total, 120 of 190 respondents (63.2%) said that they were involved in the delivery of services for PCSK9 inhibitors, GLP-1 receptor agonists, or other injectables with CV benefit (Table 2). Around two-thirds had used an injectable PCSK9 inhibitor (n = 67/97; 69.1%) or a GLP-1 receptor agonist (n = 65/97; 67.0%). Cardiology was the main specialty of the majority of respondents (n = 63/99; 63.6%), with others working in diabetology (n = 26/99; 26.3%), lipidology (n = 13/99; 13.1%), and endocrinology (n = 7/99; 7.0%). Most worked in a hospital setting (n = 72/98; 73.5%) and were prescribers (physicians and others; n = 82/99; 82.8%). Furthermore, most of those involved with injectables had been for more than 12 months (n = 63/95; 66.3%). Frequently cited roles with injectable therapies among 95 respondents included patient assessment (n = 60; 63.2%), initiation of therapy (n = 58; 61.1%), monitoring (n = 56; 58.9%), educating and counselling patients and carers (n = 53; 55.8%), and making or

receiving referrals to initiate the process (n = 52; 54.7%); less commonly cited roles included educating HCPs (n = 36; 37.9%) and organizing education for all staff (n = 16; 16.8%).

Issues with injectables

Ninety-six participants responded to the question 'Are there are particular issues you experience with injectables?'. Of these, 29 (30.2%) said they had no issues (Table 2). The remainder highlighted various concerns, the most common of which were resource (e.g. lack of specialist human resource, reimbursement issues, access problems; n = 35; 36.5%), lack of knowledge of injectables among colleagues (n = 31; 32.3%), paperwork relating to use (n = 31; 32.3%), and lack of patient knowledge about injectables (n = 27; 28.1%).

When asked to describe (in free text) the main barriers that made patients decline injectable therapies, the primary reason given among 53 respondents was 'fear of injection' (n = 30; 56.6%) (Figure 1). Other common themes were lack of awareness or education (e.g. feeling of failure, poor comprehension of disease; n = 14; 26.4%), administration issues (e.g. poor dexterity, poor eyesight; n = 8; 15.1%), cost (n = 5; 9.4%), side effects (n = 4; 7.5%), and lack of consultation time (n = 3; 5.7%) (Figure 1).

Respondents were also asked to list the main barriers to initiation of injectable therapies. These were then collated into key themes using an inductive approach. Among 50 respondents, the main cited barriers to initiation were fear of injection among patients (n = 18; 36.0%), lack of education on the HCP side (e.g. identifying eligible patients; n = 13; 26.0%), cost (n = 9; 18.0%), and legal constraints (e.g. restrictive local formularies, related paperwork; n = 8; 16.0%).

When asked to describe the main barriers to adherence with injectables among their patients, the most frequently stated themes among 43 respondents were compliance (e.g. patients not remembering to gain repeat prescription or to administer the drug; n = 14; 32.6%), side effects (n = 12; 27.9%), fear of injection (n = 10; 23.3%), and lack of patient education (e.g. poor understanding of why they need the medication; n = 8; 18.6%).

Respondents were then asked to estimate the level of patient adherence to injectable therapies with CV benefits in their experience, using a scale of 0% (no adherence) to 100% (complete adherence). Among 57 responses, the mean adherence estimate was 79.1% at 3–6 months, 74.0% at 6–12 months, and 69.6% beyond 12 months.

When invited to state the main reasons associated with discontinuation of injectables (N = 56), several key themes were identified by qualitative analysis of responses. These included: side effects (n = 26; 46.4%); perceived lack of benefit (e.g. no change in glycated haemoglobin levels, no weight loss) (n = 16; 28.6%); local reactions (n = 12; 21.4%); and fear of injection (n = 7; 12.5%).

Training

Respondents were asked to rate their confidence with various skills and knowledge relating to injectables (N = 74). Most HCPs were 'confident' or 'very confident' in all aspects. However, the parameters on which they were least confident (i.e. for which the most respondents were 'unsure' or 'not confident') were managing patients who are not adherent (n = 12; 16.2% 'unsure' or 'not confident'), troubleshooting with patients on injectables (n = 12; 16.2%), and educating colleagues and staff about injectables (n = 9; 12.2%).

