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RESEARCH ARTICLE

Pharmacy student confidence, knowledge and teaching experience in diabetes related pharmacology and therapeutics

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Abstract

Background: Pharmacists are crucial in managing diabetes, requiring appropriate confidence levels and knowledge for effective clinical decision-making. Therefore, the current study assesses correlations between student pharmacist confidence and knowledge in diabetes pharmacology and therapeutics within a UK institution. It also examines the influence of their teaching experience on these factors. **Methods:** An online questionnaire was disseminated to final-year pharmacy students (n = 47) at Ulster University. A 5-point Likert scale determined student confidence on diabetes pharmacology and therapeutics topics, with related multiple-choice questions assessing corresponding knowledge. Associations between confidence and knowledge were then determined. **Results:** Most students felt confident understanding diabetes pharmacology and therapeutics, except for treatment algorithms. They answered six out of ten knowledge domains correctly, though gaps were noted in treatment algorithms, drug options, and side effects. No overall correlation between confidence and knowledge was found, but a significant positive correlation existed regarding insulin action and recognising hypoglycemia signs. Generally, students were satisfied with their diabetes-specific teaching experience, as shown by excellent attendance, but they would welcome additional innovative teaching methods. **Conclusion:** The current study presents no overall correlation between confidence and knowledge of final-year Ulster University pharmacy students about diabetes pharmacology and therapeutics content. Whilst teaching methods were well received, more engaging tools may help address areas where knowledge gaps were identified.

Introduction

The incidence of type 2 diabetes mellitus (T2DM) is increasing at an alarming rate, fuelled largely by the worldwide obesity epidemic and an ageing population (GBD 2021 Diabetes Collaborators, 2023). Globally, over 500 million people have been diagnosed with diabetes, and this figure is expected to rise to 783 million by 2045 (Sun *et al.,* 2022). Notably, this resulted in an approximate 966 billion USD expenditure on diabetes healthcare across the world in 2021, and costs are projected to reach 1,054 billion USD by 2045 (Sun *et al.,* 2022). When viewed in the context that effective management of T2DM is difficult to achieve, with data from the USA and several European countries demonstrating less than 40% achieve target HbA1c (Lautsch *et al.,* 2022), and possibly even poorer outcomes in less developed countries (Suprapti *et al.,* 2023), there is an obvious need to improve patient care in this setting.

Pharmacists are well recognised to be centrally involved in managing T2DM (Fajriansyah *et al.,* 2020). Moreover, the role of a pharmacist has significantly evolved in recent times, and they are no longer viewed simply as medication dispensers (Twigg *et al.,* 2013) but as clinically trained professionals who can provide comprehensive T2DM care plans including lifestyle advice, in-depth information around pharmacology and therapeutics as well as recognition of early warning

signs for uncontrolled diabetes. Indeed, pharmacists tend to have consistent contact with patients (Valliant *et al.,* 2022), providing an opportunity to conduct important medication reviews and improve the standard of overall care (Stewart *et al.,* 2020). With the recent incorporation of independent prescriber readiness into Masters of Pharmacy (MPharm) degrees in the UK (Girvin *et al.,* 2023), alongside continuing advancements in therapeutics for T2DM (Davies *et al.,* 2022), pharmacists are more important than ever in developing and monitoring T2DM treatment plans (Brewster *et al.,* 2020). Therefore, both qualified and newly trained pharmacists need a high level of confidence and knowledge to allow for the provision of such services.

The results from numerous studies confirm that students from various healthcare professions are lacking in essential knowledge relating to diabetes care. Among medical students in Poland, 31% declared themselves insufficiently prepared to manage diabetes, evidenced by the fact that 50% could not identify hypoglycaemic glucose levels (Chobot *et al.,* 2021). For pharmacy students, a lack of knowledge relating to basic diabetes self-management skills has been reported of late (Axon *et al.,* 2022) that corresponds well to earlier observations (Shrader *et al.,* 2012; Morello *et al.,* 2013; Manigault *et al.,* 2020). Confidence also plays a major role in effective decision-making, with both over- and under-confidence observed in student pharmacists that could have adverse effects on clinical care (Nisly *et al.,* 2021; Abeyaratne *et al.,* 2022). Previous studies have struggled to identify a correlation between pharmacy student confidence and related knowledge across various topics (Maxwell *et al.,* 2016; Woit *et al.,* 2020; Gabbard & Romanelli, 2021). More recent investigations into a potential link between the two factors in the area of diabetes, focusing largely on available technologies, demonstrated some trends but no overall association (Axon *et al.,* 2022), although similar data from a UK institution is not available to date. Further to this, the overall teaching experience has been demonstrated to significantly impact the diabetes knowledge, aptitude and confidence of student pharmacists (Wongwiwatthananukit *et al.,* 2013; Manigault *et al.,* 2020; Kiles *et al.,* 2021; Ginzburg & Chim, 2022; Litten *et al.,* 2023), and this factor should also be considered when interpreting these types of correlations.

