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Delphi Consensus Among French Obesity Experts on Clinical Recommendations for Drug Prescription in Patients With Severe Obesity

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Keywords: body weight gain | clinical recommendations | Delphi method | drug prescription | severe obesity

ABSTRACT

Introduction: Although the physiologic alterations seen in obesity often affect the pharmacokinetics and pharmacodynamics of drugs, most clinical trials do not consider these aspects specifically for this population. To date, there is no list of potentially inappropriate medications for patients living with obesity. The aim of this study was to use the Delphi method to identify useful recommendations for the prescription of some specific drug classes in patients living with severe obesity.

Methods: We identified five therapeutic groups of drugs using data from the HEGP Clinical Data Warehouse. We conducted a literature review and sought the opinions of local experts to produce potential recommendations. We selected volunteer medical experts from the French network FORCE and set up a two-round Delphi method, concluded by a synthesis meeting, to establish a list of recommendations. In each round, the experts were asked to rate the potential recommendations.

Abbreviations: ATC, Anatomical Therapeutic Chemical; BMI, body mass index; FCRIN, French Clinical Research Infrastructure Network; FORCE, French Obesity Research Centre of Excellence.

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Results: Forty-three proposed recommendations were evaluated in the first round. The experts approved four recommendations with a strong consensus and 16 with a relative consensus. In the second round, they approved six recommendations with a strong consensus and 13 with a relative consensus.

Conclusion: This is the first study to use the Delphi method to produce a summary of consensus recommendations for several drug classes in patients living with severe obesity. It provides an expert-based consensus on the use of the five most commonly prescribed therapeutic drug classes and develops a list of recommendations for drug prescription in patients living with severe obesity.

1 | Introduction

A recent WHO report on obesity in Europe stated that almost a quarter (23%) of adults in the European region are living with obesity, characterized by a body mass index (BMI) of 30 kg/m² or more [1]. In France, the Obepi-Roche 2020 survey by the *Ligue Contre l'Obésité* estimated that 17% of the population is living with obesity and that 5.1% have a BMI ≥ 35 kg/m² [2]. The prevalence of obesity has increased significantly, continuing the trend already observed in the 1997–2012 Obepi studies [3, 4] and in several French cohorts (CONSTANCES, Esteban) [5, 6]. A recent French epidemiological survey, the OFÉO study, which included older patients, found an obesity prevalence of 18.1% [7].

Obesity is a major risk factor for developing chronic diseases, such as type 2 diabetes, cardiovascular and respiratory diseases [8], cancers, and musculoskeletal disorders. There are also links between obesity and psychiatric disorders, including major depressive disorder, anxiety disorder, alcohol use disorder, and personality disorders, and positive links with suicidal behavior and suicide attempts [2, 9]. Patients living with obesity therefore form a polymedicated population at high risk of mortality. Milder et al. showed that men living with obesity are prescribed significantly more medicines (OR = 2.27 [1.50–3.44]) than overweight men (OR = 1.18 [0.93–1.50]), compared with normal weight men, after adjustment for age, smoking, alcohol consumption and education level [10]. Moreover, class II obesity ($35 \text{ kg/m}^2 \leq \text{BMI} < 40 \text{ kg/m}^2$) and class III obesity ($\text{BMI} \geq 40 \text{ kg/m}^2$) remain highly complex pathologies in terms of drug treatment as indicated in a report from the *French Haute Autorité de Santé* [11].

Although the physiologic alterations seen in obesity often affect the pharmacokinetics and pharmacodynamics of drugs, most clinical trials do not consider these aspects specifically for the population of patients living with obesity. This lack of information on the treatment of this population may lead to suboptimal dosing when standard doses are used. Moreover, several drugs or classes of drugs used in the treatment of chronic diseases are consistently associated with weight gain as a side effect and are considered “obesogenic” [12, 13], or carry an increased risk of adverse effects due to obesity and its complications. Switching to a drug with a lower propensity to induce weight gain may be preferable [14].

To date, there is no list of potentially inappropriate medications for patients living with obesity. This situation leads to non-standardized and/or potentially inappropriate drug treatments, increasing the risk of iatrogenic events in these patients.

The aim of this study was to use the Delphi method to identify useful recommendations for the prescription of some specific drug classes in patients living with severe obesity ($\text{BMI} \geq 35 \text{ kg/m}^2$).

