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1 **Healthcare professionals' perspectives on use of PCSK9 inhibitors in cardiovascular disease: an in-**
2 **depth qualitative study**

3 **Short title: Injectables interviews**

4
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2

3 **Short title: Injectables interviews**

4 **Abstract:**

5 *Aim:* Injectable medicines such as PCSK-9 inhibitors are increasingly used to manage risk factors for
6 cardiovascular events with little information around the perceptions of healthcare professionals (HCPs)
7 on the administrative and clinical practicalities. The aim was to identify the facilitators and barriers on
8 the use of injectable therapies with CV benefits through interviews with HCPs.

9 *Methods and results:* Qualitative interviews were conducted in the United Kingdom (London and Leeds)
10 and Italy (Rome and Milan) in 2021. Coding was undertaken using NVivo and thematic analysis
11 performed. A total of 38 HCPs were interviewed, 19 in each country composing of physicians (n=18),
12 pharmacists (n=10), nurses (n=9) and pharmacy technician (n=1). Four themes emerged: (i) Clinicians'
13 previous experiences with injectable therapies (ii) Challenges with patients' behaviours and beliefs (iii)
14 Clinicians' knowledge of injectable therapies and therapeutic inertia and (iv) Organisational and
15 governance issues. The behaviour and beliefs from healthcare professionals focused on facilitating
16 behaviour change as well as the poor interdisciplinary working and collaboration. Therapeutic inertia
17 was raised where physicians either lacked awareness of injectable therapies or were unwilling to
18 prescribe them. The importance of facilitating patient education on injection techniques was highlighted
19 while organisational and governance issues identified the lack of guidance to inform practice. Clear
20 pathways are required to identify those who were eligible for injectable therapies as well as on how
21 injectables should be prescribed.

22 *Conclusion:* If medicine optimisation is to be achieved, there needs to be structured processes in place
23 to identify eligible patients and the development of educational material.

24 **Keywords:** Injectable therapies, cardiovascular disease, dyslipidemia, healthcare professionals.

25 **Novelty:**

- 26
- This study provides in-depth analysis from interviews of AHPs on novel injectable therapies in
27 two distinct locations.
 - CVD injectable therapies have different challenges compared to other injectables such as insulin.
- 28

- 1 • The study adds further knowledge to perceptions on the use of injectable therapies for
2 cardiovascular disease.
- 3 • We identified specific barriers to the administration and prescribing of injectable therapies.
4

5 Background

6 Despite mortality from cardiovascular disease (CVD) decreasing, a significant number of people continue
7 to have risk factors including dyslipidaemia (that is, increased levels of serum total cholesterol, and/or
8 high triglycerides and/or increased low-density lipoprotein cholesterol: LDL-C), which is associated with
9 a greater risk of a cardiovascular event.¹ As such, injectable therapies to lower cholesterol (PCSK9
10 monoclonal antibody medications inhibitors for example) have been shown to be effective for primary
11 prevention and secondary prevention of CVD.² Optimization in lipid therapy has been shown with
12 Evolocumab and Alirocumab as well as Inclisarin with reductions in total cholesterol and LDL-C.³ These
13 medications require regular injections for a person's lifetime and these can be administered by a
14 healthcare professional, the patient or a caregiver. A recent study reported that injectable therapies
15 were acceptable to patients whilst also highlighting several barriers in terms of their use including
16 needle phobia and lack of accessible patient educational material as well as a lack of a standardised
17 clinical support monitoring system.⁴ A survey of healthcare professionals across Europe on injectable
18 therapies for CVD revealed organisational and administrative problems as well as a lack of educational
19 material that could be used in clinical practice.⁵ The results confirmed the findings from an integrative
20 review on injectable therapies that reported a lack of studies on these novel injectable therapies.⁶ The
21 European Society of Cardiology recommend use of these medications in those at high risk of CVD with
22 nurses and allied healthcare professionals playing a key role in the assessment, treatment and
23 management of patients who require these injectable therapies. Other injectables have been developed
24 including Glucagon-like peptide 1 (GLP1-) agonists and these are in use for those with obesity and
25 diabetes and the recent 2023 European Society of Cardiology guidelines recommend GLP-1 agonists for
26 those who have or at risk of cardiovascular disease.⁷ The STEP-HFpEF trial used once weekly GLP-1
27 agonist, semaglutide for patients with heart failure and obesity demonstrated improvements in heart
28 failure symptoms and greater weight loss compared to placebo in those with heart failure with
29 preserved ejection fraction.⁸ However widespread implementation and use cannot be achieved without
30 clinicians being confident and competent in managing, educating and monitoring patients who are
31 prescribed PCSK9 inhibitors as well as GLP-1 agonists and other injectable therapies. The aims of the
32 study were to identify the education and training needs of healthcare professionals on the PCSK9

1 inhibitor injectable therapies in Italy and the United Kingdom and identify the facilitators and barriers
2 relating to their use in clinical practice.