Therefore, the primary objective of the current study was to assess final-year pharmacy student confidence and knowledge within a UK institution (n = 47, from a cohort of 59 students), namely Ulster University (UU), concentrating predominantly on pharmacology and therapeutics of diabetes management. In addition, aspects of the student experience of diabetes teaching on the MPharm degree at Ulster were also investigated since this can directly impact pharmacy student knowledge (Wongwiwatthananukit *et al.,* 2013; Kiles *et al.,* 2021; Litten *et al.,* 2023) and confidence (Ginzburg & Chim, 2022). Thus, if a poor correlation between confidence and knowledge is uncovered, it could point towards the need for modification of teaching and learning strategies.

Methods

Overview of the study design

The central hypothesis for this study was that final-year MPharm students' theoretical knowledge of diabetes pharmacology and therapeutics should have a strong positive correlation with their confidence in approaching these patients in clinical settings. Although, it should be noted that confidence in theoretic knowledge may not always directly equate to confidence in the application of such knowledge to the real life situation. In addition, student attitudes regarding their teaching experience were also investigated to uncover whether such factors impact knowledge and perceived confidence. To facilitate this, a survey-style study with convenience sampling was developed, and student responses were captured using an online questionnaire. As the questionnaire was administered to all final-year students, there was a fixed maximum sample size of n = 59. Both the project and questionnaire received ethical approval from the UU School of Biomedical Sciences Ethics Filter Committee (project number FCBMS-23-144-A) on 28th July 2023. All data were collected under informed consent, anonymised and analysed according to General Data Protection Regulation (GDPR) guidelines.

Study participants

Study participants were final-year student pharmacists (Class of 2024) attending UU. This cohort was chosen because they had completed second and third-year modules covering the cardiovascular and endocrine systems, where diabetes was a focus subject. These modules account for 20 of 120 total credits in the second year and 25 of 120 total credits in the third year of the MPharm degree at UU. Both modules embed the clinical skills to manage endocrine conditions such as T2DM alongside the pharmacology, therapeutics and related scientific basis for treatment. Module rationale aims and learning outcomes for the two specific modules are available in Supplementary File 1.

Questionnaire

The questionnaire was developed online using the Jisc® platform and divided into four sections, namely demographics, confidence, teaching experience and knowledge of diabetes-related content (Supplementary File 2). Content reliability and validity were assessed by two independent academics within the School who specialise in diabetes pharmacology and therapeutics, as well as academic members of the Ethics Filter Committee. Given that a valid questionnaire will always be reliable, feedback from this panel of academics was used to validate the questionnaire rather than conduct a full pilot study with subsequent factor analysis. The areas assessed in the questionnaire relate to the curriculum covered in the MPharm degree at Ulster, specifically pharmacology and therapeutics for the management of T2DM. Student confidence on aspects of diabetes-related pharmacology and therapeutics was evaluated using ten questions and a 5-point Likert scale, with respondent options being either strongly agree, agree, neither agree nor disagree, disagree or strongly disagree. Likewise, teaching experience was then evaluated using a further ten questions on an identical 5-point Likert scale. A separate overall satisfaction of diabetes teaching question was also employed, again assessed using a 5-point Likert scale ranging from very satisfied to very dissatisfied. In addition, within the teaching experience section of the questionnaire, the student's self-reported attendance record was appraised using a single multiple-choice question (MCQ). The final section of the questionnaire included ten MCQs to assess respondent's knowledge. Each of the ten knowledge questions was directly linked to the ten confidence questions to allow for a direct correlation analysis between confidence and knowledge across the ten separate topics. The confidence and knowledge segments of the questionnaire were deliberately separated by the teaching experience section to help avoid influencing responses to the connected confidence and knowledge questions.