2 | Materials and Methods

We identified five Anatomical Therapeutic Chemical (ATC) groups of drugs using data from the HEGP Clinical Data Warehouse. We then conducted a literature review and sought the opinions of local experts due to a lack of literature review data. The resulting potential recommendations were then validated by national expert consensus using a Delphi method. The study followed the ACCORD checklist [15].

2.1 | Identification of ATC Groups From the HEGP Clinical Data Warehouse

In 2018, out of 2318 hospital admissions of patients living with obesity ($\text{BMI} \geq 35 \text{ kg/m}^2$), 39.8% involved the administration of antithrombotic agents (ATC B01), around 20.0% of antidiabetic drugs (ATC A10, 26.0%) and antipsychotic drugs (ATC N05, 20.3%), and around 8.0% of antibacterials for systemic use (ATC J01, 8.6%) and antidepressant drugs (ATC N06, 8.0%). These five ATC groups (antibiotics, anticoagulants, antidiabetics, antidepressants, antipsychotics) were evaluated in this study.

2.2 | Formation of the National Expert Consensus Group

We selected volunteer medical experts from the French network FORCE [16] (French Obesity Research Centre of Excellence), certified by the FCRIN (French Clinical Research Infrastructure Network, <http://www.fcrin.org/>). These medical experts have extensive experience in caring for patients living with obesity, particularly severe and complex obesity. They all work in specialized obesity centers, mainly within endocrinology, diabetology, and nutrition departments. Experts may refer to the scientific literature or consult specialists in the relevant medications (in particular antibiotics or psychotropic drugs) for any specific questions. The FORCE network has experience in coordinating clinical research studies such as the Delphi consensus method. They prepared and coordinated the consensus exercise, including the organization of the two rounds, the meetings, the email reminders, and the final synthesis of the recommendations. The French language was used in the documents and meetings.

2.3 | Literature Review to Establish a List of Potential Recommendations

The Steering Committee conducted a literature review to identify potential recommendations for targeted clinical situations

and drug prescription for the five ATC groups defined, using the terms “body weight gain” and “obesity” in PubMed and Embase.

2.4 | Formalizing a List of Potential Recommendations (Level of Evidence, Quantitative Scale, and Free Text)

Members of the Steering Committee (BS, SB, GP) developed a list of potential recommendations from the references selected in the literature review. This list was completed in consultation with our hospital experts in nutrition (AR, SC), psychiatry (GA), hematology (NG), and infectiology (JLM). By round, each recommendation was presented along with the level (quality) of evidence, a quantitative scale to be completed by the national experts, and a free text box to comment on the way the proposed recommendations were defined. The level of evidence was assessed according to the three-level scale developed by the French *Haute Autorité de Santé* [17]: level A—high-quality evidence from meta-analyses or RCTs or drug monographs; level B—moderate-quality evidence from small-sized RCTs, non-randomized studies, transversal studies, cohorts; level C—evidence from case reports, non-experimental descriptive studies, or expert committee reports or opinions. We did not take kidney function into account when making recommendations. The members of the Steering Committee did not rate the proposed recommendations.

2.5 | Delphi Process

In line with the guidelines [18, 19], we set up a two-round Delphi consensus process, concluded by a synthesis meeting, to select a list of recommendations. In each round, the experts were asked to rate the potential recommendations.

In the first round, the experts were asked to rate the proposed recommendations on a quantitative scale (1, very inappropriate, up to 9, completely appropriate). They were also asked to comment on the way the proposed recommendations were defined and formulated, especially for the recommendations that were not consensual or for which there were no data in the literature. After the first round, a videoconference meeting was held to present the recommendations approved in this round (relative and strong consensus). The non-approved recommendations were discussed and clarified for the second round. In the second round, the experts were asked to rate the non-approved recommendations on a quantitative scale (1, very inappropriate, up to 9, completely appropriate). As in the first round, weekly emails were sent to the experts for 1 month to limit non-response. The final results were presented at a meeting. The Delphi method thus allowed us to define whether the recommendations achieved strong consensus, relative consensus, lack of consensus, relative non-consensus, or strong non-consensus.

