Original Article

Pioglitazone and barriers to effective post-stroke comorbidity management in stroke survivors with diabetes

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ABSTRACT

الأهداف: استكشاف العوائق التي تمنع من استخدام البيوجليتازون لدى الناجين من السكتة الدماغية ولدى مقدمين الرعاية الأولية والثانوية للسكتة الدماغية.

المنهجية: الدراسة هي دراسة استكشافية نوعية باستخدام نظرية أرضية مقاربة لتقييم استخدام البيوجليتازون كعلاج لمرض السكري المصابين بالسكتة الدماغية لتقليل المضاعفات المرتبطة به. أنشاءت الدراسة على ثلاث مجموعات بؤرية، 48 مشاركا من الناجين من السكتة الدماغية ومن أخصائيو الرعاية الصحية، في اسكتلندا وويلز خلال يناير 2019 إلى يوليو 2022.

النتائج: أثبتت نتائج الدراسة أنه عادةً ما شعر الناجون من السكتة الدماغية أن معالجة أخطار السكتة الدماغية كانت أكثر أهمية من معالجة زيادة الوزن أو علاج كسور العظام. وبدا أنهم أكثر استعدادًا لقبول الناضرار الجانبية التي يسببها البيوجليتازون أكثر من تقبل خطر الإصابة بالسكتة الدماغية. بينما قد اقترح أخصائيو الرعاية الصحية بعض الطرق لتقليل الناضرار الجانبية المرتبطة باستخدام البيوجليتازون، مثل الاختيار الفردي الأفضل، وتقليل جرعة البيوجليتازون، ومراقبة المتخصصين في الرعاية الصحية للأضرار الجانبية المبكرة، والاستخدام المبكر للعلاجات الوقائية لكسور العظام.

الخلاصة: قد تسمح هذه الاستراتيجيات بزيادة الالتزام بعلاج البيوجليتازون وزيادة ثقة المتخصصين في الرعاية الصحية في مرارساتهم السريرية. تشير النتائج إلى أن هناك حاجة إلى مزيد من البحث لتسهيل الاستخدام الأوسع للبيوجليتازون في علاج الأشخاص المصابين بالسكتة الدماغية وهناك حاجة إلى التثقيف الصحي عند استخدام أدوية السكري بعد السكتة الدماغية.

Objectives: To explore the barriers preventing pioglitazone use in stroke survivors and primary and secondary stroke care services.

Methods: A qualitative grounded theory approached design was used to assess post-stroke diabetes treatments and to assess clinical applicability of pioglitazone as a preventive treatment to minimize its side effects (SEs) associated. Three focus groups were established with 48 participants from Scotland and

Wales health board centers during January 2019 to July 2022.

Results: A qualitative grounded theory approached design was used to assess post-stroke diabetes treatments and to assess clinical applicability of pioglitazone as a preventive treatment to minimize its SEs associated. Three focus groups were established with 48 participants from Scotland and Wales health board centers during January 2019 to July 2022.

Conclusion: These strategies might allow greater treatment adherence by stroke survivors and increased confidence of the health care professionals in their practice. The findings suggest that further research will be needed to facilitate wider usage of pioglitazone in treating people with stroke and health education is necessitate when using diabetes drugs post-stroke.

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liabetes is a risk factor for the development of stroke with an incidence rate of more than doubling the risk of stroke recurrence.1 At present, there is no definitive evidence that intensive control of hyperglycemia improves the clinical outcomes of acute stroke.² The PROspective pioglitAzone Clinical Trial In macroVascular Events (PROactive)³ study demonstrated that the use of pioglitazone reduced the risk of recurrent strokes in patients with diabetes. Whether aggressive management of diabetes, using more frequently prescribed treatments, insulin or metformin, conveys stroke preventive benefits however remains unknown. Additionally, in the Insulin Resistance Intervention after Stroke (IRIS)⁴ study, the relative risk reduction of stroke with pioglitazone was 24% with a number need to treat of 36 versus placebo. These benefits are comparable to changes observed with aspirin⁵ and statins.⁶ It also reduced risk of developing diabetes and there was no increased risk of hemorrhagic stroke.⁷ The net benefits of pioglitazone however have been questioned, as it increased risk of peripheral edema, weight gain, heart failure (HF),⁸ and fracture⁹ associated side effects (SEs).

Although the European stroke guideline¹⁰ for long-term secondary prevention after transient ischemic attack or ischemic stroke stipulate that pioglitazone can be considered after a risk/benefit analysis, there is little data on the perspective of health care professionals and survivors with stroke concerning the benefits and potential SEs. Since the translation of early phase post-stroke diabetes management research will take time into later phase research translation. Gaining opinions from the health care professionals and stroke survivors' data, are crucial to understand the current circumstances, will suggest innovative ideas to redesign the clinical practice of pioglitazone use post-stroke diabetes services.

The aimed of this study was to explore the views from the health care professionals and stroke survivors to help understand the barriers for the clinical applicability of pioglitazone Comorbidity Management Post-Stroke with a focus on Diabetes (COMPOSEd). Ultimately, to determine whether further research is needed.

Methods. The protocol of the COMPOSEd study was approved by XXX Ethical Committee (XXX) with a reference of registration number (238470) in the UK Integrated Research Application System.

Study design. The study used a qualitative method based on the approach of "grounded theory"¹¹ to guide the design of focus groups (FGs) interpretation. The FGs interviews with the health care professionals and

stroke survivors were conducted in the South Wales and Scotland hospitals. The interviews were directed by researchers experienced in qualitative methodology. In qualitative study, the point using of data saturation¹² was determined the final number of FG interviews.

Participants. The health care professionals and stroke survivors participated in individual FGs, received an information sheet, and provided written informed consent. The health care professionals were approached through special interest groups and professional networks with their direct care of patients with diabetes and stroke in the Wales and Scotland health board hospitals. A minimum of 2 individuals from each gender were surveyed (stroke and geriatric consultants, occupational therapists, diabetes specialists, clinical stroke nurses, and general practitioners). Stroke survivors with a history of diabetes were identified through clinical stroke care teams. A purposive sample was undertaken to achieve a range of age, gender, disability, and socioeconomic status.

Study approach. Stroke survivor views were explored on the etiology of diabetes and stroke and on the strategies that can be used with pioglitazone to minimize weight gain and fractures SEs. Health care professionals' views were explored on the barriers associated with the use of pioglitazone pre- and post-stroke and in mitigating its associated SEs to improve stroke outcomes in clinical practice.

Format of the FGs. The FGs were formed to offer an opportunity for an in-depth exploration of participants' perspectives. A series schedule of open-ended questions was prompted, digitally recorded, to encourage further discussion with participants. The participants were asked to express their views on the pre-stroke and COMPOSED in the primary and secondary services of stroke care. The meetings were conducted in neutral territory away from participants' homes or hospitals. Participants had the opportunity to interact with others study participants or to respond individually in an un-structured discussed interviews at the end of each meeting.