Data collection

A study invitation email was distributed to all final-year MPharm students at UU on 4th October 2023. This email included information on the contents of the questionnaire and highlighted that by completion of the survey, there was an assumption that consent to participate is agreed. The questionnaire was accessed by a website link provided within the email and remained open for responses until the 31st of October, 2023. A follow-up reminder email was sent to all participants one week prior to the study closing.

Data analysis

Raw data gathered from the Jisc® platform were initially exported to Microsoft Excel (Version 16.77.1), and demographic characteristics were summarised as frequencies, including median ranges. Likert responses were number-coded as follows: strongly agree = 1, agree = 2, neither agree nor disagree = 3, disagree = 4 and strongly disagree = 5. Data relating to student attendance and their perceived experience of the teaching of diabetes topics on the MPharm were reported as frequencies. For the knowledge questions, the percent score was calculated for each of the respondents, with every correct answer contributing 10% to the final score and incorrect, blank or cases where more than one answer was selected being worth 0%. To gauge the likelihood of Type I/II statistical errors in the subsequent analysis, a *post hoc* power analysis was conducted (G*Power, Version 3.1), taking an effect size of 0.35 (Faul *et al.,* 2009). Spearman's correlation coefficient (R_S) was evaluated using IBM SPSS Statistics for Windows, version 28.0.0.1.1 (IBM Corp., Armonk, N.Y., USA) and was used to determine the overall correlation between knowledge scores and mean confidence scores. It was also used to test for correlation between confidence and knowledge for each of the ten separate topics. Note that the data gathered were paired, and it was assumed that the two variables (confidence and knowledge) had a monotonic relationship. Where appropriate, results were deemed significantly different if $P < 0.05$ and the following intervals were used for R_S: strong, 0.70 – 1.00; medium, 0.40–0.69 and weak, 0.10– 0.39. Any value under 0.009 was ignored.

Possible trends in over-confidence and under-confidence were further identified by comparing the differences between percentage score and confidence score for each individual. A knowledge score which was at least 30% less than the participant's confidence score was considered over-confidence, while a knowledge score of at least 30% more than the participant's confidence score was considered under-confidence.

Results

Response rate and demographics

A total of 47 final-year MPharm students completed the full questionnaire (79.7% response rate). Importantly, *post hoc* power analysis confirmed that a sample size of 46 was needed to give an actual power of 0.80, validating the appropriate statistical power of the current study. Table I presents information on student demographics, including gender, age and

previous experience of teaching in diabetes. The age range 21-25 had the highest proportion of respondents (n = 35), and approximately twice as many females (n = 32) than males (n = 15) completed the questionnaire (Table I). Only six students noted previous experience of diabetes-specific teaching (Table I), which included completion of a BSc Biomedical Science degree (n = 2), qualifying as a pharmacy technician (n = 2), undertaking a thesis on diabetic drugs (n = 1) and one participant did not provide specific details.

Table I: Demographic data for the final-year UU MPharm students (n = 47) included in the current study

Descriptive variable	N (%)
Gender	
Male	32 (68.1%)
Female	15 (31.1%)
Age range	
18-20	1 (2.1%)
21-25	35 (71.5%)
26-30	11 (23.4%)
Previous experience of diabetes teaching	
Yes	6 (12.8%)
No	40 (85.1%)
Unsure	1 (2.1%)

Assessment of student confidence

The internal consistency for the Likert responses for questions assessing student confidence was evaluated by Cronbach's alpha; this returned a value of 0.76. Of note, almost all students (n = 46, 98%) agreed or strongly agreed they felt confident in their knowledge of how the body controls blood glucose levels, with similar trends in terms of confidence to recognise key symptoms of hypoglycaemia and describe the incretin effect. Students were somewhat less confident about the mechanism of action and key contraindications for T2DM drugs and the T2DM National Institute for Health and Care Excellence (NICE) treatment algorithm, with less than 50% of students agreeing that they felt confident in their knowledge of this algorithm.

Assessment of student knowledge

The average percentage mark for correct responses was 55.3±16.3%, and the most common (n = 13) score was 50% (Supplementary Figure 1). The highest score was 90%, but 59% of responses (n = 28) recorded a 50% or less mark in the knowledge section (Supplementary Figure 1). Data in Figure 2 demonstrated that 6 out of 10 knowledge domains relating to diabetes pharmacology and therapeutics were answered correctly by more than 50% of respondents. The greatest number of correct responses (n = 43; 91%) were recorded for question 1 about how the body controls blood glucose levels (Figure 2), corresponding well with student confidence on this topic (Figure 1).