2.6 | Protocol Deviations

Some deviations from the study protocol were anticipated. For example, a relative consensus in the first round was finally analyzed as a strong consensus and not presented in the second

round, because one or two experts had given a score of 5 or 6 on the Likert scale. During the meeting, the experts decided to treat it as a strong consensus. Some recommendations were removed at the end of the first round, because the drugs were not routinely prescribed.

2.7 | Ethics and Funding of the Study

This study was conducted as part of the first phase of the RECOB-MED study (NCT06517303), supported by the French Ministry of Health's Research Programme on the Performance of the French Healthcare System in 2019, which focuses on developing and validating drug prescription recommendations for patients living with severe obesity. The RECOB-MED study was approved by the Ethics Committee (CERAPHP Centre) (IRB registration: #00011928, date: 2023/06/09).

3 | Results

3.1 | Time Period

Fifteen of the 47 experts contacted in December 2021, and 10 of the 13 experts contacted in December 2022 agreed to participate (42%). In the end, 11 experts participated in both rounds and evaluated the proposed recommendations (some recommendations were rated by 10 experts). The first round ran from October 2022 to January 2023. A meeting was then held in February 2023 to present the recommendations approved in this round. The second round ran from April 2023 to June 2023.

3.2 | Delphi Process

The flowchart of the Delphi process is shown in Figure 1. For the five drug classes, 43 proposed recommendations were evaluated in the first round. The experts approved four recommendations rated with a strong consensus and 16 recommendations with a relative consensus. Twenty-three recommendations did not achieve consensus and were thus proposed for the second round. In the second round, the experts approved six recommendations with a strong consensus and 13 with a relative consensus. Finally, four proposed recommendations did not achieve expert consensus (Table S1).

During the Delphi process, 39 recommendations presented by ATC drug class achieved a strong consensus (Table 1) or a relative consensus (Table 2).

3.3 | Antibiotics

Eleven proposed recommendations were assessed in the first round. Of these, two received a relative consensus for selection. Two proposed recommendations were reworded in the light of the experts' suggestions and split into two further proposed recommendations.

In the second round, 11 proposed recommendations were evaluated, of which four received a strong consensus and four a relative

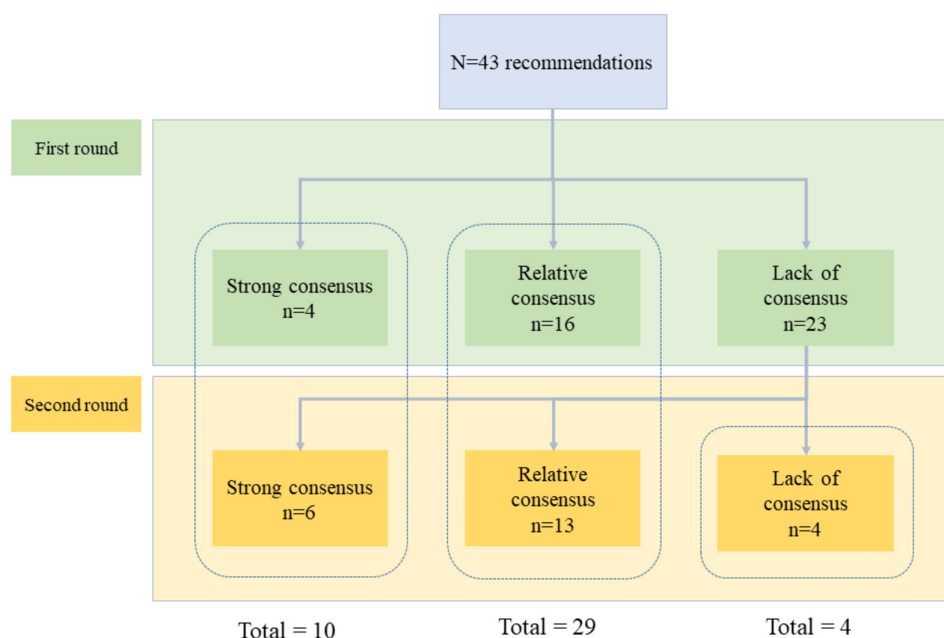


FIGURE 1 | Flowchart of the Delphi process.

consensus. Three proposed recommendations did not achieve expert consensus due to lack of agreement. Finally, we validated 10 recommendations (including one for the ideal weight calculation).