Analysis of the study data. The collection of FGs data and their analysis was performed with an iterative process. All interviews were anonymized, transcribed verbatim, and coded for qualitative analysis. A constant comparative analysis¹³ approach, using a grounded theory method, subsequently identified key points from the FGs interviews. Initially, the chunks of data were coded. The coded data comprised either of large text blocks or phrases that characterized health care professionals and stroke survivors' regarding their

Table 1 - Baseline characteristics of the participants included in the COMPOSEd study.

| | | | Participants' background |
|----------|----------|----------------|--|
| No. | Age | Gender | Baseline characteristics |
| | | | Focus group I (Glasgow) Stroke survivors |
| 1 | 55 | Female | Raised blood pressure, diabetes mellitus, ischemic stroke |
| 2 | 79 | Male | Diabetes mellitus, raised blood pressure, ischemic stroke |
| 3 | 65 | Male | Raised blood pressure, diabetes mellitus, ischemic stroke |
| 4 | 65 | Male | Raised blood pressure, diabetes mellitus, ischemic stroke |
| 5 | 66 | Female | Diabetes mellitus, raised blood pressure, ischemic stroke |
| 6 | 53 | Female | |
| | | | Diabetes mellitus, ischemic stroke, raised blood pressure |
| 7 | 65 | Male | Ischemic stroke, diabetes mellitus, raised blood pressure |
| 8 | 61 | Female | Ischemic stroke, raised blood pressure, diabetes mellitus |
| 9 10 | 62 68 | Male Female | Ischemic stroke, diabetes mellitus |
| 11 | 55 | Male | Ischemic stroke, diabetes mellitus, raised blood pressure Ischemic stroke, diabetes mellitus |
| 12 | 70 | Female | Raised blood pressure, ischemic stroke, diabetes mellitus |
| 13 | 79 | Male | Ischemic stroke, diabetes mellitus |
| 14 | 69 | Female | Ischemic stroke, diabetes mellitus, raised blood pressure, |
| 15 | 65 | Male | Ischemic stroke, diabetes mellitus |
| 16 | 50 | Female | Ischemic stroke, diabetes mellitus |
| | F | ocus group | II (Glasgow National Health Service) health care professionals |
| 1 | 50 | Female | Consultant geriatrician/stroke |
| 2 | 55 | Male | Consultant geriatrician |
| 3 | 46 | Male | Consultant / stroke |
| 4 | 45 | Female | Consultant / stroke |
| 5 | 55 | Male | Occupational therapist |
| 6 | 49 | Male | Occupational therapist |
| 7 | 52 | Female | Occupational therapist |
| 8 | 56 60 | Male Female | Diabetes specialist |
| 9 10 | 60 39 | Female | Endocrinologist Trainee doctor / stroke |
| 11 | 32 | Male | Trainee doctor / stroke |
| 12 | 40 | Male | Nurse / stroke |
| 13 | 42 | Female | Nurse / stroke |
| 13 14 | 42 39 | Female | Nurse / stroke Clinical stroke nurse |
| 15 | 35 | Female | General practitioner |
| | | | ^ |
| 16 | 32 | Male | General practitioner |
| | I | Focus group | o III (Wales National Health Service) health care professionals |
| 1 | 50 | Female | Consultant geriatrician /stroke |
| 2 | 56 | Male | Consultant / stroke |
| 3 4 | 60 50 | Female Male | Consultant / stroke |
| | 59 | | Consultant geriatrician /stroke |
| 5 | 44 | Male | Occupational therapist |
| 6 | 46 | Male | Physiotherapist |
| 7 | 51 | Female | Occupational therapist |
| 8 | 38 | Male | Endocrinologist |
| 9 | 59 | Female | Diabetes consultant |
| 10 11 | 39 35 | Female Male | Trainee doctor / stroke Trainee doctor / stroke |
| 12 | 35 30 | Female | General practitioner |
| 13 | 33 | Male | General practitioner |
| 14 | 35 | Male | Nurse / stroke |
| 15 | 40 | Male | Clinical stroke nurse |
| 16 | 46 | Female | Nurse / stroke |
| | COMI | POSEd - C | omorbidity Management Post-Stroke with a focus on Diabetes |

knowledgeable views of pre-stroke and COMPOSEd. Coded data were then individually grouped into comparable related concepts and were formed to identify

key theme and sub-themes. As groups were abstract categories, compared further, until the emerging of the core theme and sub-themes in each FG. Inconsistency

was resolved with further discussion within the study team until an agreement was achieved on the final sub-themes.

We followed the Reporting of Qualitative Research checklist¹⁵ criteria to facilitate the decision-making use of this study.

Results. During January 2019 to July 2022, 3 FG meetings with 48 participants were conducted (2 with health care professionals and one with stroke survivors). The interview meeting lasted 45 to 90 minutes. The health care professionals' FGs had 32 participants from 2 health board centers in Wales and Scotland hospitals (4 stroke and geriatric consultants, 2 stroke trainee doctors, 3 occupational therapist, 2 diabetes specialists, 3 clinical stroke nurses, and 2 general practitioners). The patients FG had 16 stroke survivors' participants from Glasgow hospital (8 men and 8 women), aged 53 to 79 years, who had hypertension and diabetes and had recovered from a stroke. The study participants baseline characteristics are explained in Table 1.

Details for participants' themes and sub-themes are detailed in Appendix 1. In the stroke survivors' FG, 3 themes (lack of stroke survivors' awareness on the etiology of diabetes and stroke, lack of stroke survivors' knowledge regarding advances in post-stroke diabetes management, and their decision making) and 2 sub-themes (diabetes and weight gain risk awareness and willingness, and diabetes and fracture risk perception and willingness) were identified. In the health care professionals' FGs, 4 themes (barriers associated with pre-stroke and COMPOSEd, lack of health care professionals' knowledge in post-stroke advance in diabetes treatments, future perspectives and clinical applicability of pioglitazone, and strategic plan to improve pioglitazone clinical practice in pre-stroke and COMPOSEd) and 2 sub-themes (weight gain and peripheral edema prevention strategies and fracture mitigation strategies) were identified.

Discussion. The COMPOSEd study draws together the views of health care professionals and survivors with stroke to investigate the feasibility of pioglitazone use post-stroke. This study aimed to assess the trade-offs between the undesirable and desirable outcomes associated with pioglitazone as a preventive treatment post-stroke to analyze and capture the barriers to its adoption among primary and secondary stroke health care services.