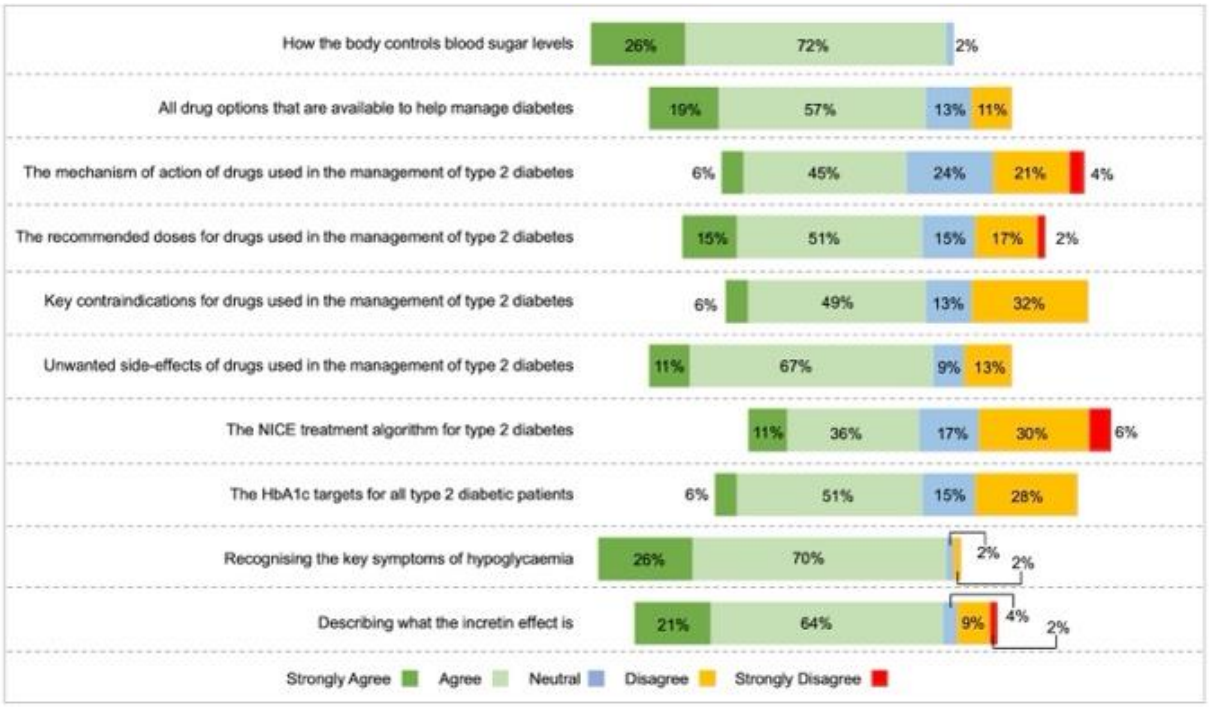

Figure 1: Student confidence

Questions 3, 5, 8, 9 and 10 related to the mode of action of pioglitazone, contraindications for glucagon-like peptide-1 (GLP-1) therapy, HbA1c targets, symptoms of hypoglycaemia and the incretin effect, respectively, were also answered correctly by over half of the participants (Figure 2). Question 7, concerning the NICE treatment algorithm for T2DM, had the most incorrect answers (n = 33; 70.2%), with question 2 relating to therapeutic options for T2DM exhibiting a similar trend of incorrect answers (n = 32; 68.1%).