3 Methods

4 The study is reported in accordance with the consolidated criteria for reporting qualitative research
5 (COREQ).⁹

6 Ethics

7
8 The study respected the principles of the Helsinki Declaration. Ethics approval was obtained from each
9 centres in Italy (Institutional Review Board Lazio 2 in Rome: ref: 22.21 and the Institutional Review Board
10 of San Raffaele in Milan ref: 365.2020). The UK site deemed the project as a service evaluation and
11 ethics approval was not required.
12

13 Design and recruitment

14 A qualitative constructionist methodology was employed to capture the experiences of healthcare
15 professionals in practice that would lead to informing and improving clinical practice.^{10,11} The study was
16 conducted between late 2020 to August 2021 using a convenience sample of clinicians working in the UK
17 (Leeds and London) and Italy (Milan and Rome). These sites were chosen as both were identified as
18 using PCSK9 inhibitors and represent locations in the north and south of Europe and these countries
19 were used as both were using PCSK9 inhibitors as treatment for cardiovascular conditions. Healthcare
20 professionals involved in care of CVD patients (i.e., registered nurses, pharmacists and/or any healthcare
21 professional directly involved in injectable therapies and included several departments - cardiology,
22 lipidology and diabetes/endocrine) were eligible and those not working with CVD patients were
23 excluded. All those who fitted the inclusion criteria were sent an email about the study and asked if they
24 wished to participate in the study and asked to contact the researchers if they wished to participate.
25

26 Materials and procedure

27 Once consent was completed, experienced qualitative researchers undertook the interviews using MS
28 Teams or Zoom (AD and MK) (this was because there were restrictions on face-to-face meetings with
29 COVID 19 restrictions).

30 Healthcare professionals were asked the following questions in a semi-structured interview. (i)
31 What are the facilitators and barriers to prescribing injectable therapies? (ii) What would help you make

1 prescribing decisions on prescribing injectable medicines and (iii) What are your educational needs in
2 relation to administering and managing injectable therapies. Participants were also asked their opinions
3 on the products, their practical use, side-effects, pharmaceutical form and storage. One change was
4 required between sites- the term 'Implementation' was used instead of 'Prescription' (in Italy, nurses
5 and pharmacist cannot prescribe these medications). The UK allows physicians and pharmacists to
6 prescribe injectable therapies but there are different constraints in Italy. These questions were based on
7 previous literature and questions that were developed for patients.

8 Interviews were conducted in the native local language (i.e., Italian and English) and lasted
9 between 30 to 60 minutes. All interviews were recorded using the built in function within Zoom and
10 Teams with the permission of the participants. In order to preserve the meaning of idiomatic
11 expressions, the interviews from Italy were not translated but directly coded into English, and a table of
12 the most significant quotations was then constructed in dual language by fluent and certified English-
13 speaking researchers.¹² Using a schematic content analysis approach, interim analysis was done and
14 highlighted emerging themes and determined data saturation using NVivo 11. Standard process of
15 inductive thematic content analysis was undertaken with 19 initial codes identified and through
16 refinement reduced to 13 final codes by EB and GL.¹³ The MIRACLE Framework was used to guide the
17 abstraction and ensure an in-depth description of the themes.¹⁴ The same process of analysis was
18 applied to identify the facilitators and barriers to using injectable therapies. All quotes from participants
19 were anonymised.

21 Results

22 Participant demographics

23 A total of 38 healthcare professionals (HCPs) were interviewed, 19 in each country and composed of
24 physicians (n=18), pharmacists (n=11) and nurses (n=9). The participants worked in cardiology, lipidology
25 and endocrinology.