The health care professionals' views of the pioglitazone applicability in clinical practices are

neutral. Their perceptions are multi-dimensional. Some avoid pioglitazone use owing to the greater treatment burden, while others do not have the knowledge of the chemotherapeutic advances in diabetes clinical studies post-stroke. These issues may be resolved through the use of knowledge, motivation, attitude, practice, and an outcomes framework.¹⁶ This may involve increased awareness and behavior change via recommendations and communications in clinical practice. Although health care professionals viewed some practical heterogeneity with chemotherapeutic advances in COMPOSEd, their preference is to devise optimal guidelines that combine flexibility with rigor for early screening of diabetes post-stroke. Additionally, a recommendation for this screening should be mentioned in the stroke survivor's hospital discharge forms.

The association between stroke survivors' willingness to accept treatment and their perceived risks associated is viewed as a significant concern. Their views on using pioglitazone are a choice between greater risks of weight gain and fractures or an improved in their long-term of stroke outcomes. The behavior of those stroke survivors reluctant to choose treatment may resonate with the loss of aversion phenomenon¹⁷—a tendency to favor avoiding loss over gaining benefits. Their preferences are to be monitored by health care professionals, who will observe for its early signs of SEs associated and will encourage survivors to engage in a rehabilitation program that will offer the caveat of being sensitive and flexible to the demand of their lifestyle.

This study highlights stroke survivors' challenges in deciding whether they will adhere to a pioglitazone regimen, given the probability of peripheral edema, weight gain, and fracture SEs. Arguably, clear approaches can address these issues. Stroke clinicians must consider stroke survivors' needs and abilities. In spite of the enhancement achieved in the IRIS4 and PROactive3 trials and the personalized medicine approach used in the IRIS⁴ trial, the successful amelioration of the excess risk of HF through dose reduction or discontinuation for IRIS stroke survivors who developed significant edema gives rise to hope. However, there is no clear consensus on the optimal approach post-stroke to alleviate weight gain or fracture associated with the use of pioglitazone. This makes it challenging to persuade survivors with stroke to accept pioglitazone use. The COMPOSEd study has produced strategies to optimize pioglitazone use and help decide the best treatment to be offered.

Peripheral edema represents a primary concern for health care professionals, while weight gain is a primary

concern for stroke survivors in this study. The peripheral edema and weight gain SEs may be explained by increased subcutaneous adipose tissue mass, rather than increased visceral deposition.¹⁸ As a result, there is a tendency for plasma volume expansion and fluid accumulation owing to sodium retention, 19 which increases the risk of HF if the levels of sodium are unchecked. In the IRIS trial,²⁰ however, stroke survivors who gained weight had fewer rate of HF hospitalizations, improved glycemic controls, and lower rates of strokes recurrent than those with higher risk of HF or those with a normal-to-low body mass index.9 In the PROactive trial,21 HF rates independently correlated with increased the incidence risk of stroke related-mortality. The COMPOSEd study suggests following the IRIS4 recommendations to use safety algorithm to trigger the dose reduction with pioglitazone for substantial edema. However, this study varies from such a personalized medicine approach in that we aimed to target those stroke survivors with a low risk of peripheral edema and weight gain development and with the highest chance of benefiting from strokes prevention. We envisage employing an early cardiac echo test and B-type natriuretic peptide screening biomarkers,²² before and after the use of pioglitazone, to monitor those survivors at high risk of HF development along with a strict caloric diet restriction²³ and exercise²⁴ with a degree of flexibility to counteract the risk of weight gain. With these approaches, we hope to mitigate the fear of physicians and stroke survivors regarding the early use of pioglitazone post-stroke.

Participants' FGs did not consider fracture to be a significant concern in prevention of stroke with the use of pioglitazone. Fractures may be explained by the increased bone resorption and decreased bone formation in mesenchymal bone stem cells, which accelerate bone loss.²⁵ In the IRIS⁸ and PROactive²⁶ trials, serious and non-serious fractures were observed among ill patients, with the majority of events were related to falls. However, neither study provided baseline data on falls nor measured the frequency of fracture-related stroke disability, which are major risk factors for fracture. Interestingly, a minority of patients with acute stroke in IRIS trial were on preventive treatments for fracture. The COMPOSEd study proposed to target people with the lowest risk of fractures and at the same time with the highest chance of benefiting from stroke prevention. This can be achieved by using the clinical scores of early fractures risk assessment (FRAX)²⁷ to exclude those with the highest risk of fractures and falls²⁸ and dual energy X-ray absorptiometry²⁹ screening, with the use of fractures secondary prevention treatments such as vitamin D³⁰ and bisphosphonates.³¹

Implications for future research. The European³² and American³³ guidelines are recommended a glycemic control of HbA1c level to be <7 % in ischemic stroke, but it is challenged the health care professionals to identify those stroke survivors with HbA1c at primary stroke centers. In this study, data on the implementation of HbA1c during rehabilitation phase of stroke emerged. Whether for an ongoing monitoring or early diagnosis, this appears to be a preferable solution for some health care professionals for early COMPOSEd. This raises the question whether a rigorous screening in stroke care can increase the possibility of detecting missing cases that appear soon after discharge and might lead to changes in their current managements.

To understand the clinical implications of pioglitazone, it is important to consider why it is utilized in post-stroke. The Council of UK Medical Research³⁴ suggested that the acceptability of drug's should be assessed to evaluates a complex intervention, with risks and benefits, as well as variability assessments in individual-level outcome. From the perspective of precision medicine,35 this study is unique from IRIS in that it aims to stratify stroke survivors whose will be most likely to benefit from the use of pioglitazone. Survivors with stroke have a doubled risk of fracture due to fall following an acute stroke.³⁶ We address this however by using the proposed alternative therapy for fractures within the critical window of the first 6 to 12 months following a stroke and by excluding those at the highest risk of fractures at baseline. Such an approach could subsequently facilitate treatment decisions and allow survivors to adopt greater ownership of their stroke condition. For health care professionals, these approaches seem logical, although financial consideration was raised in term of their implementation. However, considering the vast expenses of the UK National health services for stroke survivors with comorbidities such as stroke and diabetes,³⁷ it would be reasonable to accept these approaches for a secondary prevention of comorbidity post-stroke.

Education is essential for survivors with stroke who would welcome a sense of empowerment in managing their health needs, as well as for those in a state of flux between rejecting the guidelines and to adhering them. Given the variation in practice that emerged among health care professionals, it would be instructive to instill, through health education, a feeling of confidence in practices regarding when and which stroke survivors need to treat. Likewise, stroke survivors need simple guidance to adhere with the use of pioglitazone post-stroke. They need to be informed at what time they should be monitored for the SEs associated and under what conditions. Joint decision making involves

stroke survivors is shown to increase the likelihood of compliance.³⁸

The COMPOSEd study adopted several steps to understand the risks and benefits associated with the use of pioglitazone. Using inputs from the health care professionals' and stroke survivors' perspective and instituting appropriate health education would provide appropriate suggestions to incorporate into pioglitazone COMPOSEd and allow a flexibility in guidelines development.