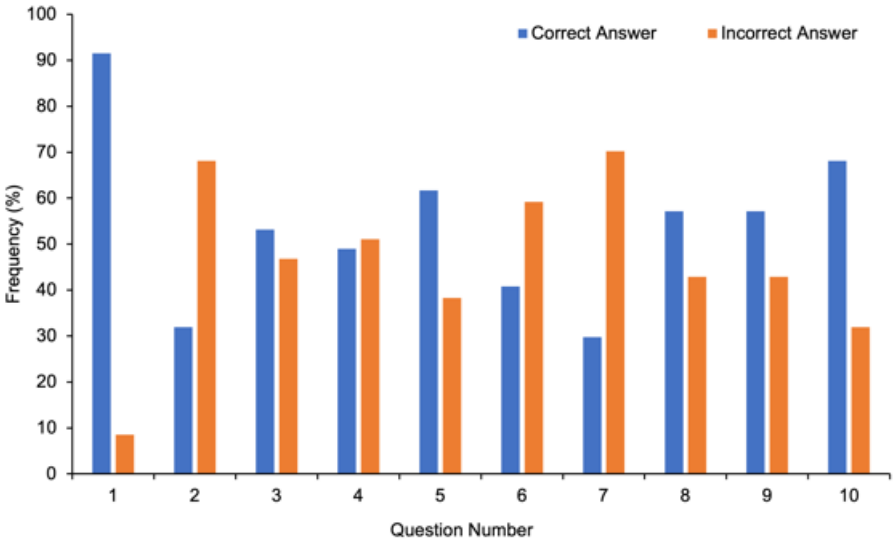

Figure 2: Correct and incorrect responses

Correlation between confidence and knowledge

Data from the questionnaire demonstrated no overall correlation between confidence and knowledge of final-year Ulster MPharm students in T2DM pharmacology and therapeutics (R_s = 0.213; P = 0.150). However, whilst data presented within Table II confirm the majority of paired confidence and knowledge questions also displayed no correlation, there were two pairs of questions, 1 and 9, where a significant association was observed (Table II). Specifically, confidence and related knowledge of how the body controls blood glucose levels were positively correlated (P = 0.02), as were confidence and knowledge relating to symptoms of hypoglycaemia (P = 0.007). No domains presented a significant negative correlation between confidence and knowledge (Table II). Interestingly, questions 2 and 6 had the most wrong answers selected (> 61%) in the knowledge domain, but conversely, these topics had a relatively high proportion of agree and strongly agree responses in the related confidence domain, possibly suggesting a degree of over-confidence. Yet no significant correlation was revealed for these question pairs (Table II; P = 0.466 and P = 0.948, respectively). Further, when comparing individual student confidence and knowledge percentage scores, a slight trend in over-confidence was found in 29.8% (n = 14) of the respondents. Specifically, these students had knowledge scores at least 30% less than their respective confidence scores. Interestingly, there were no respondents who had a knowledge score that was at least 30% higher than their confidence score.

Table II: Potential associations between final-year Ulster MPharm student confidence and knowledge in relation to specific diabetes pharmacology and therapeutic topics

Question pair assessed	Correlation coefficient (R_s)	P value
C1 vs K1	0.340	0.020
C2 vs K2	-0.109	0.466
C3 vs K3	0.008	0.955
C4 vs K4	-0.270	0.067
C5 vs K5	-0.152	0.307
C6 vs K6	-0.010	0.948
C7 vs K7	-0.123	0.409
C8 vs K8	-0.021	0.890
C9 vs K9	0.385	0.007
C10 vs K10	0.002	0.990

Spearman's correlation coefficient was used to determine the strength and direction of association between confidence and knowledge question pairs, as indicated by the positive and negative R_s values. Student (n=47) responses to knowledge (K) questions were correlated to respective related confidence (C) topics. An assumption was made that the two variables, confidence and knowledge, had a monotonic relationship.

Teaching experience

A series of ten questions were used to investigate student attendance and attitudes towards their teaching experience of diabetes-related topics in the MPharm degree program at Ulster. The internal consistency of these responses was high (Cronbach's alpha, 0.82). The findings demonstrate that most students reported that staff were encouraging, well prepared and knowledgeable, and memorising information was insufficient to pass assessments. However, it was also noted that introducing more innovative teaching methods, such as inter-professional learning, would be welcomed (Figure 3).