26 Themes

27 Four main themes were identified: (i) Clinicians' previous experiences with injectable therapies (ii)
28 Challenges with patients' behaviours and beliefs (iii) Clinicians' knowledge of injectable therapies and
29 therapeutic inertia and (iv) Organisational and governance issues. Within each of these broad themes
30 both facilitators, barriers and solutions were identified and categorised across the data (**Figure 1**).

1 *Insert Figure 1 here*

2 Theme 1: Clinicians' previous experiences with injectable therapies

3 A clinician's previous clinical experience in using injectable therapies was seen as strongly influencing
4 their ability to interact with patients who were eligible for PCSK9 inhibitors. Their previous experience of
5 educating patients on moving from oral medication to injectables and ensuring they had a good
6 injection technique was identified as important by participants.

7 *"I think often it tends to be a mental barrier doesn't it that it feels somewhat like a failure that*
8 *you are progressing to injectable therapies, and I don't know whether that's something that we*
9 *as healthcare professionals actually play into in some way ...I don't know whether we're like, OK*
10 *well this [statins] hasn't worked and therefore you are going to go onto this injectable therapy. It*
11 *kind of feels like you've failed at something, so it feels like a bit of a negative thing to start off*
12 *with."* [Physician, UK]

13 *"Some problems, for the adherence of patients, especially some who were not so keen on the*
14 *method of administration...some were a bit dazed, as if it were something a bit too invasive at*
15 *first."* [Cardiologist, Italy]

16 Clinicians' perspective on the prevalence of adverse effects and side effects noted the importance of
17 monitoring and ensuring there were no issues.

18 *"So when we follow them up, we would always ask to see if they are suffering from any adverse*
19 *effects so we would get that sort of feedback from them. Also, I ask to see how they are getting*
20 *on with the self-administration and then they can sometimes then offer extra feedback on how*
21 *they are getting on if I've not covered everything with them in the questioning."* [Pharmacist, UK]

22 Theme 2: Challenges with patients' behaviours and beliefs

23 This theme related to challenges identified by clinicians in facilitation of patient behaviour in relation to
24 injection techniques, especially with patients' needle phobia:

25 *"...I think when I speak to patients about injectable medicines there's often that fear of needles...*
26 *I think needle phobia associated pain is definitely the biggest one when I speak to patients."*
27 [Pharmacist, UK]

28 The challenges of facilitating patient education were also noted with some patients reluctant to
29 consider injectable therapies and refused to consider these therapies.

1 *“The patient who declined the therapy, according to him...he could make mistakes and we tried*
2 *several times to explain that it was quite simple, sure for us it is simple but for him it was not so,*
3 *but he was afraid, afraid to do something wrong and therefore if he was at home and he did*
4 *something wrong and he was afraid of the consequences.”* [Nurse, Italy]

5 However, participants were also able to identify benefits of PCSK9 inhibitors supports their use in
6 hypercholesterolaemia and can be shared with the patients in terms of the rapid improvement in blood
7 test results.

8 *“A very rapid fall in LDL can be seen from the very first course of treatment.”* [Pharmacist, Italy]

9 Theme 3: Clinicians’ knowledge of injectable therapies and therapeutic inertia
10 A theme around healthcare professionals’ therapeutic inertia (therapeutic inertia is defined as the
11 attitude of the physician who, even if aware of the fact that the patient doesn’t reach the treatment’s
12 target, doesn’t adopt the needed measures to solve the problem and it can also refer to missed
13 application of new therapies), with lack of knowledge and awareness about these injectable therapies
14 identified. Participants stated that senior clinicians often lacked awareness of these therapies in terms
15 of availability and potential benefits.

16 *“...beyond an inevitable therapeutic inertia that means that any new therapy has to be*
17 *metabolised before it can become common practice.”* [Cardiologist, Italy]

18 The lack of awareness and the therapeutic inertia highlights the issue of identifying patients who are
19 eligible for these medications or not being able to prescribe them.

20 *“I think also people lack knowledge about [the injectables team]....I don’t think in terms of my*
21 *practice or people that I work with there is a disinterest or barrier to using injectable therapies*
22 *it’s just understanding how it works and how to get people on them.”* [Physician, UK]

23 There was clearly a lack of knowledge about injectable therapies, namely PCSK9 inhibitors, from
24 participants’ interactions with their professional colleagues. Further education for clinicians was
25 suggested as a way to improve the level of preparation and education for patients.

