Supplementary Material

Barriers and Strategies to Optimize the Use of Glucagon-Like Peptide 1 Receptor Agonists in People with Type 2 Diabetes and High Cardiovascular Risk or Established Cardiovascular Disease: A Delphi Consensus in Spain

Manuel Botana López[1,†], Miguel Camafort Babkowski[2,†], Raquel Campuzano Ruiz[3,†], Ana Cebrián Cuenca[4,†], Manuel Gargallo Fernández[5,†], Héctor David de Paz[6], Jennifer Redondo-Antón[7], Esther Artime[7], Silvia Díaz-Cerezo[7], Miriam Rubio de Santos[7,*]

[1] Servicio de Endocrinología, Hospital Universitario Lucus Augusti, Lugo, Spain
[2] Servicio de Medicina Interna, ICMiD, Hospital Clínic, Barcelona; Departamento de Medicina, Universidad de Barcelona, and CiberOBN, Instituto de Salud Carlos III, Madrid, Spain
[3] Servicio de Cardiología, Hospital Universitario Fundación de Alcorcón, Madrid, Spain
[4] Medicina Familiar y Comunitaria, Centro de Salud Cartagena Casco, Cartagena, Spain; Biomedical Research Institute of Murcia (IMIB), Murcia, Spain
[5] Servicio de Endocrinología y Nutrición, Hospital Universitario Infanta Leonor, Madrid, and Fundación Jiménez Díaz, Madrid, Spain
[6] Outcomes'10, Parque Científico, Tecnológico y Empresarial, Jaume I University, Castellón de la Plana, Spain
[7] Eli Lilly and Company, Alcobendas, Madrid, Spain
[†] These authors contributed equally and on behalf of their medical societies.

* Correspondence Details:
Name: Miriam Rubio de Santos
Address: Eli Lilly and Company,
            Avda. de la Industria 30,
            Alcobendas, 28108 Madrid, Spain
Phone: +34 634220677
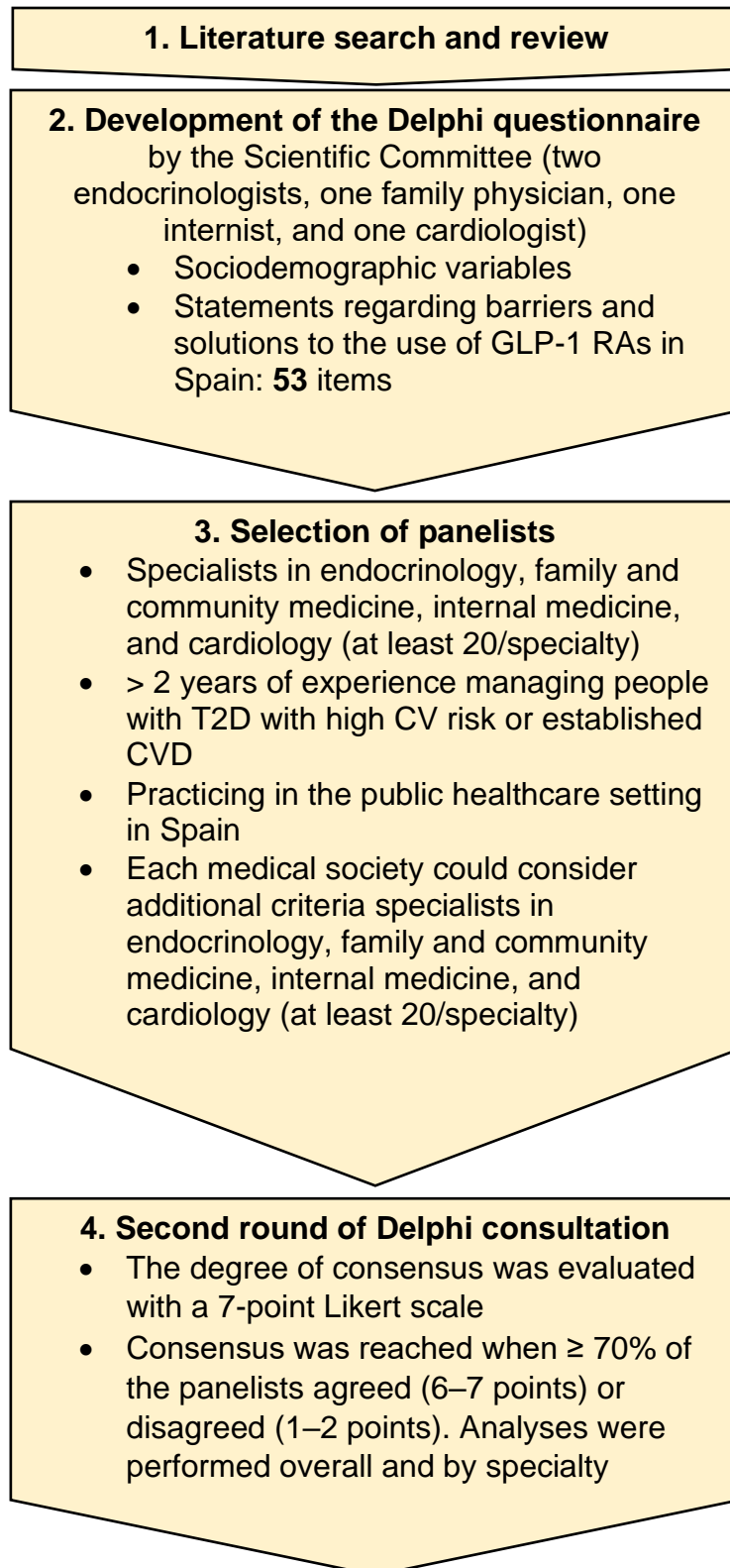Email: rubio_miriam@lilly.com