Strengths and limitations. To guarantee the best clinical outcome achievable with the available resources, as a theoretical framework for acceptability,39 the COMPOSEd study combined the insights of health care professionals and stroke survivors to explore the applicability of pioglitazone use. Although we ensured equal opportunities to the participants to respond to our FGs' questions, our study may be subject to a dominant respondent bias, where some participants may have continuously dominated the talk and influenced their opinions of the other respondents. To increase the probability of experience diversity, the health care professionals were recruited from the primary and secondary Wales and Glasgow stroke centers. However, social desirability bias may exist, where the professionals would answer in a way they thought they should answer rather than what they would actually practice in clinical settings. Even though patients with stroke were recruited from a single hospital in Glasgow, theoretical saturation was assured, 40 and may still recognize a pattern of clinical practices that could inform a design of future clinical study.

Conclusion. The COMPOSEd study suggested exploring methods to reduce pioglitazone-associated SEs from the perspective of health care professionals and stroke survivors. Typically, stroke survivors felt that addressing stroke risk was more important than addressing weight gain or fracture treatmentrelated SEs. Health care professionals recommend exploratory approaches to mitigate the SEs associated with pioglitazone use, such as dose reduction, better selection of individual, early use of fracture preventive managements, and health care professionals monitoring for early SEs sign. These strategies would be beneficial in the advancement of care in the treatment of stroke survivors with diabetes post-stroke, might allow greater treatment adherence by them, and increase the confidence of health care professionals in their practice. Before the widespread use of pioglitazone, further research is necessitated to identify those stroke survivors for whom the risks might be acceptable with greatest stroke preventive benefits. The findings of this study inform the future of post-stroke trial design.

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Appendix 1 - Stroke survivors

Lack of patients' awareness on the etiology of stroke and diabetes

Stroke survivors were aware of the possibility of the complications of diabetes before they had their stroke, but were frustrated to learn that the onset of diabetes is often attended by another stroke or a heart attack.

'I'm not aware of a diabetes threat. If it concerned me, it would deal with medication'. ... 'I' ve never linked to stroke'. 'Diabetes causing circulation, amputations, and kidney problems ...' 'How would I know if I had diabetes?'... 'I discovered ... because of my heart attack, they said. ... "Oh, you've got T2DM ... don't know your sugars because ..." 'My uncle died of a heart attack. ... He had a stroke ... was diabetic ... did not put (it all) together. I should have because he had ...' (Stroke Survivors Scotland)

Participants cited several examples of their experience in monitoring diabetes. Some participants were positive about monitoring their blood sugar and already knew that consuming high-sugar foods was an important risk factor for diabetes before stroke. They realized that with diabetes, they needed to monitor their blood sugar levels and watch their diet closely.

"If I am concerned, I manage ... I just had three chocolate Easter eggs; it will go up. Then, when I fast, it'll come down'. Before my stroke, I was aware I shouldn't eat chocolate. ... Most people who have diabetes get to the point where they know what they are taking, ... because trying to cut back sugar ..." (Stroke Survivors Scotland)

Others were surprised to learn that they had diabetes and stated that after learning about it, they had not worried about blood-sugar monitoring until the diabetes was complicated by stroke.

" ... don't self-test. ... Then on we go, have a stroke, recover from a stroke. ... Nobody at the start said ... What can you do? ... Unless your diabetes got really bad, you`re insulin dependent. ... My GP said, "Are you living on jelly-babies?" My blood sugar was so high. ... " "Anything sweet, never rationed myself before a stroke ... I still like them, but I believe it is true ... not just in case you have diabetes should you cut down sugar. If you are taking in an awful lot of sugar, it can ... actually cause a stroke." (Stroke Survivors Scotland)

Participants were uncertain whether they had been tested for diabetes at a hospital or clinic following their stroke. However, a few were aware that their blood sugar levels were monitored annually at the clinic.

"Haven't had any monitoring."... "The only thing I'm aware of was when I had a review with a GP once a year." ... "My blood sugar, weight, and blood pressure were monitored by the practice nurse twice a year." (Stroke Survivors Scotland)

Lack of patients' knowledge regarding advanced post-stroke diabetes treatment

Stroke survivors did not know that new treatments were available for diabetes, one that decreased the chance of stroke even for those without diabetes. Once informed that a drug could reduce the likelihood of another stroke by 24%, all participants were quite interested but also wanted to know if any side effects (SEs) were associated.

"Depending on what stroke I had, the likelihood of having another... I rather think about that first, but yes" \dots "I'd like know more about ... SEs." (Stroke Survivors Scotland)

Diabetes and weight gain risk awareness and willingness

The survivors stressed that they were not aware of the SEs of diabetic treatments, particularly weight gain. They also noted that their post-stroke weight gain had adverse emotional, physical, or mental effects.

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"I put on loads of weight since ... stroke. ... I lost it, ... being exhausted all the time ... try to go to classes, ... getting my mobility better. ... Then I'm not all right with a stroke. ... It throws you back again." "I was told when you're tired, ... lie down. You'll feel better." "Then you get lazy." "Putting more strain on the heart. ... It could restrict ... mobility, wouldn't like." (Stroke Survivors Scotland)

Stroke survivors were reluctant to decide about starting a new treatment based on their previous stroke-related disabilities. Some were shocked or disappointed to find out that they would have to learn to manage their stroke-related disabilities incrementally when they transitioned from acute hospital care to living independently. However, those with more severe stroke experiences seemed more willing to risk gaining weight than those with less severe stroke and better prognosis.

"Your own mind would be, well, ... going to manage weight, almost like diet, exercise, gyms, just to compensate. ... If you want to make yourself better, you must lose weight and do all the rest of it, balance one against the other." "Everybody in a situation like that tries to lose weight ... would work at it but would high for some, low for others" ... "would be too much to ask somebody who's just back recovering from a stroke." "It takes so long to deal with the shock of the life-changing experience that just happened. Everything has been over. ... It's hard enough." (Stroke Survivors Scotland)

With this, we attempted to explore their views on the degree of weight gain that would be unpleasant for them. Some responded that they feared that a weight gain of a stone and a half (10 kg) would put them at a higher risk of movement restrictions. Some participants felt that the treatment benefit of greater stroke prevention would leave them with a better quality of life, which somewhat alleviated their weight gain concerns on if there were alternative modalities to mitigate the increased risk of weight gain.