26 *“The patient who renounced to the therapy maybe because he was not convinced from the*
27 *beginning and we tried to make him understand how important could be to enter in this*
28 *therapeutic plan for his characteristics, at the beginning he accepted, but in the moment of the*

1 *explanation of how the drug had to be prepared and then how it had to be administered he did*
2 *not feel able...* [Nurse, Italy]

3 The need for further education for clinicians was seen as important as a lack of preparedness in dealing
4 with patients' questions could negatively affect patients' decisions to consider injectable therapies.

5 *"I can see how as a clinician who doesn't come across them it could be quite confusing when you*
6 *see them because it's a monoclonal antibody and usually that sparks alarm bells. But it just*
7 *requires a bit more education to make sure people don't panic when they see them."* [Physician,
8 UK]

9 Theme 4: Organisational and governance issues

10 The final theme identified was around organisational and governance issues and ensuring there was a
11 clear pathway from identification for clinical need to prescription of an injectable product.

12 *"There was a disparity between the indications of the guidelines in terms of the target to which*
13 *access was given and the indications of the AIFA [Italian authority for prescribing], and therefore*
14 *of the therapeutic plan."* [Cardiologist, Italy]

15 The lack of clear evidence-based guidelines was raised by participants.

16 *"I don't think the current guidelines out there are accessible enough for health care professionals*
17 *to guide us in when we need to be, you know, prescribing someone injectable therapies. So, I*
18 *don't think there's that much awareness around the protocols so if you don't know about*
19 *something you can't really feel confident about prescribing it, especially if it's something like an*
20 *injectable therapy."* [Physician, UK]

21 Barriers to management in both primary and secondary care settings were noted in both locations.

22 Poor interdisciplinary working, collaboration, and communication was also identified as a challenge in
23 both countries where not all those working in a hospital are familiar with these therapies:

24 *"I think we all need to be singing off the same hymn sheets/algorithm and I don't think we are*
25 *currently. You write letters to GPs, and they may check people's traditional cholesterol profile*
26 *without LDLs or non-HDLs and apply primary prevention algorithms so making sure everyone*
27 *across the patch....I will write to GPs sometimes and say can you put this chap on 80mgs of*
28 *Atorvastatin and see what his lipids are like in another 3-months, and they'll come back a year*
29 *later with 20mgs of Atorvastatin and no blood test done."* [Physician, UK]

1 In terms of governance, in Italy, there was a lack of integrated care and communication between the
2 hospital setting and primary care and the need for several blood tests that must be organised by the
3 hospital.

4 *“Three cholesterol samples in recent months also required hospital reorganisation.”*

5 [Cardiologist, Italy]

6 *“This is because the family doctor is hardly involved. The family nurse is unfortunately a figure
7 that is not yet identified. Thus, the patient does not have many points of reference.”*

8 [Cardiologist, Italy]

9 Facilitators and barriers

10 As well as identifying the themes above, participants were specifically asked if there were any
11 facilitators and barriers to prescribing PCSK9 inhibitors and they were able to identify several of each.
12 There were several existing facilitators identified including patients previous experience of injectables
13 such as insulin and the clinical goal reached are a good stimulus for the use of PCSK-9 inhibitors. One
14 cardiologist in Italy commented that people with diabetes who had been using insulin did not
15 experience the same level of hesitation when considering PCSK9 inhibitor injectables:

16 *“The diabetic patient is used to a different approach.”*

17 [Cardiologist, Italy]

18 Interestingly word of mouth was a powerful existing facilitator (**Supplementary Table 1**).

19 Discussion

20 This is the first in-depth qualitative paper examining healthcare professionals’ perceptions on use of
21 PCSK9 inhibitors in Europe. All healthcare professionals who were invited to participate did so, and we
22 included a wide variety of professionals. Healthcare professionals from several specialties participated
23 and they were directly involved in PCSK-9 prescribing that included cardiology, lipidology and
24 endocrinology. The results have added context from a qualitative perspective confirming the findings
25 from a previous European-wide survey of 192 respondents that was undertaken as an earlier
26 component of this project.⁵

27 Clinicians’ knowledge of injectable therapies was a key theme identified with respondents
28 raising some of the issues they have to manage in their clinical practice including teaching patients
29 about self-administration, and good injecting technique. Previous studies have focused on clinical