Table 2 Responses to questions on use of injectables

Question	*n* (%)
In your practice, are you involved in the delivery of services for PCSK9 inhibitors, GLP-1 agonists, or other injectables with CV benefit? (*n* = 190)	
Yes	120 (63.2)
No	70 (36.8)
Which injectables are currently in use in your workplace?[a] (*n* = 97)	
PCSK9 inhibitors	67 (69.1)
GLP-1 agonists, e.g. liraglutide and semaglutide	65 (67.0)
Other	7 (7.3)
What is your specialty?[a] (*n* = 99)	
Cardiology	63 (63.6)
Diabetes	26 (26.3)
Lipidology	13 (13.1)
Endocrinology	7 (7.0)
Other	14 (14.1)
What type of setting do you work in? (*n* = 98)	
Cardiology ward setting in hospital	39 (39.8)
Out-patients department in hospital	19 (19.4)
Primary care	16 (16.3)
Clinic setting in hospital	10 (10.2)
General ward in hospital	4 (4.1)
Other	10 (10.2)
Are you a prescriber? (*n* = 99)	
Prescriber (physician)	53 (53.5)
Prescriber (non-physician)	29 (29.3)
Supplementary prescriber	3 (3.0)
Not a prescriber	14 (14.1)
How long have you been involved in the delivery of injectables? (*n* = 95)	
Less than a month	3 (3.2)
1–12 months	29 (30.5)
More than 1 year	63 (66.3)
What is your involvement in injectable therapies?[a] (*n* = 95)	
Assessing patients for potential injectables therapy	60 (63.2)
Initiating injectables therapy	58 (61.1)
Monitoring injectables therapy	56 (58.9)
Educate and counsel patients/carers about injectables	53 (55.8)
Make/receive referrals to initiate the process	52 (54.7)
Educate health professionals about injectables	36 (37.9)
Reviewing and auditing injectables as a therapy	34 (35.8)
Administering injectables therapy	20 (21.1)
Organizing education for all staff on injectable therapies	16 (16.8)
Other	5 (5.3)
Any there are particular issues you experience with injectables?[a] (*n* = 96)	
Resource issues	35 (36.5)
Lack of knowledge from colleagues on injectable therapies	31 (32.3)
Paperwork around injectables (i.e. demonstrating eligibility, getting local approval)	31 (32.3)
Patient lack of knowledge on injectables	27 (28.1)
Lack of clear guidance on which patients who are eligible for injectables	18 (18.8)
Lack of clarity on who should be initiating injectables	15 (15.6)
Lack of policy/guidance in my workplace on injectables	10 (10.4)
Other	5 (5.2)
No issues	29 (30.2)

CV, cardiovascular; GLP-1, glucagon-like peptide-1; PCSK9, proprotein convertase subtilisin/kexin type 9.
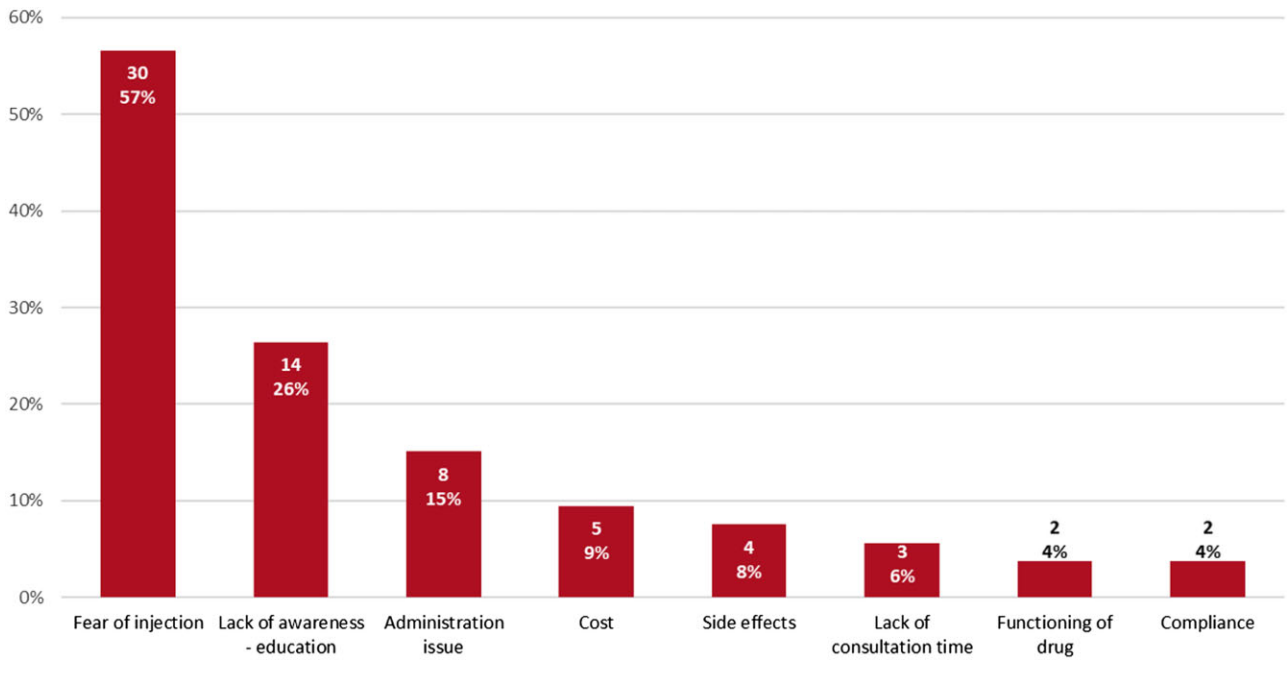[a]Respondents were allowed to select all the options that applied.