1. Literature search and review

2. Development of the Delphi questionnaire
by the Scientific Committee (two endocrinologists, one family physician, one internist, and one cardiologist)
- Sociodemographic variables
- Statements regarding barriers and solutions to the use of GLP-1 RAs in Spain: **53** items

3. Selection of panelists
- Specialists in endocrinology, family and community medicine, internal medicine, and cardiology (at least 20/specialty)
- > 2 years of experience managing people with T2D with high CV risk or established CVD
- Practicing in the public healthcare setting in Spain
- Each medical society could consider additional criteria specialists in endocrinology, family and community medicine, internal medicine, and cardiology (at least 20/specialty)

4. Second round of Delphi consultation
- The degree of consensus was evaluated with a 7-point Likert scale
- Consensus was reached when ≥ 70% of the panelists agreed (6–7 points) or disagreed (1–2 points). Analyses were performed overall and by specialty

Fig. S1 Scheme of the Delphi consultation process. *CV* cardiovascular, *CVD* cardiovascular disease, *GLP-1 RAs* glucagon-like peptide 1 receptor agonists, *T2D* type 2 diabetes

Table S1 The Delphi questionnaire

SECTION A

Sociodemographic characteristics and of clinical practice

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1. Gender:
   - ☐ Man
   - ☐ Woman

2. Age: ___ years

3. Specialty:
   - ☐ Family and Community Medicine
   - ☐ Endocrinology
   - ☐ Internal medicine
   - ☐ Cardiology

4. Years of experience in the management of people with T2D and/or high-risk CV or CVD established (not counting years of residence): ___ years

5. Approximately, what number of patients do you see weekly in your practice? ___ patients

6. Approximately, what percentage of patients seen in your practice have a diagnosis of T2D? ___ %

7. Approximately, what percentage of people with T2D seen in your practice have high CV risk or established CVD? ___ %

8. Approximately, in what percentage of people with T2D and high CV risk or established CVD have you prescribed treatment with GLP-1 RA? ___ %

Characteristics of the working place

9. Autonomous Community in which he/she practices his/her profession:

10. Do you belong to any working groups related to diabetes and/or CV risk?
    - ☐ Yes
    - ☐ No

11. Level of care of your main workplace:
    - ☐ First level of care (primary care centers, health centers)
    - ☐ Second level of care (specialty centers and area hospitals)
    - ☐ Third level of care (reference hospitals)

12. Is there a diabetes unit in your workplace?
    - ☐ Yes
    - ☐ No

SECTION B

Barriers to GLP-1 RA use in people with T2D with high CV risk or established CVD

Treatment
1. The choice of drug T2D treatment is complex due to the large number of pharmacological agents available.
2. The traditional stepwise approach to T2D treatment contributes to the late use of GLP-1 RAs.