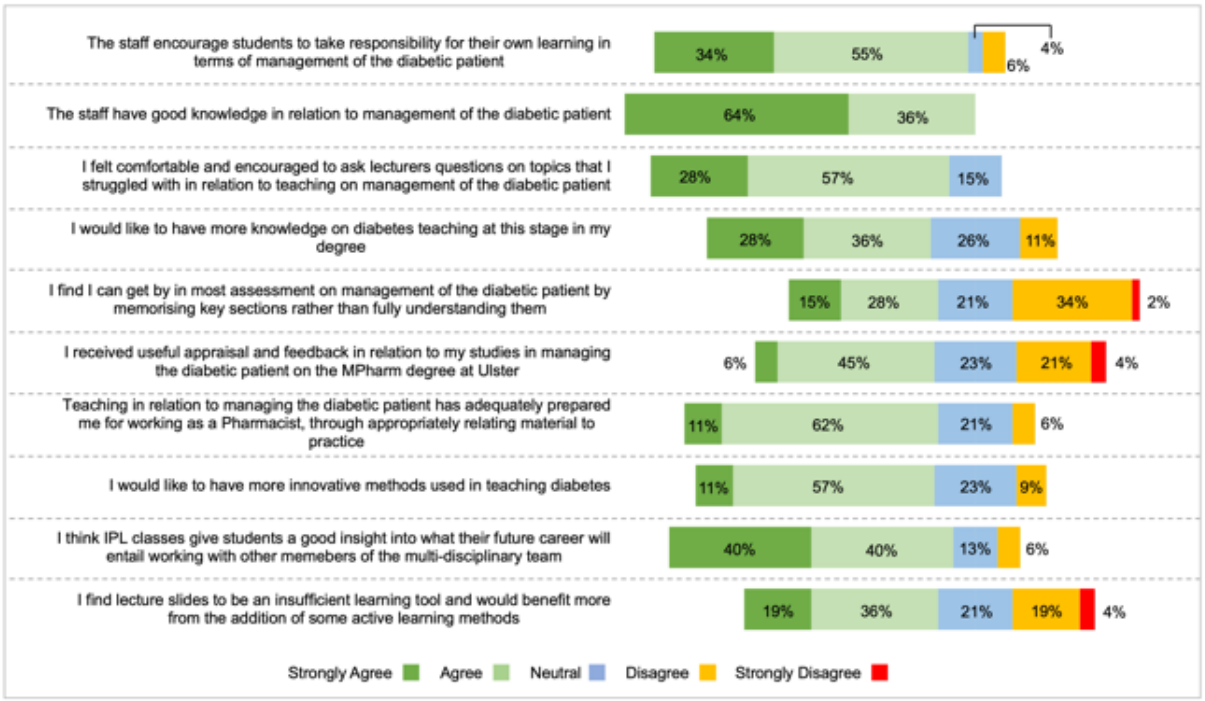

Figure 3: Student views on teaching

Reassuringly, in terms of the overall academic experience of diabetes-specific teaching, most students were either satisfied or very satisfied (n = 42; 89.4%), with no student stating any dissatisfaction in this regard (Figure 4).

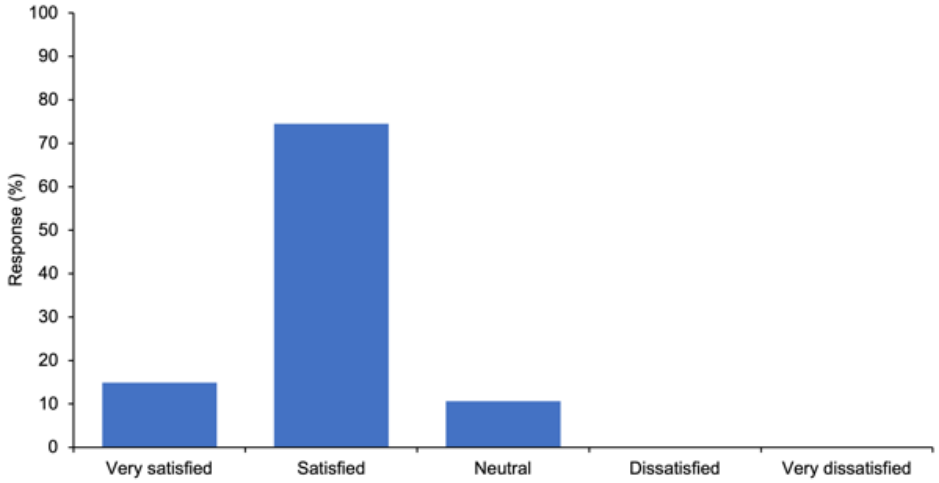

Figure 4: Overall student satisfaction

When probed about class absenteeism over the previous academic year, 40 of the 47 participants (85.1%) stated they attended all classes. Importantly, the electronic Qwickly attendance tool is used for all MPharm classes at UU, and of the 38 sessions chronicled on this system for the cardiovascular and endocrine module in this cohort's third year of study, only four students (6.7%) recorded absences of more than five classes over these 38 sessions, with n = 29 displaying 100% attendance.