Figure 1 Main barriers likely to make patients decline the use of injectable therapies with cardiovascular benefit when indicated (N = 53).

Table 3 Training undertaken to deliver injectable therapies (N = 97)

	Respondents, n (%)
From colleagues in practice	50 (51.5)
Directly from pharmaceutical representative	47 (48.5)
Face-to-face training	31 (32.0)
Online or e-learning	30 (30.9)
Shadowing, observing, mentoring and peer review	30 (30.9)
Workshop	20 (20.6)
Other	10 (10.3)

Respondents were allowed to select all the options that applied.

When asked about the type of training undertaken on injectables, the most common sources were colleagues in practice (n = 50/97; 51.5%) and pharmaceutical representatives (n = 47/97; 48.5%) (Table 3).

With regard to the types of training needed to maintain skills and knowledge in this area (N = 69), the most commonly cited first preference was face-to-face training (n = 30; 43.5%), followed by online learning (n = 18; 26.1%). Respondents were then asked to rate different types of face-to-face training on a scale of 1 (low priority) to 5 (high priority). Among 60 responses, the highest mean priority scores were for: simulation training with actor and role playing with different scenarios (mean score: 3.50); workshop with role play (3.48); and case study and peer review (3.48). Similarly, when asked about preferred formats for online learning (N = 52), the highest mean priority scores were for case study with interactive review (3.87), videos (3.77), and interactive online training packages with lectures (3.60).

Finally, with respect to specific aspects of injectable therapy that respondents wanted to learn more about (N = 63), the majority were focused on increasing their knowledge about injectables, in particular the side effects (n = 41; 65.1%) and access to evidence-based materials demonstrating their benefits (n = 38; 60.3%).

Type of injectable used

A sub-analysis was made based on responses to the question 'Which injectables are currently in use in your workplace?', comparing results between respondents from centres using only PCSK9 inhibitors (n = 41) vs. those using only GLP-1 receptor agonists (n = 39); respondents working in institutions where both are used (n = 26) were excluded.

There were few clear differences between the two groups. However, respondents from institutions using only GLP-1 receptor agonists were somewhat more confident than those using only PCSK9 inhibitors. For example, 78.9% (n = 15/19) vs. 61.1% (n = 11/18), respectively, were 'confident' or 'very confident' in managing challenges at assessment. Glucagon-like peptide-1 receptor agonist users were also more confident than PCSK9 inhibitor users in understanding screening for eligibility for injectables, assessing adherence, and supporting adherence.

With regard to specific aspects of injectable therapy that respondents wanted to learn more about, those from centres using only PCSK9 inhibitors were most likely to want to know about side effects (64.7%; n = 11/17) whereas GLP-1 receptor agonist users were more likely to want to hear about the underlying evidence base (66.7%; n = 10/15).

Discussion

This survey-based study assessed the views of HCPs involved in providing injectable therapies with CV benefit and identified barriers and

facilitators of use. Although 63.2% of respondents had used these treatments, it is likely that the majority of non-responders had no such experience. Indeed, our expectation was that only a small proportion of those sent the survey would have used these relatively new therapies.