3. Injectable treatments have traditionally been used in later stages of the disease, limiting the early access to GLP-1 RAs.

4. The inertia of using the most potent drugs for later stages of the disease limits the early use of GLP-1 RAs.

5. There is therapeutic inertia that induces a glycocentric approach to diabetes and does not cover the CV risk prevention approach.

6. Restrictions at the regional or center level (1st, 2nd, and subsequent lines of treatment) limit the early access to GLP-1 RAs.

7. The belief that the adherence and persistence rate of GLP-1 RAs is lower compared to other treatments limits their prescription.

8. The injectable route of administration is a barrier for physicians in prescribing GLP-1 RAs.

9. The potential gastrointestinal adverse effects limit GLP-1 RAs prescription.

10. GLP-1 RAs cost is a barrier for patients who do not meet the inspection visa requirements (obesity), though they could take advantage of their CV benefit.

11. Many healthcare professionals overestimate patients' refusal of injectable drugs.

Healthcare process

12. The inspection visa administrative procedures limit the prescription of GLP-1 RAs in clinical practice.

13. The inspection visa requirements (obesity) limit GLP-1 RAs prescription in people with T2D with high CV risk or established CVD.

14. GLP-1 RAs use recommendations included in some CPGs are not focused on CV risk control in people with T2D.

15. The absence of multidisciplinary teams limits the access to GLP-1 RAs for people with T2D with high CV risk or established CVD who could benefit from their use.

16. The absence of comprehensive and individualized treatment strategies based on comorbidities of people with T2D limits the use of GLP-1 RAs.

17. Not considering CV risk as a switching treatment factor in people with T2D and high CV risk or established CVD limits the prescription of GLP-1 RAs.

18. The assumption that GLP-1 RAs cannot be prescribed within my specialty (due to the inspection visa requirements) represents a barrier to their prescription.

Healthcare organization and resources

19. The lack of time in the consultation room limits the adherence to CPG recommendations on using GLP-1 RAs in clinical practice.

20. The lack of support staff to assess CV risk and/or educate patients on their treatment limits the GLP-1 RAs prescription.

21. The absence of a shared electronic medical record history between specialties limits GLP-1 RAs prescription in people with T2D with a high CV risk of established CVD.

Healthcare education and training

22. The lack of awareness of the importance of CV prevention in people with T2D limits the use of GLP-1 RAs.

23. The lack of awareness or conviction of the GLP-1 RAs benefits people with T2D limits their use.

24. Healthcare professionals are unfamiliar with using GLP-1 RAs for CV risk control.

Potential strategies to optimize the use of GLP-1 RAs and improve adherence to the recommendations of the Clinical Practice Guidelines

1. Develop and implement simple treatment algorithms based on patient comorbidities.

2. Develop and implement treatment algorithms common to all specialties.

3. Promote a more patient-centered approach in treatment selection (based on personal medical history, lifestyle behaviors, and CV and metabolic risk factors).

4. Educate patients in the care of their disease.

5. Promote shared decision-making models that incorporate patients' values and preferences in treatment selection (shared decision-making tools, nursing involvement, etc.).

6. Inform patients about the essential characteristics of their treatment, including possible adverse events and the recommendations to minimize them.

7. Implementation of automatic treatment renewal by electronic prescription.

8. Review the GLP-1 RAs inspection visa requirements, including the indication for people with T2D with established CVD

9. Create automated alert systems for people with T2D with established CVD who are not receiving adequate treatment based on their CV risk.

10. Consider all people with T2D as high CV risk patients.

11. Implement treatment optimization protocols in people with T2D with hospital admissions due to a recent CVD.

12. Promote the optimal management of people with T2D after CVD through their inclusion in cardiac rehabilitation programs.

13. Increase the nursing involvement in screening for comorbidities and/or patient education.

14. Create the nurse/case manager figure to facilitate transversal patient care.

15. Establish a rapid and fluid collaboration culture between professionals (multidisciplinary/interdisciplinary) appropriate to each center's characteristics, ensuring minimum coordination/referral criteria between specialties.

16. Establish a multidisciplinary and bidirectional e-consultation model.

17. Promote the cooperation between scientific societies to develop updated multidisciplinary consensus guidelines that consider the importance of CV risk control.