"I would do anything not to be overweight.... wouldn't consider drugs if I knew I'm going to be overweight... if I put a half-stone on, I would quite happily take it off again so that... really freaks me out."... "You'd find a stone and a half alarming, but you'd say, "Can I manage and keep pills?"... "What's "alternative", then? ... If somebody said, "This a drug will help, but you're going to put on a stone, but you're never going to take it off, but it's going to give you another 10 years"... "Better to manage that than manage after-stroke effects."... "Bit heavier... but, still, being here beats the alternative." (Stroke Survivors Scotland)

We emphasized that the post-stroke mobility obstacles of survivors would be more manageable if the treatment-associated weight gain were monitored with professional healthcare assistance. As such, their GPs could arrange with the NHS to monitor them for early signs of weight gain and provide instructional peer support to help them take good care of themselves and focus on their capacity to optimize their lifestyles through a balanced diet, exercise, and encouragement from families, friends, and/or spouses.

"It's not ... about diet; it's about diet and mobility. They have to go hand in hand to lose weight effectively ... balancing that." ... "A doctor's going to say, there's ways (that) will motivate you ... when get to stage that you have had a stroke and you're getting better, it gives you more ... opinions on it to make you go and motivated to do it if you want. ... There will always be people who won't, but if people want to motivate themselves with a doctor's words, great." ... "Would have thought post-stroke ... a lot of self-motivation considering what I had before, but it just wasn't there. ... Try as I might, I could not. ... I want there to be weekly at least that kind of clinic, gym to help, because I would find the motivation because ... I try really easily really difficult, but if I had professional help, doing it, encouraging myself, would make that easier." (Stroke Survivors Scotland)

Paradoxically, some stroke survivors seemed to look for formal instructions from healthcare providers that allowed them to passively adhere to professional recommendations, rather than engage in the active self-motivation required to understand the rationales behind the recommendations. Hence, we worked to develop their expertise, and establish harmony and concordance between patients and healthcare providers (HPs).

"We instantly jump to the NHS to provide answers but should look at ourselves first ... having somebody help ... look at yourself before you jump to someone to do magic." "How you live life, trying to manage it all together rather than saying."

... "It's about smoking if you smoke, family ... other pressures ... looking at your lifestyle rather than getting a half-stone off." "If somebody really convinced me 10 years before, "Don't smoke, and you won't have a heart attack", I would've stopped. If somebody said, "Take this pill, and you won't have a stroke," I'd bite their arm off to go after it." ... "I'm one least affected by a stroke. ... I do not want another. ... I am concerned about diabetes sneaking up on me. ... I don't know how to cure it ... just stop eating sugar?" (Stroke Survivors Scotland)

Diabetes and fracture risk perception and willingness

Stroke survivors had a diverse range of fall experiences and were unaware that their risk of suffering a fracture was somewhat increased post-stroke. Some felt lucky to survive their strokes, even with their recurrent falls. However, falling was a painful experience that affected them adversely, even with fracture-prevention assistance.

"I'm surprised I haven't broken anything. ... I fall all the time, but I didn't know there's more risk of fall and chance of fracture post-stroke." ... "You've got humerus ... everything from council. I press an alarm at home for falls; I fall a lot. ... I lose balance going from room to room. Put your hand up, down you go, on the floor; you can't help yourself." ... "When I fell, I broke my hand. The nurse said, "look at your bones." They are like tissue paper and take nothing to snap, which is why I have broken my ankle. It is a nightmare, broken bones ... all pain ... the mobility side of it. I've been diagnosed with osteoarthritis in my hips ... since the stroke." (Stroke Survivors Scotland)

Some felt helpless and pessimistic due to fractures. In this regard, they felt more anxious about having another stroke that might disable them temporarily or permanently than they did about a fracture that would heal with time. Those who had been reflecting on their history of fractures seemed more willing to take the risk associated with new treatment than those who had not experienced a fracture.

"A fracture will mend with treatment. You can build up strength in physical things, but the stroke left a weakness that—nothing is coming back for the brain to send messages. It is totally life-changing overnight. ... (One second,) you are at work, the next, lying in a hospital bed. Your life has changed. You will never work again, drive ... automatically think I did not want a stroke, breaks a leg, ... then you get to those who do not know how bad ... a stroke is, a break is. A break's a break." ... "You can have quite a minor stroke, quite a serious fracture, but generally, a stroke's worse." ... When you say fracture, somebody thinks, ... falling ... a fractured arm, those levels are like levels of stroke. They're not easy, ... like it or not." ... "I wouldn't like it either, but a stroke is devastating." (Stroke Survivors Scotland)

As one possible fall prevention practice, some participants actively engaged in risk assessments. They also tried taking secondary preventive courses to help them cope with their disabilities, especially their strength and balance limitations. Such skills are difficult to adopt even with the help of a rehabilitation trainee, therapy exercise, or consultations on falls with a specially trained nurse.

"Move things out of the way that's going to obstruct me.... I skip over things, fall, even with plenty of room, get away from rugs, stuff like that."... "My sight to the left's really bad.... I catch a foot, and down I go. The physiotherapist suggested going to a strength and balance class... to try to avoid falls. The consultant says, "I'm going to send the falls nurse to you"... They tried for weeks, ... but I could not kneel to get up. ... They teach how to get up if you fall, but it just is not happening.... If I am down, ... somebody has got me up." (Stroke Survivors Scotland)

To ensure success, such activities should be paired with flexibility program and motivational efforts. One suggested strategy to counterbalance fracture risk was to explore the participants' thoughts on adjunct medical treatment with bisphosphonates. Some studies found it difficult to accept this treatment. They seemed frightened of taking on more polypharmacy, since post-stroke-related disability left them with swallowing issues, even if such alternatives would mitigate fracture risk and minimize the chance of future strokes.

"...more drugs always scary...got stuck in throat..." "I take many tablets, can't take anything else...I went from one to 15 tablets ...struggle, ...difficult to swallow...choked me...got worse since I had a stroke." "If guarantee you're not have another stroke?" ... "you will get balance...If take this, ... What get away with? ... how Γ ll able to cope, if I do not take

this, where I'm heading? ... A question of balance, relying on person talking to you, doctor works out that balance, ... take this ... this goes-down, ... be in perfect weight, but might have another bad stroke..." (Stroke Survivors Scotland)

Survivors' decision-making

Survivors were quite satisfied with participating in future trials that involved drugs that might lower their stroke recurrence. However, they were more concerned about weight gain than fractures. They also preferred to have a bone scan before and after the study, which seemed to be a crucial factor in their decision-making process.