3.4 | Anticoagulants

Thirteen proposed recommendations were assessed in the first round. Of these, six received a relative consensus for selection. Of the seven recommendations presented in the second round, two were incorporated into another recommendation because they related to the same pharmacological drug, and one was deleted because the drug was not widely used. These changes were made following the experts' suggestions.

In the second round, four proposed recommendations were evaluated and a relative consensus was reached. Finally, 10 recommendations were validated.

3.5 | Antidiabetics

Four proposed recommendations were assessed in the first round. Of these, one received a relative consensus for selection. One proposed recommendation was split into two based on the experts' suggestions.

In the second round, four proposed recommendations were assessed; two received a strong consensus and two a relative consensus. Finally, five recommendations were validated.

3.6 | Antidepressants

Nine proposed recommendations were assessed in the first round. Of these, three received a strong consensus and four a relative consensus for selection.

In the second round, two proposed recommendations were assessed; one received a relative consensus and one did not achieve expert consensus due to lack of agreement. Finally, eight recommendations were validated.

3.7 | Antipsychotics

Six proposed recommendations were assessed in the first round. Of these, one received a strong consensus and three a relative consensus for selection.

In the second round, two proposed recommendations were assessed and received a relative consensus. Finally, six recommendations were validated.

4 | Discussion

In this study, for the first time, we developed a list of potential recommendations for drug prescription in patients living with severe obesity. We validated 39 recommendations, of which 10 achieved a strong consensus and 29 a relative consensus. Four recommendations did not achieve expert consensus due to lack of agreement, including two recommendations for antibiotics.

For antibiotics, Castro-Balado et al. [62] and Caubergs et al. [63] confirmed the five recommendations presented. In line with our study, they found highly heterogeneous or even conflicting dosage recommendations in the scientific literature, and agreed that therapeutic drug monitoring is essential for optimal adjustment of drug dosages in this population.

For anticoagulants, our recommendations and routine clinical practices are based on the available scientific literature. Abilgaard et al. proposed a reduced weight-based dose of enoxaparin 0.8mg/kg twice daily in patients with a BMI ≥ 40 kg/

TABLE 1 | Recommendations with strong consensus (n = 10).

Round N°	Recommendation submitted for experts approval	Level of evidence	References	Expert opinion	Median rate	Min rate	Max rate	Number of experts
Antibiotics (n = 4)								
2	Prescription of vancomycin Warning when prescribing drug: Loading dose: Adjust dose according to actual body weight Maintenance dose: Adjust dose according to therapeutic drug monitoring	B	[20-22]	Strong consensus	9	7	9	11
2	Prescription of trimethoprim/ sulfamethoxazole Warning when prescribing drug: Adjust dose according to adjusted body weight Dose calculation: https://abxBMI.com	B	[20, 21, 23]	Strong consensus	9	7	9	11
2	Prescription of teicoplanin Warning when prescribing drug: Loading dose: Adjust dose according to actual body weight Maintenance dose: Adjust dose according to therapeutic drug monitoring	Expert opinion required	[22]	Strong consensus	9	7	9	11
2	Prescription of metronidazole or doxycycline No warning when prescribing drug	Expert opinion required	[20, 22]	Strong consensus	9	7	9	11
Antidiabetics (n = 2)								

(Continues)

TABLE 1 | (Continued)

Round N°	Recommendation submitted for experts approval	Level of evidence	References	Expert opinion	Median rate	Min rate	Max rate	Number of experts
2	Prescription of NPH insulin, insulin degludec, insulin glargine, insulin detemir Warning when prescribing drug: - When starting treatment: Reassessment of the risk–benefit balance, after medical advice from a diabetologist Prescription of metformin or a GLP-1 receptor agonist (exenatide, liraglutide, dulaglutide, semaglutide) or an SGLT2 inhibitor (dapagliflozin, empagliflozin) is preferred. When continuing treatment: do not stop insulin treatment.	A	[12, 24–33]	Strong consensus	9	8	9	11
2	Prescription of metformin, exenatide, liraglutide, dulaglutide, semaglutide, dapagliflozin, empagliflozin, acarbose, sitagliptin, vildagliptin No warning when prescribing drug	A	[12, 26, 28–34]	Strong consensus	9	7	9	11
Antidepressants (<i>n</i> = 3)								
1	Prescription of dosulepin, clomipramine, trimipramine, imipramine, amitriptyline, doxepin, maprotiline for major depressive disorder Warning when prescribing drug: Third-line treatment to be considered in the event of treatment failure	A	[29–31, 35, 36]	Strong consensus	9	8	9	10
1	Prescription of fluoxetine, vortioxetine, moclobemide, milnacipran No warning when prescribing drug	A	[29–31, 35, 37]	Strong consensus	9	7	9	10
1	Prescription of sertraline, venlafaxine, duloxetine, fluvoxamine No warning when prescribing drug	A	[12, 29–31, 35, 37]	Strong consensus	9	8	9	10
Antipsychotics (<i>n</i> = 1)								