18. Implement shared access systems of the medical records to facilitate communication between specialties.

19. Encourage the creation of diabetes units, coordination groups, or care committees.

20. Increment the consultation time for those patients who require it.

21. Facilitate prescription activities in the consultation room (for example, through direct access to the treatment algorithms in the electronic medical record).

22. Promote the divulgation of the new treatment algorithms by the different scientific societies and/or the industry.

23. Implement treatment adherence evaluation systems accessible to all involved specialties.

24. Train health care professionals (including administrators) on the central role of CV risk in people with T2D.

25. Promote and develop training initiatives on GLP-1 RAs efficacy and CV benefit.

26. Promote training programs adapted to different professional profiles (residents, GPs, experts, etc.), including the training on fundamental concepts to reach less experienced professionals in the use of GLP-1 RAs.

27. Define innovative training strategies (e.g., case studies, on-line, etc.).

28. Promote incentivized training programs (within working hours, integrated within promotion plans, etc.).

CPG clinical practice guideline, *CV* cardiovascular, *CVD* cardiovascular disease, *GLP-1 RAs* glucagon-like peptide 1 receptor agonists, *T2D* type 2 diabetes

Table S2 Potential barriers to the use of GLP-1 RAs: results by subgroups

Barriers	Agreement (6–7), %			
	Endocrinology (*N* = 33)	Cardiology (*N* = 22)	Internal medicine (*N* = 22)	Family and community medicine (*N* = 19)
Treatment				
1. The choice of drug T2D treatment is complex due to the large number of pharmacological agents available	39.4	13.6	45.5	36.8
2. The traditional stepwise approach to T2D treatment contributes to the late use of GLP-1 RAs	90.9	72.7	81.8	73.7
3. Injectable treatments have traditionally been used in later stages of the disease, limiting the early access to GLP-1 RAs	72.7	77.3	77.3	80.0
4. The inertia of using the most potent drugs for later stages of the disease limits the early use of GLP-1 RAs	78.8	63.6	77.3	63.2
5. There is therapeutic inertia that induces a glycocentric approach to diabetes and does not cover the CV risk prevention approach	90.9	86.4	81.8	68.4
6. Restrictions at the regional or center level (1st, 2nd, and subsequent lines of treatment) limit the early access to GLP-1 RAs	90.9	90.9	68.2	73.7
7. The belief that the adherence and persistence rate of GLP-1 RAs is lower compared to other treatments limits their prescription	18.2	0.0	22.7	5.3
8. The injectable route of administration is a barrier for physicians in prescribing GLP-1 RAs	57.6	59.1	59.1	52.6
9. The potential gastrointestinal adverse effects limit GLP-1 RAs prescription	21.2	9.1	13.6	15.8
10. GLP-1 RAs cost is a barrier for patients who do not meet the inspection visa requirements (obesity), though they could take advantage of their CV benefit	93.9	86.4	90.9	85.0
11. Many healthcare professionals overestimate patients' refusal of injectable drugs	84.8	81.8	68.2	65.0
Healthcare process				
12. The inspection visa administrative procedures limit the prescription of GLP-1 RAs in clinical practice	84.8	81.8	72.7	57.9
13. The inspection visa requirements (obesity) limit GLP-1 RAs prescription in people with T2D with high CV risk or established CVD	84.8	77.3	86.4	70.0