1 outcomes and prescription practices with a paucity of information on clinicians' previous experience
2 with injectable therapies for CVD. ^{15,16} This theme relates to the theme on clinicians' knowledge of
3 injectables and the need for education when novel therapies are introduced. Formal education and
4 training for all healthcare professionals was one of the main themes identified; this highlights the
5 importance of having clinicians who are competent and confident in providing advice and education to
6 patients and their caregivers. Critically, this included those who were familiar with these therapies
7 (training on injectable techniques and how to respond to patients' beliefs around injectable therapies),
8 as well as managing lack of awareness of these medications as identified by therapeutic inertia. Despite
9 the publication of a clinical practice guideline that includes excellent infographics, participants clearly
10 require local educational opportunities in their workplace. ¹⁷ The authors also recognised some of their
11 recommendations were weak which also highlighted that the majority of published guidelines (from
12 European Society of Cardiology and American Heart Association for example), did not systematically
13 assess the cardiovascular benefits of adding PCSK9 inhibitors and/or ezetimibe for all risk groups across
14 primary and secondary prevention. As well as considering what medication is clinically appropriate,
15 clinicians need to discuss options with patients and their families and cannot under-estimate the
16 importance of shared decision-making. ¹⁸ Previous studies have shown that once these therapies are
17 initiated, there was a high adherence rate within the first six months and significant reductions in MACE
18 in patients with CVD. ^{16,19,20} In terms of what needs to be done, the development and use of
19 educational materials for both healthcare professionals and patients/caregivers is key as well as the
20 development of clearer guidance and pathways to improve delivery and optimisation of these
21 medications.

22 Regarding the theme of healthcare professionals' perceived challenges with patient behaviour
23 and beliefs, this theme confirms findings from in-depth interviews with patients. ⁴ Needle phobia is not
24 unique to CVD injectable therapies and is a well-known barrier to injectable therapy initiation,
25 particularly in those with diabetes. ^{21,22}

26 The theme of organisational and governance issues builds on findings in previous studies
27 although they did not specifically explore reasons for this other than reporting high rates of
28 discontinuation. ^{15,16,19,20} Our study is unique in undertaking a qualitative approach to exploring the
29 organisational and governance issues. Having the prescription of PCSK-9 inhibitors limited to hospitals is
30 associated with a significant administrative burden for these centres and clearly, improvements in the
31 administration and distribution of injectable therapies is needed if wider use is to be achieved. A

1 previous study highlighted the importance of community pharmacists benefit in improving delivery of
2 these medications and their role in monitoring patients and reducing the barriers.²³ Post COVID-19,
3 there is evidence supporting patients' preferences for local appointments and the ability to collect
4 medications from their local pharmacies rather than have to go to the hospital.⁴ A Spanish study
5 undertaken during the pandemic demonstrated that home delivery of medication was advantageous to
6 patients and good lipid control was maintained.²⁴ One issue noted a lack of homogeneity in prescriptions
7 between the various Italian regions. However, the national scientific societies are working with the
8 Italian Medicines Agency (AIFA) to reduce some of the differences. A new update from AIFA is expected
9 shortly. Interestingly, cost did not come up as a theme.

10 It was reassuring that there were existing facilitators identified by the participants that included
11 the clinical benefits of PCSK9 inhibitors in terms of their lipid profile and patients who had prior
12 experience of injectables such as insulin as well as the importance of word-of-mouth amongst patients.

13 Limitations need to be acknowledged, the study was undertaken in two European countries and
14 other countries may have revealed different themes and contextual barriers. Only healthcare
15 professionals working with the hospital sector were approached to participate in this study as at the
16 time of the data collection, neither country were prescribing these medications in primary care. It may
17 be that different perceptions would now be observed within the primary care setting where prescribing
18 of PCSK-9 prescriptions is in practice. The participants only had experience in PCSK9 inhibitors, which
19 may be seen as a limitation, however the principles of injectable therapies are similar and thus this is
20 not viewed as a major limitation. There still remains a paucity of education on these novel injectables
21 therapies for healthcare professionals.

22 Conclusion

23 The interviews with healthcare professionals identified several themes and provided some suggestions
24 on how the delivery and education could be improved. The development and availability of educational
25 material for both patients and healthcare professionals have the potential to optimise the use of
26 injectable therapies and help reduce the initial fears and reluctance around commencing injectable
27 therapies. The findings could be used to develop educational material that can be implemented into
28 practice and improve uptake and maintenance of injectable therapies.