"Biggest worry... weight gain"... "I could deal with fracture...no problem." "Ask your GPs get bone density scan, ... it in not an unpleasant experience, ... after you have had an x-ray, the stroke nurse will explained to you, ... how bones are made, how you are going to stop producing them after age of 30 years ... made you more aware ... if needed put you on a drug..." (Stroke Survivors Scotland)

Healthcare professionals

Barriers associated with diabetes comorbidity management, pre- and post-stroke

People with transient ischemic attacks (TIAs) might experience cognitive or mood deficits depending on their level of physical decline or mental state. In the rehabilitation phase, if the ischemia progresses and becomes associated with diabetes, this can create a barrier to the HPs controlling the target HbA_{1c} level and to the patients adhering to treatment.

"It's very challenging when newcomers who have swallow problems take that NG into the mix of problems for diabetic patients. Suddenly, treatment becomes very complicated. ... In the re-habitation phase, a lot of them are less familiar with ... management trying to discuss and provide input in that phase. If their blood sugar is reading 230, get dehydrated, drowsy, and therefore do not, their optimum is kind of an initial-phase problematic. Suddenly, that whole tightly controlled ... goes out of the window ... making sure do not have problem with their ability to take part in rehab. My target difference, compared to the discharge target, is in the low teens. Below that is a risk when they go home." (Geriatrician/ Stroke Consultant, Wales)

"No clear-cut guidelines to managed." (Endocrinologist, Wales)

The primary HPs and stroke trainees emphasized that the stroke survivors' blood sugar was not monitored acutely post-stroke and the regular detection of HbA_{1c} before or after the onset of diabetes was insufficient. These might be challenging due to the increase in stroke survivors' hospital referrals brought by shortage of diabetes nurses, lack of a trainee program and practical experience, or the complexity of fasting glucose test organization.

"We looked at it in our unit. Recently, we were not great with the HbA1c, quality project, screening how many folks had glucose checks. The vast majority went home without them." "The issue is, if we pick up, we pick up quite a lot." (Stroke Trainee Doctor, Scotland)

"It's a challenge getting enough diabetes nurses. We are working hard to train a diabetic team, quite often doing blood tests. We bring them in three months later, but we are not actually changing management. We are trying to intensify our treatment to make sure HbA1c".... "We're treating to target getting patients to comply, and we're picking up more pre-diabetics, even people who don't...look at risk of pre-diabetes. Then you have the whole cohort that needs education, monitoring." (GPs, Scotland)

"We are quite bad doing fasting glucose. Everybody gives random ..., and it's difficult to organize fasting glucose ..." (Geriatrician/Stroke Consultant, Scotland)

Although stroke nurses often identify people with diabetes at clinics, most patients were not screened post-stroke or after their hospital discharge with an HbA_{1c} test. Providers proposed that it is crucial to perform such monitoring

after an acute stroke. This can be ensured by highlighting the need for this testing in patients' discharge letters or getting them enrolled in a pre-diabetic health modification program.

"In the clinic, if an HbA1c has not been done, I'll probably order one. But managing it all is difficult. With a new diagnosis, I would not be rushing it as some sort of back-up, nine times out of ten in the acute phase. But if they do not have diabetes, they have poor HbA1c. You start by asking about tablets; are they taking them? ... Maybe what their diet what should be, and mention that in a letter by default, pass it onto primary care. As I am aware, T2DM management is seen more in primary care than type 1 in hospital." (Stroke Nurse, Scotland)

"Problem is, when people come in post-stroke, no regular check-up takes places. There's no opportunity to come and say, "You've just been discharged after having a stroke. Can you think of anything you need?" It does not happen with a practice nurse or GPs. Even a year later, with their check-up with a nurse, I do not think a diabetes screen is done. They do BP, cholesterol. It wasn't on QOF."... "I don't think many GPs look at a discharge letter. ... We should see this person, and there should not be barriers, for a one-year review ... or financial barriers. It is just not done in this culture. I do not think a stroke one-year review was all that thorough, anyway. The BP aim is 150/90 on QOF, cholesterols, HbA1c would probably be more useful." (GPs, Scotland)

"I wouldn't state that on a discharge letter unless a patient arrived symptomatic and we had suspicions, but not routinely post-stroke." (Stroke Trainee Doctor, Scotland)

"We have a program for pre-diabetics, but it has been overwhelmed, with a massive waiting list to get into." (Occupational Therapist, Wales)

From the perspective of geriatric/stroke consultants, stroke survivors are routinely screened for cholesterol but not specifically for diabetes at secondary healthcare centers. This is crucial for elderly patients in terms of starting them on high dose statins early post-stroke to limit expensive referrals to the NHS service. However, there is no standardized guideline to follow, and no diabetes testing has been shown to identify high risk individuals who need post-stroke screening.

"The cholesterol part of an annual review, in a sense, doesn't matter. They are getting started on high-dose statin. They are not tolerant unless there's familial hyperlipidemia. You've got an injectable thing that costs millions of pounds checking lipid and doing nothing with it, whereas, think in terms of a black box process, wouldn't it be better to check HbA1c for BP?" (Geriatrician/Stroke Consultant, Scotland)

Lack of knowledge of HPs in relation to post-stroke advances in diabetes management

The focus group for primary care physicians revealed a substantial discrepancy in the optimal approach to managing diabetes post-stroke. Although the National Institute for Health and Care Excellence (NICE) guidance was available, there was a lack of guidance to support the exact time to check those with acute stroke presentation at risk of diabetes, or how to determine whether they had been diagnosed with diabetes post-stroke at the hospital or after hospital discharge.

"We don't have clear-cut guidelines for HbA1c. If 40 and above is diabetes, depending on the age of patients, the functional level before a stroke and co-morbidities make sure diabetes control is good as possible. Being a diabetologist, my goal differs from a stroke physician, that is to prevent them from having further strokes because diabetes is the starting point for strokes." (Endocrinologist, Wales)

"An initial assessment should be able to look at the BM part of neurological assessment. In the case of an acute stroke or high BM, undertaking stress hypoglycemia. It is viewed as an insulin deficit because of body stress. We can't due to a stroke but due to illness. If there is no history of diabetes or pre-diabetes, an acute stroke maintains between seven to 12. Post-discharge needs to do glucose tolerance, with fasting blood sugar later, in the rehab phase." (Geriatrician/Stroke Consultant, Wales)

The focus group for stroke consultants highlighted that diabetes treatments appeared to vary among clinicians within the primary and secondary care sectors and even within the same care center. This may be attributed to different patient characteristics, and that no universal rule of thumb exists for diabetes management when diabetes is complicated with cardiovascular disease, including stroke. This makes diabetic combination therapies difficult to manage, as they require more time and resources.