Barriers	Agreement (6–7), %			
	Endocrinology (*N* = 33)	Cardiology (*N* = 22)	Internal medicine (*N* = 22)	Family and community medicine (*N* = 19)
14. GLP-1 RAs use recommendations included in some CPGs are not focused on CV risk control in people with T2D	24.2	54.5	31.8	21.1
15. The absence of multidisciplinary teams limits the access to GLP-1 RAs for people with T2D with high CV risk or established CVD who could benefit from their use	63.6	54.5	18.2	5.3
16. The absence of comprehensive and individualized treatment strategies based on comorbidities of people with T2D limits the use of GLP-1 RAs	81.8	77.3	68.2	47.4
17. Not considering CV risk as a switching treatment factor in people with T2D and high CV risk or established CVD limits the prescription of GLP-1 RAs	75.8	86.4	77.3	70.0
18. The assumption that GLP-1 RAs cannot be prescribed within my specialty (due to the inspection visa requirements) represents a barrier to their prescription	42.4	50.0	36.4	5.3
Healthcare organization and resources				
19. The lack of time in the consultation room limits the adherence to CPG recommendations on using GLP-1 RAs in clinical practice	54.5	45.5	40.9	31.6
20. The lack of support staff to assess CV risk and/or educate patients on their treatment limits the GLP-1 RAs prescription	60.6	40.9	40.9	21.1
21. The absence of a shared electronic medical record history between specialties limits GLP1-RAs prescription in people with T2D with a high CV risk of established CVD	45.5	27.3	18.2	26.3
Healthcare education and training				
22. The lack of awareness of the importance of CV prevention in people with T2D limits the use of GLP RAs	84.8	90.9	72.7	63.2
23. The lack of awareness or conviction of the GLP-1 RAs benefits people with T2D limits their use	78.8	90.9	72.7	63.2
24. Healthcare professionals are unfamiliar with using GLP-1 RAs for CV risk control	69.7	81.8	72.7	73.7

Data after the two rounds of Delphi consultation are included here (i.e., results from the round in which each statement reached consensus or results from the second round for those items not reaching consensus)

In green, the barriers that reached ≥ 70% of consensus; in red, the barriers that did not reach 70% of consensus

CPG clinical practice guideline, *CV* cardiovascular, *CVD* cardiovascular disease, *GLP-1 RAs* glucagon-like peptide 1 receptor agonists, *N* number of physicians, *T2D* type 2 diabetes

Table S3 Potential strategies to optimize the use of GLP-1 RAs and improve adherence to the recommendations of clinical practice guidelines: results by subgroups

Potential solutions	Agreement (6–7), %			
	Endocrinology (*N* = 33)	Cardiology (*N* = 22)	Internal medicine (*N* = 22)	Family and community medicine (*N* = 19)
1. Develop and implement simple treatment algorithms based on patient comorbidities				
Suitability	87.9	81.8	90.9	90.0
Feasibility	75.8	72.7	81.8	85.0
2. Develop and implement treatment algorithms common to all specialties				
Suitability	78.8	86.4	95.5	90.0
Feasibility	57.6	45.5	72.7	47.4
3. Promote a more patient-centered approach in treatment selection (based on personal medical history, lifestyle behaviors, and CV and metabolic risk factors)				
Suitability	93.9	81.8	90.9	95.0
Feasibility	81.8	81.8	72.7	78.9
4. Educate patients in the care of their disease				
Suitability	87.9	90.9	90.9	90.0
Feasibility	60.6	36.4	77.3	47.4
5. Promote shared decision-making models that incorporate patients' values and preferences in treatment selection (shared decision-making tools, nursing involvement, etc.)				
Suitability	84.8	81.8	81.8	95.0
Feasibility	54.5	31.8	40.9	47.4
6. Inform patients about the essential characteristics of their treatment, including possible adverse events and the recommendations to minimize them				
Suitability	90.9	90.9	81.8	80.0
Feasibility	93.9	72.7	77.3	78.9
7. Implementation of automatic treatment renewal by electronic prescription				
Suitability	97.0	90.9	95.5	90.0

Potential solutions	Agreement (6–7), %			
	Endocrinology (*N* = 33)	Cardiology (*N* = 22)	Internal medicine (*N* = 22)	Family and community medicine (*N* = 19)
Feasibility	90.9	81.8	81.8	90.0
8. Review the GLP-1 RAs inspection visa requirements, including the indication for people with T2D with established CVD				
Suitability	100.0	95.5	95.5	95.0
Feasibility	75.8	50.0	59.1	68.4
9. Create automated alert systems for people with T2D with established CVD who are not receiving adequate treatment based on their CV risk				
Suitability	93.9	95.5	81.8	90.0
Feasibility	66.7	54.5	50.0	63.2
10. Consider all people with T2D as high CV risk patients				
Suitability	84.8	81.8	77.3	63.2
Feasibility	81.8	81.8	72.7	57.9
11. Implement treatment optimization protocols in people with T2D with hospital admissions due to a recent CVD				
Suitability	87.9	95.5	90.9	85.0
Feasibility	81.8	81.8	68.2	78.9
12. Promote the optimal management of people with T2D after CVD through their inclusion in cardiac rehabilitation programs				
Suitability	87.9	86.4	77.3	100.0
Feasibility	84.8	59.1	45.5	42.1
13. Increase the nursing involvement in screening for comorbidities and/or patient education				
Suitability	81.8	95.5	90.9	95.0
Feasibility	63.6	68.2	54.5	84.2
14. Create the nurse/case manager figure to facilitate transversal patient care				
Suitability	78.8	72.7	68.2	60.0
Feasibility	48.5	40.9	27.3	57.9