29

1 **CRedit statement:** GL & EV devised the study, MK, GC, FD undertook the interviews, EB, GL, AD, RK
2 analysed the data, all authors contributed to the writing of the paper.

3 **Declaration of competing interest** No conflicts of interest.

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8 publication. In addition, they did not have access to the data.

9
10 **Data availability statement:** Due to the nature of the data collected, it is not possible to share it.

11 12 **References**

13 1. Hedayatnia M, Asadi Z, Zare-Feyzabadi R, Yaghooti-Khorasani M, Ghazizadeh H, Ghaffarian-Zirak R et
14 al. Dyslipidemia and cardiovascular disease risk among the MASHAD study population. *Lipids in Health*
15 *Dis; 2020: 19;42.*

16
17 2. Rached F, Santos RD. The role of statins in current guidelines. *Curr Atheroscler Rep.* 2020; **22**, 50. doi:
18 10.1007/s11883-020-00861-9 pmid: 32770357

19
20 3. Khatib R, Khan M, Barrowcliff A, Ikongo E, Burton C, Mansfield M et al. Innovative, centralised,
21 multidisciplinary medicines optimisation clinic for PCSK9 inhibitors. *Open Heart* 2021; **9**: e001931. doi:
22 10.1136/openhrt-2021-001931

23

- 1 4. Lee GA, Durante A, Baker E, Vellone E, Caggianelli G, Dellafiore F, et al. Patients' perceptions on the
2 facilitators and barriers using injectable therapies in cardiovascular disease: a qualitative international
3 study. *J Adv Nurs* 2023; **79** (12): 4687-4696. <https://doi.org/10.1111/jan.15739>
- 4
- 5 5. Khatib R, Angus N, Hansen T, Lambrinou E, Vellone E, Khan M et al. Perceptions of injectable therapies
6 with cardiovascular benefit: An ACNAP survey of healthcare professionals to explore facilitators and
7 barriers. *Eur J Cardiovasc Nurs* 2022; **21**:430-437. <https://doi.org/10.1093/eurjcn/zvab106>
- 8
- 9 6. Lambrinou E, Kyriakou M, Lakatamitou I, Angus N, Khatib R, Vellone E et al. Facilitators and barriers in
10 delivering and managing injectable therapies in chronic conditions: An integrative review. *Eur J*
11 *Cardiovasc Nurs* 2020; **19**(8): 663-680. [10.1177/1474515120939007](https://doi.org/10.1177/1474515120939007)
- 12
- 13 7. Marx N, Federici M, Schütt K, Müller-Wieland D, Ajjan RA, Antunes MJ, et al. ESC Scientific Document
14 Group , 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes:
15 Developed by the task force on the management of cardiovascular disease in patients with diabetes of
16 the European Society of Cardiology (ESC), *Eur Heart J*, 2023; **44** (39): 4043-4140.
17 ehad192, <https://doi.org/10.1093/eurheartj/ehad192>
- 18
- 19 8. Kosiborod MN, Abildstrøm SZ, Borlaug, BA, Butler J, Rasmussen S, Davies M, et al. for the STEP-
20 HFpEF Trial Committees and Investigators. Semaglutide in Patients with Heart Failure with Preserved
21 Ejection Fraction and Obesity. *NEJM*; 2023; **389** (12): 1069-1084. DOI: 10.1056/NEJMoa2306963
- 22
- 23 9. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-
24 item checklist for interviews and focus groups. *Int. J. Qual. Health Care*. 2007; **19** (6), 349–357
- 25
- 26 10. Doyle L, McCabe C, Keogh B, Brady A, McCann M. An overview of the qualitative descriptive design
27 within nursing research. *J Res Nurs*. 2020; **25**(5), 443-455.
- 28
- 29