(Continues)

TABLE 1 | (Continued)

Round N°	Recommendation submitted for experts approval	Level of evidence	References	Expert opinion	Median rate	Min rate	Max rate	Number of experts
1	Prescription of clozapine Third-line treatment, which should not be stopped or dose-adjusted (except in the case of agranulocytosis). Do not change treatment, or wait for specialist psychiatric advice	A	[13, 29, 31, 35–40]	Strong consensus	9	8	9	10

Abbreviations: DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; ND, no data; NPH, neutral protamine Hagedorn; SGLT2, sodium-glucose linked transporter 2.

m² and no dose capping for tinzaparin in patients with a body weight < 140 kg [64].

The Delphi experts were more cautious about the use of direct oral anticoagulants even in patients with a lower BMI. Recent publications support the use of standard fixed-dose rivaroxaban and apixaban in such patients with venous thromboembolism or atrial fibrillation [64, 65]. The ISTH Scientific and Standardization Committee 2021 guidelines concluded that the use of all direct oral anticoagulants is appropriate in patients with a BMI ≤ 40 kg/m² and weight ≤ 120 kg [54]. A meta-analysis of the efficacy and safety of direct oral anticoagulants in patients with a BMI ≥ 30 kg/m² showed that the use of these drugs in patients living with obesity was associated with a significant 20% reduction in the composite endpoint (stroke, systemic embolism, myocardial infarction, or all-cause mortality) compared with warfarin [66]. Rosolsky et al. summarized the use of direct oral anticoagulants in a single sentence: “In 2022, for treatment of acute venous thromboembolism, body weight should not be a significant factor in deciding which anticoagulant to use” [67].

For people with type 2 diabetes, significant weight loss is a key goal, often leading to improvements in glycemic control and cardiovascular risk factors. Our five recommendations are in line with the Francophone Diabetes Society and the *French Haute Autorité de Santé* [68, 69], which favor the prescription of drugs with a weight-loss effect, namely SGLT2 inhibitors, GLP-1 receptor agonists, and GIP/GLP-1 receptor agonists. Metformin and DDP-4 inhibitors can be used and show a neutral or mild effect on weight loss [70]. We did not make a recommendation for tirzepatide (GIP/GLP1 receptor agonist) because it is not yet available in France. Finally, acarbose was not mentioned by the experts society and French Authority [68, 69], but it has mild weight-loss effects [70].

For antidepressants, our eight recommendations are in line with the literature [71]. If possible, a switch to fluoxetine may improve the weight profile. Mirtazapine and paroxetine are associated with the highest risk of weight gain. However, the risk-benefit balance of switching antidepressants during euthymia must be weighed. We did not look at bupropion because it is only indicated for smoking cessation in France.

For antipsychotics, our six recommendations are in line with the literature. Atypical antipsychotics are commonly prescribed to treat schizophrenia and other psychotic disorders, and also bipolar disorders with some differences in indications between molecules. However, they can cause metabolic syndrome, particularly in terms of weight gain. Olanzapine and clozapine are associated with the highest risk of metabolic syndrome, whereas quetiapine, risperidone, and amisulpride cause moderate changes [72]. Switching to aripiprazole may improve the weight profile and other cardiometabolic outcomes [73]. However, switching antipsychotics in psychiatrically stable patients must be balanced against the risk of decompensation and done in concordance with the indication.

There are several limitations to this study. The aim was not to cover all possible drug prescriptions, but to focus on the most commonly prescribed drugs. All of the experts recognized the

TABLE 2 | Recommendations with relative consensus ($n = 29$).