Potential solutions	Agreement (6–7), %			
	Endocrinology (*N* = 33)	Cardiology (*N* = 22)	Internal medicine (*N* = 22)	Family and community medicine (*N* = 19)
15. Establish a rapid and fluid collaboration culture between professionals (multidisciplinary/interdisciplinary) appropriate to each center's characteristics, ensuring minimum coordination/referral criteria between specialties				
Suitability	93.9	86.4	95.5	95.0
Feasibility	72.7	45.5	50.0	57.9
16. Establish a multidisciplinary and bidirectional e-consultation model				
Suitability	81.8	86.4	81.8	100.0
Feasibility	75.8	77.3	68.2	73.7
17. Promote the cooperation between scientific societies to develop updated multidisciplinary consensus guidelines that consider the importance of CV risk control				
Suitability	87.9	90.9	95.5	95.0
Feasibility	81.8	72.7	81.8	63.2
18. Implement shared access systems of the medical records to facilitate communication between specialties				
Suitability	87.9	95.5	100.0	95.0
Feasibility	60.6	81.8	72.7	80.0
19. Encourage the creation of diabetes units, coordination groups, or care committees				
Suitability	87.9	59.1	54.5	68.4
Feasibility	75.8	31.8	31.8	36.8
20. Increment the consultation time for those patients who require it				
Suitability	97.0	86.4	86.4	95.0
Feasibility	36.4	27.3	13.6	15.8
21. Facilitate prescription activities in the consultation room (for example, through direct access to the treatment algorithms in the electronic medical record)				
Suitability	81.8	77.3	63.6	80.0
Feasibility	33.3	50.0	27.3	40.0

Potential solutions	Agreement (6–7), %			
	Endocrinology (*N* = 33)	Cardiology (*N* = 22)	Internal medicine (*N* = 22)	Family and community medicine (*N* = 19)
22. Promote the divulgation of the new treatment algorithms by the different scientific societies and/or the industry				
Suitability	81.8	95.5	81.8	80.0
Feasibility	75.8	90.9	63.6	85.0
23. Implement treatment adherence evaluation systems accessible to all involved specialties				
Suitability	84.8	90.9	77.3	100.0
Feasibility	66.7	63.6	36.4	52.6
24. Train health care professionals (including administrators) on the central role of CV risk in people with T2D				
Suitability	90.9	95.5	95.5	90.0
Feasibility	72.7	63.6	50.0	52.6
25. Promote and develop training initiatives on GLP-1 RAs efficacy and CV benefit				
Suitability	84.8	95.5	86.4	95.0
Feasibility	81.8	81.8	72.7	80.0
26. Promote training programs adapted to different professional profiles (residents, GPs, experts, etc.), including the training on fundamental concepts to reach less experienced professionals in the use of GLP-1 RAs				
Suitability	93.9	95.5	86.4	75.0
Feasibility	87.9	72.7	81.8	78.9
27. Define innovative training strategies (e.g., case studies, on-line, etc.)				
Suitability	87.9	81.8	59.1	75.0
Feasibility	90.9	68.2	72.7	84.2
28. Promote incentivized training programs (within working hours, integrated within promotion plans, etc.)				
Suitability	84.8	81.8	59.1	95.0
Feasibility	45.5	31.8	40.9	42.1

Data after the two rounds of Delphi consultation are included here (i.e., results from the round in which each statement reached consensus or results from the second round for those items not reaching consensus)

In green, the barriers that reached ≥ 70% of consensus; in red, the barriers that did not reach 70% of consensus

CV cardiovascular, *CVD* cardiovascular disease, *GLP-1 RAs* glucagon-like peptide 1 receptor agonists, *GPs* general practitioners, *N* number of physicians, *T2D* type 2 diabetes