"The issue is, we pick up quite a lot of new diagnoses of diabetes when they come with a stroke. Management simply 10 years ago gave them metformin, and your job was done. There are many variations now, and we struggle to keep up with them." ... "How should we personalize that?" ... We have got two thoughts when people become inpatients. Is this person persistently hyperglycemic in the ward? Do they have osmotic symptoms? I would introduce treatment to control prior to discharge, then get one eye on cardiovascular risk reduction. Metformin is still at the center." (Geriatrician/Stroke Consultant, Scotland)

There was some disagreement when selecting post-stroke antidiabetic treatments among practitioners. Their preference ranged from sulfonylureas for those with an acute presentation of uncontrolled glycaemia to metformin ± DPP4-Is for those who needed long-term management. The nature of the disagreement differed with the severity of glycemia. In general, their guidelines depended on the treating consultants' preference, their diabetes management post-stroke experience, or the primary care location. This reflects the complexity of diabetic drugs and perhaps highlights the use of these new antidiabetic cumulative SE profiles for long-term use, the polypharmacy argument, and the rapidly growing advances in clinical trials that require professionals to update their practice regularly.

"There is guidance, but it's not familiar with all parts of the problem. My practice nurse does most of it; I am quite deskilled." (Geriatrician/Stroke Consultant, Wales)

"We use metformin, lot of sitagliptin, but wouldn't necessarily." (GPs, Scotland)

"If the patient has osmotic symptoms, really high glucose, we want to keep that down, gliclazide. Beyond that, we need a little bit of education." "In hospital, we use gliclazide, then refer patients to get them tidied up." (Geriatrician Consultant, Scotland)

"Metformin is still at the center of use, with blood pressure discussion, because we're starting at least three drugs to reduce it – that's four drugs with SEs – in people a bit less well if they've been in hospital long enough. If they are stable over a few weeks, we pass them to primary care and think about metformin." (Stroke Consultant, Scotland)

"It seems to depend on where you are."... "There is a lot of local guidelines. Metformin's first, followed by gliclazide, then whether alogliptin is used. It comes down to local consultant preference. I don't know what the evidence is or what should be best." (GPs, Scotland)

Pioglitazone clinical applicability and future perspectives

The debate over glucose-lowering therapies for stroke prevention is complicated. The use of pioglitazone was questionable, but it did reduce the net cardiovascular mortality and stroke risk compared to sulfonylureas. However, it seemed challenging to convince practitioners to start treating people with diabetes post-stroke due to associated SEs. Similarly, sulfonylureas have negative cardiovascular effects within a long-term period, but even with such unfavorable aspects, it is still on the market. However, metformin, empagliflozin, and semaglutide did not decrease stroke endpoints as pioglitazone. Hence, selecting a combined therapy can be difficult for practitioners because of the lack of practical expertise regarding such newly emerged drugs. Thus, further research is required to increase the confidence in using pioglitazone. Determining the long-term safety profile is an important and high-priority step.

"Everyone around the table seems to prefer antibodies to pioglitazone, if you're going to do all that stuff. People are a bit circumspect about using." (Geriatrician Consultant, Scotland)

"Thinking about the polypharmacy of low-hanging fruit, what to take away first, what to stop if it's telling. There are too many tablets, a lot of work to make it available, make people comfortable prescribing it routinely." (Stroke Consultant, Scotland)

"With diabetes management, patients don't buy it fully. It is difficult to sell them a drug that has all those SEs. Primary care isn't keen to prescribe it anymore." (GPs, Scotland)

"It's difficult enough to get a patient to take metformin. If gliclazide came on the market now, it would not get licensed. It's a very nasty drug, but it drags down blood sugar." ... "We've not had a very positive response." (Consultant Geriatrician/Stroke, Scotland)

"Commonly, stroke people are elderly. We're not aggressive in sort of keeping sugars low." (GPs, Scotland)
"The famous cardiovascular benefits of metformin are impressive, but it's ... just kind of hive knowledge." ... "If we are running > 12, with osmotic symptoms, dehydration and hyperosmolar, but it is not best for achieving what we are looking for in the short-term concerning reassurance, maybe more weeks aren't good enough." (Consultant Geriatrician/Stroke, Scotland)

"Many GPs feel deskilled and uncomfortable prescribing empagliflozin or semaglutide. Everybody likes metformin, and Sitagliptin now is more common. Generally, I do not like to prescribe things that come from secondary care. Maybe they become familiar, but initially are quite difficult." (GPs, Scotland)

"Many new drugs come on the market, and it's quite hard to stay on top of them all." "Even in a very competitive market, insulin and many different drugs keep changing, and it's hard for us." (Endocrinologist, Wales) "Pioglitazone, probably people are a bit more anxious than others." (GPs, Scotland)

"I wouldn't see myself prescribing it unless there are a lot of bigger numbers, longer-term safety follow-up, and a drug with attendant consequences wasn't anticipated in initial trials. I do not want to sound too pessimistic, but I am thinking about hypertension and diabetes, the stroke population changing. It is older people with three to four strokes, lots of comorbidities. I wonder if trials are moving things way forward." (Geriatrician/Stroke Consultant, Scotland)

Weight gain and peripheral edema preventive strategies

The feasibility of using pioglitazone in patients with diabetes and stroke was questioned by the focus groups of HPs. We attempted to explore their views and learned that they were afraid to use pioglitazone due to intensifying specialty bias associating pioglitazone with weight gain or peripheral edema. If there were some favorable effects from using pioglitazone that would eliminate the negative impacts of the different drugs used in diabetes comorbidity management, it would promote polypharmacy compliance.

"If they are taking tablets but think they are gaining weight, does that affect their compliance? Once they go home and start feeling better, they think, I will not take my medication today, and they start playing around with it." ... "My trials were reading quite bad; individuals are different. Some very select individuals I could make a case for it, but because the cardiovascular comorbidity rate is so high and undiagnosed rates of CHD and LVSD reasonably high, HF... we have other treatments that work, that are anti-hypertensive. There is this idea that pioglitazone lowers BP; is that really doing a lot for diabetes or just giving an anti-hypertensive effect? If we try to add another, are we going to have them not taking something else? Hence, the polypharmacy argument." ... "The incremental benefit we seem to get isn't great. There are other things in our toolbox we can use for diabetes. They are probably going to get amlodipine. Then, any benefit with pioglitazone is lost because all medications stay in a box." (Geriatrician/Stroke Consultant, Scotland)

Pioglitazone would be promising in clinical practice if its SE profile can be mitigated. For peripheral edema, one possible mitigation strategy would be to target a population that does not have heart failure (HF) or that has a relatively low risk of HF. This calls for monitoring early signs of HF using specific blood tests or echo detection.