Round N°	Recommendation submitted for experts approval	Level of evidence	References	Expert opinion	Median rate	Min rate	Max rate	Number of experts
2	Ideal weight calculation: Formula 1: $K + 0.89 \times (\text{size} - 152.4)$ Formula 2: $K + 2.3 \times (\text{size} / 2.54 - 60)$ K (male) = 49.9, K (female) = 45.4	Expert opinion required		Relative consensus	7	5	9	11
Antibiotics ($n = 5$)								
1	Prescription of beta-lactams Warning when prescribing drug: When starting treatment: <ul style="list-style-type: none"> Consider the upper limit of normal dosage for the infection being treated. For severe infections: therapeutic drug monitoring is highly recommended and continuous infusion is preferred. -When continuing treatment: Follow the advice of a senior infectious disease physician and consider dose adjustment based on therapeutic drug monitoring results for severe infections. 	B	[20–22, 41]	Relative consensus	8	5	9	11
1	Prescription of fluoroquinolones (ciprofloxacin, (lev) ofloxacin, moxifloxacin) Warning when prescribing drug: Consider the upper limit of normal dosage for the infection being treated.	B	[20–22, 41, 42]	Relative consensus	8	5	9	11
2	Prescription of aminoglycosides (tobramycin, gentamicin, amikacin) Warning when prescribing drug: <ul style="list-style-type: none"> -When starting treatment: Dose adjustment according to adjusted body weight Dose calculation: https://abxBMI.com -When continuing treatment: Follow the advice of a senior infectious disease physician and consider dose adjustment based on therapeutic drug monitoring results. 	B	[20–22]	Relative consensus	9	6	9	11
2	Prescription of daptomycin Warning when prescribing drug: Dose adjustment according to adjusted body weight Dose calculation: https://abxBMI.com	A	[20, 21]	Relative consensus	9	6	9	11

(Continues)

TABLE 2 | (Continued)

Round N°	Recommendation submitted for experts approval	Level of evidence	References	Expert opinion	Median rate	Min rate	Max rate	Number of experts
2	Prescription of colistin Warning when prescribing drug: Dose adjustment according to ideal body weight Maximum dose of 12 MIU (400 mg) in order to limit the risk of nephrotoxicity	A	[20, 21, 29, 43]	Relative consensus	8	5	9	11
Anticoagulants (<i>n</i> = 10)								
1	Prescription of fluidione, acenocoumarol, warfarin Effect: increased time to achieve target INR No warning when prescribing drug	C	[44]	Relative consensus	9	5	9	11
1	Prescription of enoxaparin BMI 35–39.9 kg/m² Warning when prescribing drug: - Therapeutic dosing: prescribe enoxaparin 100 IU/kg/12h without dose capping for bodyweight - Prophylactic dosing outside the context of bariatric surgery: prescribe enoxaparin 4000 IU/24 h - Prophylactic dosing in the context of bariatric surgery: prescribe enoxaparin 4000 IU/12 h	C	[45–47]	Relative consensus	8	5	9	11
1	Prescription of enoxaparin BMI 40–50 kg/m² Warning when prescribing drug: - Therapeutic dosing: prescribe enoxaparin 100 IU/kg/12h without dose capping for bodyweight - Prophylactic dosing: prescribe enoxaparin 4000 IU/12h	C	[46–50]	Relative consensus	8	5	9	11
1	Prescription of enoxaparin BMI > 50 kg/m² Warning when prescribing drug: - Therapeutic dosing: prescribe enoxaparin 100 IU/kg/12h without dose capping for bodyweight - Prophylactic dosing outside the context of bariatric surgery: prescribe enoxaparin 4000 IU/12h - Prophylactic dosing in the context of bariatric surgery: prescribe enoxaparin 6000 IU/12h	C	[45–47, 49–51]	Relative consensus	7	5	9	11
1	Prescription of argatroban No warning when prescribing drug	C	[52]	Relative consensus	8	5	9	11

(Continues)

TABLE 2 | (Continued)