With regard to treatment initiation, key barriers were highlighted at system level (e.g. access, reimbursement, paperwork, and lack of consultation time) as well as HCP-related issues (e.g. lack of knowledge around injectables). In addition, respondents suggested a number of important patient-related factors, including poor disease comprehension, lack of patient education, and fear of injection. These are novel findings in the use of injectable therapies in CV medicine, but they align with previous experience in other disease areas.[10,11]

Respondents suggested that, once initiated, adherence with injectable therapies is generally high—the mean adherence was estimated at ~80% in the first 6 months of treatment. This aligns with a recent Italian study demonstrating an adherence rate of 79.9% during the first few months of PCSK9 inhibitor treatment.[18] Generally, adherence with injectable PCSK9 inhibitors appears to be higher than with oral statins.[19] Adherence with such medications has been strongly linked with reductions in MACE in patients with CVD.[20]

Respondents also noted that patient adherence with injectable treatments typically declines with time. They identified several barriers to maintaining adherence, including a lack of patient education (e.g. around why they need the medicine), problems with side effects/local reactions, perceived lack of benefit, ongoing fear of injection, and memory issues.

Levels of uptake of PCSK9 inhibitors have been lower than expected (in the UK at least).[21] The barriers identified here go some way towards explaining the shortfall. Key facilitators of increased initiation and adherence with injectables are likely to include enabling access at a system level, improved education of patients and HCPs, and greater provision of patient adherence support tools. These should be focused around a patient-centred, shared decision-making approach.[1] Education of patients and their caregivers is a key step towards medication adherence and sustained lifestyle change.[22–24] Meanwhile, training of HCPs should be focused on specific needs. The survey suggested that respondents were least confident around 'troubleshooting' with patients and managing non-adherence, as well as more general needs relating to side effects and supporting data. The preferred format for maintaining skills was face-to-face training. These findings align with the results of another recent ACNAP survey of CV nurses, which found that almost half did not feel educationally fully prepared for their jobs, with risk factor management being a key area of concern; again, respondents cited face-to-face training as their preferred format for advanced learning.[25]

There are several methods by which the uptake of injectable therapies could be improved:

(1) Patient and caregiver starter packs to enhance treatment acceptance and adherence (potentially including multimedia resources such as apps and video content); key elements should include:
  - The rationale for using these treatments;
  - How to use the injection device; and
  - A timetable for recording the treatment schedule and prescription renewal dates.

(2) Practical prescribing guidelines to help HCPs identify eligible patients, and provision of treatment schemes and key local procedures.
(3) Adequate HCP training around patient interactions (e.g. troubleshooting, managing non-adherence).
(4) Further evidence on the efficacy and tolerability of these treatments.

Over half of survey respondents were non-physicians and many of the findings—and action areas—are particularly relevant to these groups, including nurses. For example, with appropriate training, nurses and pharmacists can play a key role in educating patients on the rationale for using injectable therapies, optimal technique, and troubleshooting around common barriers such as needle anxiety.

The focus of these action plans may need to differ between centres using PCSK9 inhibitors vs. GLP-1 receptor agonists, particular given greater general experience levels with the latter. The current study suggested that confidence may be lower among prescribers of PCSK9 inhibitors, and hence further practical training of HCPs might be required. However, the analysis was based on a small sample and more research is needed. The next phase of this project is to undertake focus groups and interviews with patients, carers and HCPs and perform thematic analyses. These data will be used in conjunction with the survey results to develop educational material for patients and HCPs—including nurses and pharmacists—and pilot their feasibility.

We should acknowledge the limitations of this work. In particular, a total response of <200 participants may be construed as low and the survey was only developed in English (the official language of the ESC). However, the survey was distributed across a wide variety of professionals with the expectation that the majority would not be directly involved in delivering injectable therapies. There was also a heavy weighting of respondents towards a small number of countries (particularly the UK and Italy) and hence responses may have been influenced by local cultural issues or considerations specific to their national healthcare services; generalization of the findings should therefore be undertaken with caution. Furthermore, consideration of patient-related adherence factors was based on the opinions of HCPs rather than patients themselves.

Conclusion

The numbers of patients with elevated CV risk who are prescribed injectable therapies is likely to increase in the coming years, and this will create new challenges. There are many potential barriers to initiation and adherence with these treatments, including issues at healthcare system, HCP and patient levels. However, these concerns could be at least partially addressed through a few simple facilitators—based primarily on enhanced education and training of patients and HCPs, and greater deployment of patient support tools for maintaining long-term adherence.

Data availability

The data underlying this article are available in the article. Additional detailed data can be requested from the authors with permission from ESC ACNAP.

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