"It's feasible, but will it be more treatment burden? Giving three tablets for those three SEs of another tablet, that is another four tablets on top of statin, antiplatelets, three antihypertensive, PPIs."... "I wouldn't concomitantly be treating with other medicines to prevent SEs, to get them onto, given absolute benefits...being attractive to them. ... There may be selected patients who are at risk of complicated HF. I do not see it would be easy to routinely add them to a list, but if you know their hearts in good nick, you want an echo as prerequisite before starting on them relative to other drugs like BNP levels." (Geriatrician/Stroke Consultant, Scotland)

Fracture mitigation strategies

From the perspective of occupational therapists, people with diabetes can manage their blood sugar levels well before they can have a stroke. However, they were concerned that the target HbA_{1c} would be difficult to manage rapidly following a stroke. Their decisions on treatment choices were based on clinical judgment that called for aggressive glycemia control founded on risk factors such as increased hypoglycemia complications, low energy, likelihood of falls, swallowing status, and size of the infarct, which may prevent stroke survivors from entering an early rehabilitation program.

"If somebody becomes functionally disabled because of a stroke, they have cognitive problems. If they had diabetes before and were managing well, now they cannot. If we suddenly make them strictly, super-tightly controlled in the first two months, post-stroke ... in hospital in the re-habitation phase, we have problems. Either we cannot have rehab because of recurrent hypos or had them during the night, they are too tired or lethargic, they had a swallowing problem, or they were less familiar with diabetes management. We're trying to provide input in the acute phase, though there are concerns patients might not be able to adhere to their medication once they get home." ... "Current guidance and implications for older patients is try to go for higher targets, even if they're not as young as stroke diabetics. They're trying to exercise prevention with slightly less tight control with hypos and falls." (Occupational Therapist, Wales)

Secondary HPs supported the use of physiotherapists after the patient rehabilitation phase because this would help patients improve their functional disabilities through their engagement with and motivation for regular physical assistance and a health education program. This would also help patients improve their outlook, take greater ownership of their condition, improve their adherence to medication regimens, and facilitate subsequent treatment decisions.

"From the patients' perspective, six months, twelve months down the line, that might be helpful for lifestyle change and exercise programs. It's difficult." (Occupational Therapist, Wales)

"Is there intervention needed for those people? Do they need more input than they're currently getting regarding diabetes education post-stroke?"... "We've got to look at what the failure rate is afterwards. Because as somebody who fails on diets, medications every now and again, it is all about being fully committed to doing something, and some people are, others not." (Geriatrician/Stroke Consultant, Wales)

One possible modality to alleviate breaks was a Dual Energy X-ray Absorptiometry (DEXA) bone density scan before, and then annually after initiating pioglitazone treatment in selected patients without fractures. This might be achieved through appropriate patient safety counseling and early Fracture Risk Assessment Tool (FRAX) scores to encourage the use of substitute preventive therapies such as bisphosphonates in patients with or at risk of low bone mass. Implementing this approach would be relatively expensive.

"If they do not fall regularly with a fragility fracture, maybe we could use FRAX to estimate the osteoporotic risk before starting. We tell them we are going to roughly double it. We might not cross the threshold putting on bisphosphonates to go down that route but discuss using them." (Geriatrician/Stroke Consultant, Scotland)

"If I had infinite time and resources to do personalized medicine ... DEXA ... maybe not much, ... but is that practical? I am thinking about economics. Is money that plentiful to invest worth a modest gain?" (Geriatrician/Stroke Consultant, Wales)

Strategies to improve outcomes clinical practice in diabetes co-morbidity management pre- and post-stroke

The focus groups' HPs complained that stroke services are too medically oriented and that flexibility in stroke management guidelines needs to be improved. They suggested that early diabetes comorbidity detection and post-stroke management guidelines should be modifiable and should be supported and fostered by policymakers. These guidelines need to be clear, up to date, adjustable over time, and easily followed using applicable standardized mnemonic recommendations. Thus, it may guide the communication and professional gap between primary and secondary healthcare systems. These goals are challenging to achieve. However, yearly diabetes detection

and examinations in the primary and secondary sectors with dietician assistance or patient home visits could be appropriate suggestions and would provide an impetus for HPs to act.

"NICE is very woolly, just give the whole option of drugs." (GPs, Wales)

"If there's robust evidence and guidelines that are clear, GPs used to adjust their practice with the times. What became problematic was if guidelines were not current, you cannot follow them. Evidence is a bit wishy washy. Things come up all the time, and you have to change your practice. We still do not know about pioglitazone. When something comes out, it is given bad press, and it is difficult for people to get their head away from it. In primary care, there has been a change in monitoring now. GPs practice in clusters, and diabetes is becoming so specialized. Whether having a GP or a specialist is needed and becoming a problem is a minefield. We are becoming deskilled doing it. There's one GP in our practice who's about to retire, and we don't know what's going to happen." (GPs, Scotland)

"On the flip side, the thing that revolutionized BP treatment was ABCD. If we operationalize for something simple, is what we need? The GGC flowchart is incredibly complicated." Consultant Geriatrician/ Stroke, Scotland)

"It starts with metformin, doesn't it?" (GPs, Scotland)

"It's relatively simple, but tinker with step two when they're inpatients. The basics are simple, with new drugs with which we are less comfortable, and we are playing with. We are not happy with sugars but sending them home. Who takes ownership of that?" ... "If it becomes routine that everybody gets an HbA1c diagnosis annually, but it would be fairly cheap" ... "If somebody is found high HbA1c the minute he or she is discharged, it is mentioned in the letter, they'll automatically add it. In primary care, it would be done annually." ... "Some of the initial patients in secondary care are people who've been diagnosed. The dietician should be available to come, speak with the new diagnosis before he or she gets drugs." (Stroke Consultant, Scotland)

The synergy between a primary care team charged with acute stroke and glycemia management and secondary services charged with cognitive rehabilitation would be promising. To resolve the issue of NHS staff and hospital space shortages, these goals could be achieved by assigning specialized consultants to GP surgeries for at least one to two days per week or month. In the future, it is vital to discharge patients to their homes, rather than to nursing homes, and to employ a clinical pharmacologist who aids the stroke team with decisions regarding drug interactions and in calculating safe dosages, especially for elderly patients with diabetes or renal comorbidities.

"If there are problems with administering drugs like insulin and anything from a post-stroke function, they should return to secondary care and the stroke specialist." ... "Finding the right place to control." (Geriatrician/Stroke Consultant, Wales)

"In the Cardiff and Vale Trust, they assigned consultants to GP surgeries. They've saved £81,000 to £170,000." (Endocrinologist, Wales)

"We tend to use eGFR, which was reported by the lab. It is not easy. The computer does not calculate it, so you've to do that extra step. It's a much more thorough application than pharmacists do." (GPs, Wales)

"We're getting lots false-okay eGFRs. ... They assume everyone is 1.7 m tall and have a body mass of whatever. ... If an 85 to 90 years old person does not weigh much, the eGFR is far lower. We're trying to improve discharge to home, not be reliant on the nursing home for medication administration." (Geriatrician/Stroke Consultant, Wales)