Round N°	Recommendation submitted for experts approval	Level of evidence	References	Expert opinion	Median rate	Min rate	Max rate	Number of experts
1	Prescription of fondaparinux BMI 35–39.9 kg/m² Warning when prescribing drug: - Prophylactic dosing: prescribe 5 mg/24 h - Therapeutic dosing: prescribe 10 mg/24 h if weight > 100 kg - Therapeutic dosing in acute coronary syndrome: prescribe 2.5 mg/24 h	A	[47, 53]	Relative consensus	9	5	9	11
2	Prescription of rivaroxaban, apixaban, dabigatran Warning when prescribing drug: In the context of bariatric surgery, or outside the context of surgery, consider prescribing vitamin K antagonists	C	[54]	Relative consensus	9	5	9	10
2	Prescription of tinzaparin Warning when prescribing drug: Consider prescribing enoxaparin: - Therapeutic dosing: prescribe enoxaparin 100 IU/kg/12 h without dose capping for bodyweight - Prophylactic dosing outside the context of bariatric surgery: prescribe enoxaparin 4000 IU/24 h if BMI between 35 and 39.9 kg/m ² , prescribe enoxaparin 4000 IU/12 h if BMI between 40 and 50 kg/m ² - Prophylactic dosing in the context of bariatric surgery: prescribe enoxaparin 4000 IU/12 h	A	[45–48, 50, 55]	Relative consensus	9	5	9	10
2	Prescription of fondaparinux ≥ BMI 40 kg/m² Warning when prescribing drug: Consider prescribing enoxaparin: - Therapeutic dosing, prescribe enoxaparin 100 IU/kg/12 h without dose capping for bodyweight - Prophylactic dosing outside the context of bariatric surgery: prescribe enoxaparin 4000 IU/12 h - Prophylactic dosing in the context of bariatric surgery: prescribe enoxaparin 4000 IU/12 h	Expert consensus required	[45–48, 50, 55]	Relative consensus	9	5	9	10
2	Prescription of danaparoid No warning when prescribing drug	C	[56]	Relative consensus	9	8	9	10
Antidiabetics (<i>n</i> = 3)								

(Continues)

TABLE 2 | (Continued)

Round N°	Recommendation submitted for experts approval	Level of evidence	References	Expert opinion	Median rate	Min rate	Max rate	Number of experts
1	<p>Prescription of glimepiride, gliclazide, glibenclamide, glipizide</p> <p>Warning when prescribing drug:</p> <p>- No drug initiation as a first-line therapy, prescribe metformin instead. If metformin is not tolerated or contraindicated, prescribe a DPP-4 inhibitor (sitagliptin, vildagliptin) or a GLP-1 receptor agonist (exenatide, liraglutide, dulaglutide, semaglutide) or an SGLT2 inhibitor (dapagliflozin, empagliflozin).</p> <p>- In the case of ongoing regular treatment, reassess the risk-benefit balance, on the advice of a diabetologist and favor metformin in combination with a DPP-4 inhibitor (sitagliptin, vildagliptin) or a GLP-1 receptor agonist (exenatide, liraglutide, dulaglutide, semaglutide) or an SGLT2 inhibitor (dapagliflozin, empagliflozin).</p>	A	[12, 13, 26, 28–33]	Relative consensus	9	6	9	10
2	<p>Prescription of repaglinide</p> <p>Warning when prescribing drug:</p> <p>- GFR > 30 mL min⁻¹, do not initiate drug as a first-line therapy. In the case of ongoing regular treatment, reassess of the risk-benefit balance, on the advice of a diabetologist. Consider switching to metformin.</p> <p>- GFR < 30 mL min⁻¹, do not initiate drug as a first-line therapy. In ongoing regular treatment, reassess the risk-benefit balance, on the advice of a diabetologist. Consider switching to vildagliptin (DPP-4 inhibitor) or a GLP-1 agonist.</p>	C	[12, 26, 28–33]	Relative consensus	9	5	9	11
2	<p>Prescription of fast acting insulin</p> <p>No warning when prescribing drug (acute clinical situation)</p>	A	[13, 28, 30, 36]	Relative consensus	9	8	9	10
Antidepressants (n = 5)								
1	<p>Prescription of mirtazapine</p> <p>Warning when prescribing drug:</p> <p>Consider prescribing fluoxetine or vortioxetine if weight gain is observed during treatment. Seek specialist psychiatric advice when changing medication.</p>	A	[12, 29–31, 35–37]	Relative consensus	9	6	9	10

(Continues)

TABLE 2 | (Continued)