- 1 11. Sandelowski M, Barroso J. Classifying the findings in qualitative studies. *Qual health res* 2003; **13(7)**,
2 905-923.
- 3
- 4 12. Younas A, Fàbregues S, Durante A, Ali P. Providing English and native language quotes in qualitative
5 research: a call to action. *Nursing Open* 2022; **9(1)**, 168-174.
- 6
- 7 13. Newell, R., Burnard, P. Research for evidence-based practice in healthcare. John Wiley & Sons, 2010.
- 8
- 9 14. Younas, A., Fàbregues, S., Durante, A., Escalante, E. L., Inayat, S., & Ali, P. (2023). Proposing the
10 "MIRACLE" narrative framework for providing thick description in qualitative research. *International*
11 *Journal of Qualitative Methods*, 22, 16094069221147162.
- 12
- 13 15. McCormick, D., Bhatt, D.L., Bays, H.E., Taub, P.R., Caldwell, K.A., Guerin, C.K., Steinhoff, J., Ahmad, Z.,
14 Singh, R., Moreo, K. and Carter, J., (2020). A regional analysis of payer and provider views on cholesterol
15 management: PCSK9 inhibitors as an illustrative alignment model. *Journal of managed care & specialty*
16 *pharmacy*, 26(12), 1517-1528.
- 17
- 18 16. Piccinni, C., Antonazzo, I.C., Maggioni, A.P., Pedrini, A., Calabria, S., Ronconi, G., Dondi, L., Martini,
19 N., Roberto, G., Sampietro, T. and Sbrana, F. (2020). PCSK9 inhibitors' new users: analysis of prescription
20 patterns and patients' characteristics from an Italian real-world study. *Clinical Drug Investigation*, 40,
21 173-181.
- 22
- 23 17. Hao Q, Aertgeerts B, Guyatt G, Bekkering G E, Vandvik P O, Khan S U et al. PCSK9 inhibitors and
24 ezetimibe for the reduction of cardiovascular events: a clinical practice guideline with risk-stratified
25 recommendations *BMJ* 2022; **377** :e069066 doi:10.1136/bmj-2021-069066
- 26

- 1 18. Hendriks J, Lee G. Shared Decision Making – The patient on the forefront of care coordination. *EHI -*
2 *Qual Care Clin Outcomes*; 2020; **6**: 231-233. <https://doi.org/10.1093/ehjqcco/qcaa039>
3
- 4 19. Kosmas CE, Silverio D, Ovalle J, Montan PD, Guzman E. Patient adherence, compliance, and
5 perspectives on evolocumab for the management of resistant hypercholesterolemia. *Patient Prefer*
6 *Adherence* 2018; **12**: 2263–2266.
7
- 8 20. Bansilal S, Castellano JM, Garrido E, Wei HG, Freeman A, Spettell C et al. Assessing the impact of
9 medication adherence on long-term cardiovascular outcomes. *J Am Coll Cardiol* 2016; **68**: 789–801.
10
- 11 21. Taylor S, Thompson F and McDermott R. Barriers to insulin treatment among Australian Torres Strait
12 Islanders with poorly controlled diabetes. *Aust J Rural Health* 2016; **24**:363–370.
13
- 14 22. Papasporou M, Laschou VC, Partsiopoulou P, et al. Fears and health needs of patients with diabetes:
15 a qualitative research in rural population. *Med Arch (Sarajevo, Bosnia Herzegovina)* 2015; **69**: 190195.
16
- 17 23. Dixon DL, Saseen JJ. Pharmacist-administered long-acting injectable PCSK9 service: A solution to
18 improve patient access and adherence. *J Amer Pharm Assoc* 2021; **61 (3)**: e83-e85.
19
- 20 24. Seijas-Amigo J, Gayoso-Rey M, Mauriz-Montero MJ, Suarez-Artime P, Casa-Martinez A, Dominguez-
21 Guerra M et al. Impact of the COVID-19 pandemic in the lipid control of the patients that start PCSK9
22 inhibitors. *Clinica e Investigacion en Arteriosclerosis : Publicacion Oficial de la Sociedad Espanola de*
23 *Arteriosclerosis*: 2022; S0214-9168(22)00018-3. DOI: 10.1016/j.arteri.2022.01.003.
24

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Healthcare professionals' perspectives on use of PCSK9 inhibitors in cardiovascular disease:
an in-depth qualitative study



to identify the facilitators and barriers on the use of injectable therapies with cardiovascular benefits through interviews with healthcare professionals



Four themes



Formal education and training are needed by healthcare professionals along with improved administrative processes if there is to be medication optimisation of injectable therapies in cardiovascular disease

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Graphical Abstract
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