Discussion

The present study was designed to address the need for an improved understanding of undergraduate pharmacy student confidence in relation to associated knowledge within the area of diabetes therapeutics and to consider if the student teaching experience impacts this. Reassuringly, a questionnaire response rate of approximately 80% is highly favourable when compared to other online surveys in the healthcare field (Atallah *et al.,* 2023). Importantly, completion rates yielded adequate power and reduced the likelihood of type II error (Serdar *et al.,* 2021). In good agreement, surveys that focus on education and are relevant to the target group do tend to report higher participation rates (Wu *et al.,* 2022). Taken together, it is likely subsequent observations and analyses are representative of the target population, namely final-year pharmacy students studying at UU. Moreover, the demographic data collected was directly in line with the makeup of the final-year MPharm student cohort.

In terms of knowledge assessment, encouraging data confirmed students' understanding of rudimentary blood glucose regulation, which is comparable to recent observations with final-year student nurses (Wallymahmed, 2022). Pinpointing signs of hypoglycaemia was also understood by over two-thirds of respondents, which was slightly superior to responses from 2nd-year medical students on a similar topic (Beverly *et al.,* 2019). However, knowledge gaps were also observed, especially around T2DM NICE guidelines, related drug options and their side-effects profiles. That said, accessibility of information linked to aspects such as disease treatment guidelines has dramatically improved in recent times, and this could represent a confounding factor. Nonetheless, it is very much anticipated that future pharmacists will encounter people living with T2DM, especially as the prevalence of this disease continues to increase (Sun *et al.,* 2022), underlining a need for an improved knowledge base in these areas. Whilst this lack of expertise can be addressed through modification to pedagogical practices, such as greater use of metacognitive prompts (Colthorpe *et al.,* 2019), it is concerning that patterns in suboptimal knowledge of T2DM persist with respect to fully trained healthcare professionals (HCPs). For example, a recent systematic review noted that less than 50% of HCPs across Europe, Asia and the USA could identify appropriate therapeutic targets and lifestyle interventions for people with pre-diabetes (Teoh *et al.,* 2023), perhaps contributing to increased T2DM incidence. Thus, reports of benefits to the undergraduate pharmacy student experience through the introduction of diabetes-specific teaching elements such as active learning in the laboratory setting (Darbishire *et al.,* 2009), simulation experiences (Westberg *et al.,* 2010) as well as instructor-led modelling and role-playing exercises (Sterrett *et al.,* 2012), merit consideration in terms of addressing knowledge gaps. In addition, encouraging pharmacy students to self-regulate their learning and employ self-reflective strategies has also been shown to improve student learning outcomes (Colthorpe *et al.,* 2019). Such interventions will be considered as part of improving teaching strategies moving forward. Moreover, probing the styles of teaching and learning strategies that students considered to enhance their knowledge retention and confidence would have been a useful addition to the current survey.

It is noteworthy that pharmacist's knowledge of pharmacology and therapeutics has previously been documented to be superior to medical practitioners (Keijsers *et al.,* 2015), highlighting the benefits of a multidisciplinary approach to both education and patient care, but corresponding studies with UU medical students would be needed to confirm this. However, the finding links well with the current study, where UU pharmacy students clearly understood the need for inter-professional learning and use of innovative teaching methods to enhance their teaching experience. Furthermore, David Kolb, the renowned educational theorist, highlights the benefits of this type of experiential learning, allowing students to apply integrated knowledge in a real-world multi-disciplinary setting (Kolb, 1984). Moreover, it is encouraging to note the recent focus on experiential learning for undergraduate pharmacy student education in the UK (GPhC, 2021), the benefits of which have long been proposed (Beck, 2000). Indeed, as the 17th-century philosopher and physician, John Locke, quipped, 'No man's knowledge here can go beyond his experience'.