Round N°	Recommendation submitted for experts approval	Level of evidence	References	Expert opinion	Median rate	Min rate	Max rate	Number of experts
1	Prescription of paroxetine Warning when prescribing drug: Consider prescribing fluoxetine or vortioxetine if weight gain is observed during treatment. Seek specialist psychiatric advice when changing medication, particularly due to the risk of withdrawal symptoms.	A	[12, 29–31, 35–37]	Relative consensus	9	6	9	10
1	Prescription of agomelatine Warning when prescribing drug: Consider prescribing fluoxetine or vortioxetine. Seek specialist psychiatric advice about changing medication.	A	[12, 29–31, 35, 37]	Relative consensus	8	5	9	10
1	Prescription of mianserin Warning when prescribing drug: Consider prescribing fluoxetine or vortioxetine if weight gain is observed during treatment. Seek specialist psychiatric advice about changing medication.	A	[12, 29–31, 35, 37]	Relative consensus	9	6	9	10
2	Prescription of iproniazid, tianeptine Warning when prescribing drug: Third-line treatment in case of therapeutic failure with monitoring of the weight trend	Expert opinion required	[29]	Relative consensus	8.5	7	9	10
Antipsychotics (<i>n</i> = 5)								
1	Prescription of olanzapine Warning when prescribing drug: Consider prescribing aripiprazole if weight gain is observed. Seek specialist psychiatric advice when changing medication.	A	[12, 13, 29–31, 35–40, 57–59]	Relative consensus	9	6	9	10
1	Prescription of aripiprazole, pimozide, amisulpride, haloperidol, flupentixol No warning when prescribing drug	A	[12, 29–31, 35, 37–40, 57–59]	Relative consensus	9	6	9	10
1	Prescription of chlorpromazine, levomepromazine, cyamemazine, sulpiride, tiapride, loxapine No warning when prescribing drug (acute clinical situation for agitation or severe anxiety)	C	[30, 35, 40, 57, 58, 60]	Relative consensus	9	5	9	10

(Continues)

TABLE 2 | (Continued)

Round N°	Recommendation submitted for experts approval	Level of evidence	References	Expert opinion	Median rate	Min rate	Max rate	Number of experts
2	Prescription of risperidone, paliperidone, quetiapine Warning when prescribing drug: Consider prescribing aripiprazole if weight gain is observed during treatment. Seek specialist psychiatric advice when changing medication	A	[12, 29–31, 35–40, 57, 58, 61]	Relative consensus	9	5	9	10
2	Prescription of zuclopenthixol No warning when prescribing drug (acute clinical situation)	Expert opinion required	[60]	Relative consensus	9	5	9	10

Abbreviations: BMI, body mass index; DPP-4, dipeptidyl peptidase-4; GFR, glomerular filtration rate.

importance of making drugs recommendations but admitted that it was difficult due to the lack of evidence-based literature, meaning that a large proportion of prescriptions are based on clinical expertise. The Delphi method has been criticized for forcing consensus without allowing participants to discuss the issues, but the meetings we organized limited this aspect and provided a space for experts to give constructive feedback. The Delphi method is flexible and allows a large number of experts to contribute to a relatively inexpensive process with no geographical limitations. The anonymity of the process prevents any of the experts from dominating the others. Many experts say they rely on clinical experience, given the lack of scientific literature on the subject. However, specialists in the pathologies requiring these prescriptions (such as antibiotics or psychotropic drugs) are not experts in obesity, and obesity specialists are not experts in the pathologies in question. This finding calls for more pharmacological studies to be carried out in the population of people living with obesity.

5 | Conclusion

This is the first study to use the Delphi method to produce a summary of consensus recommendations for several drug classes in patients living with severe obesity. It provides an expert-based consensus on the use of the five most commonly prescribed ATC drug classes and develops a list of recommendations for drug prescription in patients living with severe obesity.

To provide an additional perspective for this work, an overview of actual drug prescription in patients with severe obesity will be conducted using a data warehouse to assess whether the prescriptions are in line with the recommendations. Moreover, to translate future recommendations into clinical recommendations in hospital information systems, experts could be asked to assess the feasibility of implementing the indicators using a validated tool such as the GuideLine Implementability Appraisal instrument.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

All data are presented in the results section.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.