Previous observations from the MPharm degree at Ulster recognised a close connection between attendance and academic achievement (Irwin *et al.,* 2018). Early work by Colby presented data to suggest that academic performance only significantly

diminishes when students do not attend 70% of their classes (Colby, 2004), whereas the threshold for the pharmacy degree at Ulster was substantially different with significant consequences to performance when students fail to attend 30% or more of classes (Irwin *et al.,* 2018). However, on deeper analysis of current self-reported student absenteeism data, no correlation between student attendance and overall knowledge was detected. Nonetheless, it is reassuring that current attendance figures are favourable when compared to other healthcare degree courses (Laird-Fick *et al.,* 2018; Moores *et al.,* 2019). In that regard, there are various complex factors that motivate student attendance (Field, 2012), but good pedagogical practices do contribute to enhanced student engagement (Westrick *et al.,* 2009) and these are actively fostered for all MPharm teaching at Ulster (Beggs, 2022). Although further corroboration is required, this observation also fits well with the high level of student satisfaction reported here in terms of diabetes-specific teaching.

An appropriate degree of confidence is crucial for all HCPs. Under-confidence can hinder efficiency, while over-confidence potentially increases the risk of medical errors (Borracci & Arribalzaga, 2018). Over the years, there has been a suggestion that pharmacists can lack confidence in their clinical decision-making skills (Rosenthal *et al.,* 2010; Frankel & Austin, 2013; Cope *et al.,* 2020; Anakin *et al.,* 2021; Abeyaratne *et al.,* 2022; Mertens *et al.,* 2024). For example, a recent study revealed that only 32% and 58% of Japanese and Irish pharmacists, respectively, felt confident in their ability to advise on diet-related measures for diabetes (Mittal *et al.,* 2023), notwithstanding that provision of this type of specific patient care may fall more under the remit of a dietician within the multidisciplinary healthcare team. Overall, no correlation between actual and perceived knowledge was found, in harmony with a recent report investigating pharmacy student knowledge of diabetes-related topics (Axon *et al.,* 2022). However, there was an observable association between increased confidence and respective knowledge when students were specifically probed on the control of blood glucose levels and symptoms of hypoglycaemia. Possible aspects of over-confidence were recognised in around 30% of the respondents, but over-estimation of knowledge has been demonstrated previously when pharmacy student confidence is assessed using a questionnaire-type tool (Steuber *et al.,* 2017; Nisly *et al.,* 2021).

Although the current study was adequately powered and yielded robust findings around undergraduate pharmacy student confidence and related knowledge, alongside the impact of their teaching experience on these factors, there are still some limitations. The survey was restricted to final-year student pharmacists from one UK school of pharmacy and thus may not be representative across all regions. The content of the survey focused on pharmacology and therapeutics, and future work may want to consider other aspects of diabetes management, such as patient education and self-care, recognising and responding to symptoms, and medicine use reviews. In addition, follow-up studies would be interesting to assess the effectiveness of teaching interventions aimed at addressing areas where knowledge was found to be lacking, such as T2DM treatment guidelines and drug side-effects profiles. Finally, whilst the reliability and validity of the questionnaire were confirmed prior to data collection, the lack of clear correlations could also have been related to student perceptions of the connection between confidence and knowledge question pairs. As such, by their nature, knowledge questions were generally related to explicit topics, whereas the assessment of perceived student confidence took a more holistic approach. This limitation may also have been a factor in the unique observations of student over-confidence relating to drug options for diabetes and their related side-effect profiles. This being the case, findings from the current study could be used to refine future survey instruments through a more robust statistical validation using factor/principal component analysis.

Conclusion

In conclusion, the current study presents no overall correlation between confidence and knowledge of final-year MPharm students at Ulster in relation to diabetes pharmacology and therapeutic content. However, for two domains, regulation of blood glucose and symptoms of hypoglycaemia, a significant positive association between confidence and knowledge was detected. Although almost all students were satisfied with the quality of diabetes-specific teaching they received, there was enthusiasm for an enhanced experience of more innovative teaching methods such as flipped classrooms, problem-based learning or simulations. This could be particularly relevant to areas where both confidence and knowledge were found to be lacking and suggests the need for additional training or modification to teaching and learning strategies around these specific topics.

Conflict of interest

The authors declare no conflict of interest.

Authors' contribution

All authors contributed equally to the conception and design, analysis and interpretation of data. NI drafted the manuscript, with all other authors revising it critically for important intellectual content. All authors approved the final version of the manuscript.

Data availability and sharing

The authors declare that the data supporting the findings of this study are available within the article. Any additional raw data supporting the conclusions of this article will be made available by the lead author without undue reservation.

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